Operative versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears: A Multicenter Randomized Controlled Pragmatic Trial

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Operative versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears: A Multicenter Randomized Controlled Pragmatic Trial

Arthroscopic Rotator Cuff (ARC) Clinical Trial

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Version Number: 5.0 | 2 January 2026

PROTOCOL REVISION HISTORY

Version Number	Version Date	Summary of Revisions Made:
0.5	15 Sep 2017	Draft version for DSMC review
0.6	26 Sep 2017	Draft version after DSMC review – clarifications, additions, and corrections
1.0	3 Oct 2017	Version submitted to IRB
2.0	12 Dec 2018	GENERAL: Contact info updated, new study radiologist added, minor qualifications & clarifications added, and correction of minor typos and grammatical errors throughout • **Reasons for withdrawal Revised (5.5.1)** – Randomized subjects who are later found to meet an exclusion criterion will not be withdrawn from the study. • **6-mo PT Report Timepoint Added (6.5.2)** – For subjects who have not started physical therapy by the one-month mark (or for whom treating PT info is not available), an additional PT Report Form will be sent at 6 months. • **Collection of Crossover Treatment Data (6.5.5)** – Provisions added for collection of treatment data for crossover patients when possible/feasible • **PCP/Non-Op Provider Referrals (7.1)** – Provision added for recruitment via referral by PCPs / Non-operative providers to study physicians (as appropriate) • **Follow-up (7.4.1 & 2)** – Clarification added regarding what is/is not a protocol deviation with regards to patient follow-up and treatment timeline • **Physical Therapy Diary (7.4.2)** – Provision added to collect PT Diary info from crossover/delayed treatment subjects at 12 months as appropriate • **Protocol Deviation Clarified (16.6)** – Definition revised to accord with guidelines of the reviewing, single IRB (VUMC) and distinction added between protocol deviations and protocol violations. • **Appendices** - List of appendices updated to include new study documents and reorganized to group related documents together by type
3.0	1 Dec 2020	**GENERAL:** (throughout entire protocol)

Version Number	Version Date	Summary of Revisions Made:
		• Changed age range to 40-84 from 50-84 • Adjusted duration of main study and sub-study windows to make consistent throughout • Eliminated research MRI for determination of eligibility at enrollment - eligibility of all subjects will be based on standard-of-care, clinical MRI (5.3.3, 7.2, 7.3, 8.1 & Appendix A – Schedule of Events) • Provisions for remote enrollment procedures added (7.0, 8.0) • Standardized language throughout • Minor qualifications & clarifications added • Correction of minor typos and grammatical errors • List of appendices updated to include new study documents **PI/Site Information** • Nitin Jain change of institution & title • John E. Kuhn added as Co-PI at VUMC • List of performance sites & site PIs moved to Appendix **Study Schematic** • Modified to reflect baseline procedures are performed prior to randomization. **Surgery (6.1.2)** • Clarified that surgeons may perform additional/alternative surgical procedures intraoperatively as necessary & that post-op protocol modifications are allowable in such cases **Physical Therap**y (6.3.2) • Added/clarified allowable modifications to the post-operative PT protocol. • Added telehealth as a visit option **Treating Surgeons (6.5.1)** • Added provision for how Surgery Report Form is completed if surgery is performed by an outside or non-ARC surgeon **MRI Review by Study Radiologist (6.5.4)** • Removed de-identification of MRIs as procedure since it is not scientifically required **Pre-Screening (7.1)** • Added provision for screening of self-referred patients & pre-visit contact of prospective subjects by research personnel (where allowed) **Clinic Screening (7.2)**

Version Number	Version Date	Summary of Revisions Made:
		• Eliminated research MRI at screening **Enrollment/Baseline (7.3)** • Included electronic consent and remote enrollment procedures • Added provision for modification &/or non-performance of physical exam as needed **Follow-Up Questionnaires (7.4.1)** • Added follow-up contact by site physician/staff • Clarified patient failure to complete a follow-up questionnaire not a protocol deviation **Physical Therapy Diary (7.4.2)** • Removed redundancies and abbreviated descriptions (details moved to SOP) **Study Procedures (8.1)** • Added that subsequent standard of care MRI/imaging during study period may be collected & reviewed **Adverse Events (9.1.2)** • Added Blood Clot/ DVT to list of AEs **Adverse Event Reports (9.2)** • Added that SAEs/AEs can be reported through REDCap by the sites **Seriousness of Event (9.3.3)** [previously named Severity of Event] • Included list of events that will be determined serious per FDA **Data Analysis Plan (12.4)** • Updates to sensitivity analysis **MRI/ X-Ray Images (13.2.5)** • Removed de-identification of the MRI/ X-Ray via DicomCleaner • Added potential review of subsequent clinical MRIs performed during study period **Quality Control & Assurance (14)** • Sections updated to reflect actual practices including but not limited to Double Data Entry **Publication Guidelines (17.3)** • Added specificity for authorship on primary and subsequent publications

Version Number	Version Date	Summary of Revisions Made:
		SPIRIT GUIDELINES: added to sections and created new sections to ensure protocol's compliance with SPIRIT guidelines • Added clinicaltrials.gov NCT number • **Personnel Role Descriptions (1.1)** – New section describing each role within the study. • **Subject Injury (15.6)** – added new section with language from Informed Consent Form • **Communication of Protocol Changes (15.7)** – added new section regarding how protocol changes will be disseminated • **Conflict of Interest (15.8)** – added new section • **Publication/ Data Sharing Policy (17)** – reorganized section and added new sections & information re: data sharing and dissemination of results
4.0	15 Apr 2021	**GENERAL:** • Dr. John E. Kuhn removed as co-PI of the study • Sample size change: from 700 participants to 316 participants **Effect Size and Alternative Hypothesis (12.3.2) & Sample Size Projections (12.3.3)** • Updated to reflect change in sample size
5.0	2 Jan 2026	**GENERAL:** Sample size change from 316 participants to 180 participants (an additional 20 may be recruited to allow for loss to follow-up and crossovers) • PI contact information • PCORI Contract Number **Sections updated to reflect change in sample size:** • Protocol summary and study schematic • 4.1 Primary Study • 5 Study Enrollment and Withdrawal • 12.2.1 Primary Analysis (Heterogeneity of Treatment Effects Analysis) • 12.3.2 Effect Size and Alternative Hypothesis • 12.3.3 Sample Size Projections • 12.4 Sensitivity Analyses

Version Number	Version Date	Summary of Revisions Made:
		Sub-Study updated to make explicit that it is exploratory and not funded by PCORI in the following sections: • 4.2 Exploratory Sub-study • 5.3.3 Compensation • 5.5.1 Reasons for Withdrawal • 7.4.1 Follow-Up Questionnaires (± approximately 4-6 weeks from follow-up time point) • 7.5 Follow-up Visit and MRI (2-10 years after treatment for exploratory sub-study) • 8.1 Study Procedures/evaluations • 9.1 Specification of Safety Parameters • 10 Study Oversight • 10.1 Data and Safety Monitoring Committee (DSMC) • 12.5 Exploratory Sub-study • 13.1 Source Documents • 13.2.5 MRI/X-Ray Images

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STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Conference on Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and PCORI Terms of Award. All personnel involved in the conduct of this study have completed human subjects protection training and Good Clinical Practice (GCP) training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

To be signed by all of the following:

- Principal Investigator
- Co-Investigators
- Clinical Site Investigators (Site PIs)
- DSMC Members



"Operative versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears: A Multicenter Randomized Controlled Pragmatic Trial"

Protocol Version 5.0

2 January 2026

I have read and understand the information in this Study Protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

Signed: _____ Date: _____

Name:

Title:

Site/Location:

Study Role:

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LIST OF ABBREVIATIONS

AE	Adverse Event
ASA	American Society of Anesthesiologists
ASES	American Shoulder and Elbow Surgeons
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Forms
DAG	Data Access Group
DCC	Data Coordinating Center
DDE	Double Data Entry
DSMC	Data & Safety Monitoring Committee
DSMP	Data & Safety Monitoring Plan
eCRF	Electronic Case Report Form
FWA	Federal wide Assurance
GCP	Good Clinical Practice
HEP	Home Exercise Program
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intent-to-Treat Analysis
MD	Medical Doctor / Physician
MOON	Multicenter Orthopedic Outcomes Network
MOOP	Manual of Operating Procedures
MRI	Magnetic Resonance Imaging
N	Number (typically refers to subjects)
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PCORI	Patient-Centered Outcomes Research Institute
PCP	Primary Care Provider

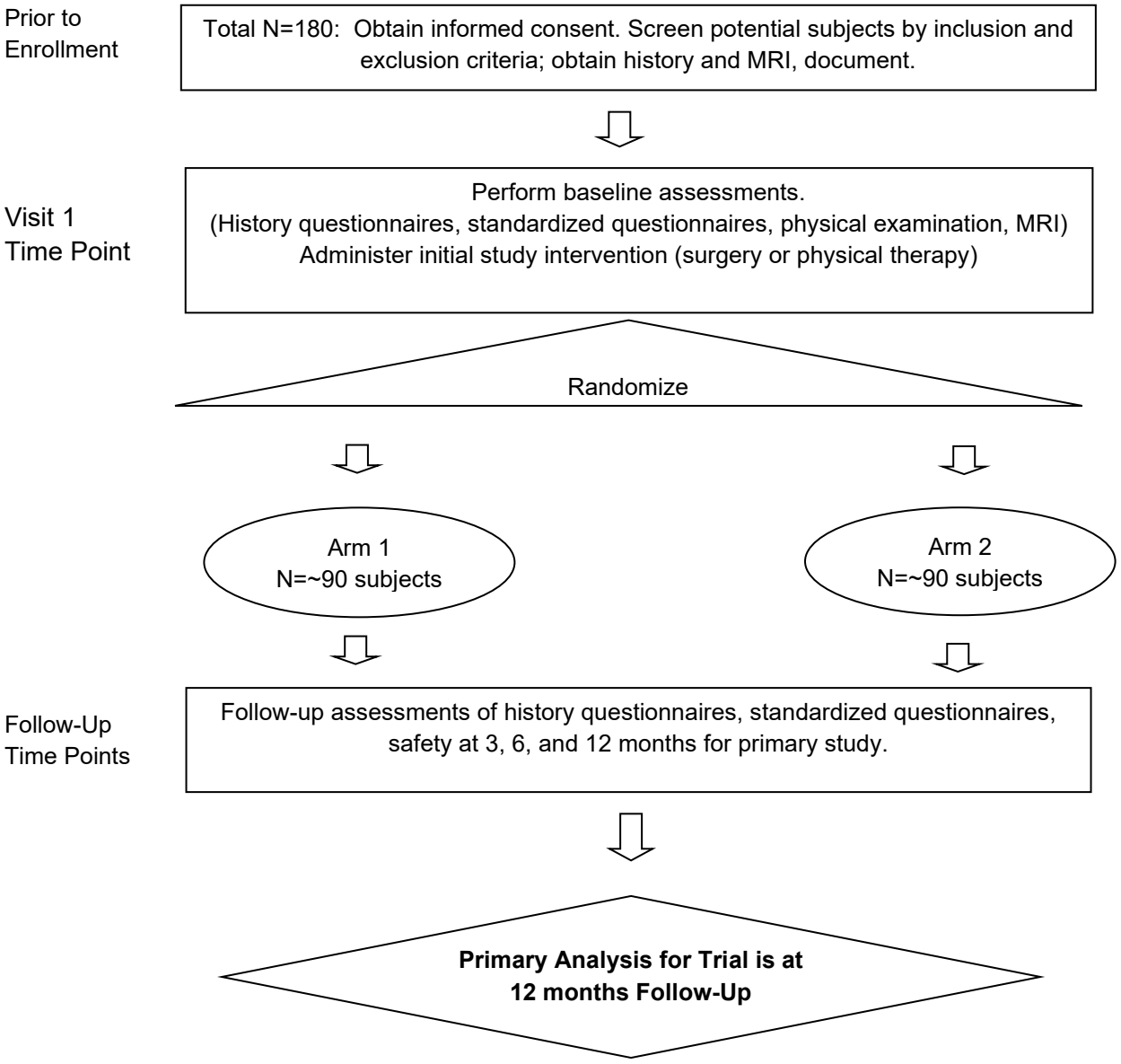
PHI	Protected Health Information
PI	Principal Investigator
PT	Physical Therapy
QA	Quality Assurance
QC	Quality Control
RA	Research Assistant/Research Coordinator
REDCap	Research Electronic Data Capture
ROM	Range of Motion
DASH	Disabilities of Arm, Shoulder, and Hand Questionnaire
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SPADI	Shoulder Pain and Disability Index
UP	Unanticipated Problem
US	United States
WHO	World Health Organization

PROTOCOL SUMMARY

Title:	Operative versus non-operative treatment for atraumatic rotator cuff tears: A multi-center pragmatic randomized controlled trial
Précis:	This is a randomized controlled trial in patients with atraumatic rotator cuff tears. The study will recruit approximately 180 patients randomized to arthroscopic surgery versus physical therapy treatments. The primary study and analysis will compare pain and function (measured by SPADI) at approximately one (1) year follow-up.
Objectives:	To compare pain and function in patients undergoing operative versus non-operative treatment of atraumatic rotator cuff tears at approximately 12 months of follow-up To assess effects of rotator cuff tear size and age on comparative outcomes (measured by SPADI) in operative versus non-operative treatments for atraumatic rotator cuff tears at approximately 12 months of follow-up Primary Outcome: SPADI Secondary: ASES
Population:	Patients of age ≥40 to <85 years diagnosed with a rotator cuff tear (with MRI confirmation) who are fit for either arthroscopic rotator cuff surgery or physical therapy will be recruited.
Sample Size:	180 subjects (an additional 20 may be recruited to allow for loss to follow-up and crossovers)
Phase:	III
Number of Sites:	16+
Description of Intervention:	Operative intervention includes arthroscopic rotator cuff surgery followed by post-operative physical therapy. Non-operative intervention includes physical therapy only.
Blinding:	None
Study Duration:	Approximately 7-9 years for the primary study

Estimated Time to Complete Enrollment:	Approximately 5.5-7 years

Schematic of Study Design:



1 KEY ROLES AND CONTACT INFORMATION

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1.1 Personnel Role Descriptions

Principal Investigator – Also the sponsor of the trial. Responsible for initiation, oversight and maintenance of trial as a whole. Primary author of study protocol and has ultimate authority over publication of protocol. Works with study statisticians for analysis and interpretation of study data.

Site Principal Investigator – Named at each study site/ institution. The primary physician responsible for oversight of study activities at that specific site.

Recruiting Physician – Responsible for recruitment and enrolment of patients. Determines eligibility and initializes study procedures. Reports to site PI.

Site Lead Physical Therapist – Responsible for communicating trial physical therapy protocols to treating physical therapist. Reports to site PI.

Trial Lead Physical Therapist – Responsible for training and overseeing Site Lead Physical Therapists.

Coordinating Center Staff –

Trial Project Manager – Oversees and trains research personnel, oversees data management and administrative tasks related to trial.

Data Manager – Responsible for data monitoring and reporting of SAEs/ AEs.

Research Study Coordinators – Assist with set-up of sites, training of staff, primary data entry, follow-up of all study participants and primary contact for

patients. Perform various administrative tasks. Share duties with site coordinator/ recruiters.

Research Assistants/Coordinators (RAs):

Site Coordinator – Oversees recruitment and enrollment activities at local site. Reports as needed to site PI, project manager, and coordinating center staff.

Site Recruiter – Responsible for completion of recruitment and enrollment activities at local site. Reports to site coordinator.

2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Shoulder symptoms accounted for 11.5 million ambulatory care visits in 2010 in the United States[1]. Rotator cuff tears are one of the leading causes of shoulder pain and disability and accounted for an estimated 272,148 ambulatory surgeries in 2006[2 3]. Despite the lack of evidence on operative versus non-operative treatment for rotator cuff tears, there has been an increase in surgery as the initial treatment for rotator cuff tears over time and billions of dollars spent by our healthcare system on these treatments[4]. This lack of evidence and the urgent need for research in this area is highlighted by the American Academy of Orthopaedic Surgeons[5], Agency for Healthcare Research and Quality[6], and Cochrane reviews[7 8].

We will compare operative and non-operative treatment in patients with atraumatic rotator cuff tears. Operative treatment includes arthroscopic rotator cuff surgery followed by post-operative physical therapy. Non-operative treatment includes physical therapy (without surgery).

2.2 Rationale

Our interest is in treatment for chronic degenerative rotator cuff tears. Therefore, patients ≥40 years of age will be eligible. Acute traumatic tears will be excluded because they are treated surgically as per expert opinion[9 10]. Since rotator cuff specific literature on what constitutes trauma is unavailable, we draw from the osteoporosis literature and use the criteria proposed by Mackey et al.[11] Patients reporting severe trauma will be excluded whereas those with low velocity trauma will still be included since the low velocity trauma likely exacerbated a pre-existing rotator cuff tear. Both partial-thickness and full-thickness tears will be included since the dilemma of operative versus non-operative treatment applies to both settings. Patients with Grade IV fatty infiltration will not be included since these patients may not be candidates for surgery in clinical practice. Patients with isolated subscapularis tears will also be excluded since these tears are usually traumatic and treated surgically. Detailed inclusion and exclusion criteria are presented in Sections 5.1 & 5.2.

Both operative and non-operative treatments are standards of usual care. Operative treatment will include arthroscopic rotator cuff surgery. The standards of care/protocol for operative treatment are included in Supplemental Materials. As in usual clinical practice, patients will have post-operative physical therapy after surgery. The post-operative physical therapy lasts for approximately 4 months. A standardized post-operative physical therapy regimen for this trial is included in Supplemental Materials.

Patients randomized to non-operative treatment will only receive physical therapy. This usually lasts for approximately 3 months. A standardized non-operative physical therapy regimen for this trial is included in Supplemental Materials.

2.3 Hypotheses

Our hypotheses for the primary analysis at approximately year one follow-up are:

Hypothesis 1: Patients undergoing operative treatment will have significantly greater improvement in pain reduction and function (measured by baseline to 12 month change in SPADI)[12] as compared with those treated non-operatively at approximately 12 months of follow-up.

Hypothesis 2a: Operative treatment will be more effective than non-operative treatment in cuff tears of increasing size.
Hypothesis 2b: Operative treatment will be more effective than non-operative treatment of rotator cuff tears with decreasing age.

2.4 Potential Risks and Benefits

2.4.1 Potential Risks

Potential physical risks include:

- fatigue due to answering study questionnaires
- pain and discomfort during the physical exam

The medical risks of participating in this study are those inherent to assigned treatments which are standards of care.

- For **physical therapy**, the risks include (but are not limited to) increased pain or no improvement of pain and function, and adhesive capsulitis (frozen shoulder).
- For **surgery**, the risks include (but are not limited to) those commonly associated with surgery, such as: post-operative bleeding or infection, blood clot, hospital readmission, complications related to anesthesia, and, in rare cases, death. Other risks for surgical treatment of rotator cuff tear include nerve injury, adhesive capsulitis (frozen shoulder), and no improvement of pain & function.

MRI Risks: There are no known major risks associated with an MRI scan. But it is possible that harmful effects could be discovered in the future. Known risks include claustrophobia, nausea, dizziness, flashing lights in eyes, and metallic taste.

In addition, there may be risks associated with the study that are unknown or unexpected.

2.4.2 Potential Benefits

There are no direct benefits to subjects participating in the study. Knowledge gained about the effectiveness of surgery versus non-operative treatments may benefit future patients and providers.

3 OBJECTIVES

3.1 Study Objectives

Aim 1: To compare pain and function in patients undergoing operative versus non-operative treatment of atraumatic rotator cuff tears at approximately 12 months of follow-up.

Aim 2: To assess effects of rotator cuff tear size and age on comparative outcomes (measured by SPADI) in operative versus non-operative treatments for atraumatic rotator cuff tears.

3.2 Study Outcome Measures

Patients with rotator cuff tear present with shoulder pain and loss of function. Hence, our outcomes are patient-reported measures of pain and function.

3.2.1 Primary Outcome

The primary outcome measure for this study is the difference between baseline and approximately 12-month SPADI[12].

3.2.2 Secondary Outcome

The secondary outcome measure for this study is the difference between baseline and approximately 12 month ASES[13].

Both, the SPADI and ASES, have shown to be reliable and valid in patients with shoulder pain.

4 STUDY DESIGN

4.1 Primary Study

This is an unblinded, multi-center, pragmatic randomized controlled clinical trial of operative versus non-operative treatments for atraumatic rotator cuff tears. A sample size of approximately 180 patients will be enrolled with approximately equal numbers of patients randomized to operative treatment (surgery + post-op physical therapy) and non-operative treatment (physical therapy without surgery). Both treatments are current standards of care. The duration of enrollment is expected to last approximately 5 years. For the main study and analysis, a 12-month follow-up is needed, with the duration of the primary study lasting for approximately 7-9 years.

Upon enrollment at baseline, patients will fill out study questionnaires, undergo a brief physical examination, and, if applicable, have a research MRI. Follow-up for the primary study will be performed via questionnaires at 3, 6, and 12 months.

4.2 Exploratory Sub-study

An exploratory sub-study will follow subjects after the primary end point of one (1) year for the trial has been met. The sub-study is not funded by PCORI and will follow subjects via questionnaires at yearly intervals for up to 10 years (i.e., for 9 years after the primary end point). The sub-study may also include a physical examination and research MRI at 2-10 years interval from enrollment. The objective of the sub-study is to assess longer-term patient-reported outcomes of operative and non-operative treatments (measured by SPADI and ASES) in patients with rotator cuff tears. It will also assess whether structural changes such as tear size and fatty infiltration of the rotator cuff muscle are different in the operative and non-operative groups.

5 STUDY ENROLLMENT AND WITHDRAWAL

Target Sample Size:	180 participants
Gender:	Both genders
Age:	≥40 years to <85 years
Demographic Group:	All demographic groups included
General Health Status:	Patients with shoulder pain and/or loss of function, and atraumatic rotator cuff tear

Screening estimates to achieve 180* participants:

- Expected number screened in clinic: 16,000
- Expected number eligible for study: 2,250

*An additional 20 patients may be recruited within the allocated timeframe to allow for loss to follow-up and crossovers

5.1 Subject Inclusion Criteria

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

- Aged ≥40 years to <85 years
- Shoulder pain and/or loss of active motion, strength or function
- MRI-confirmed partial- or full-thickness supraspinatus and/or infraspinatus tear of 4cm or less in longitudinal dimension
- Medically fit for surgery, defined as Category I-III per American Society of Anesthesiologists (ASA) Physical Status Classification (see Table 1: ASA Physical Status Classifications and Examples)
- Ability and willingness to provide informed consent

TABLE 1. ASA Physical Status Classifications and Examples

ASA Physical Status Classification	Definition	Examples
ASA I	A normal healthy patient	Healthy, nonsmoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; one or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥ 40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA <60 wk, history (>3 mo) of MI, CVA, TIA or CAD/stents
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (<3 mo) MI, CVA, TIA or CAD/stents; ongoing cardiac ischemia or severe valve dysfunction; severe reduction of ejection fraction; sepsis; DIC; ARD; or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction

ASA Physical Status Classification	Definition	Examples
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

ARD, acid reflux disease; **ASA**, American Society of Anesthesiologists; **BMI**, body mass index; **CAD**, coronary artery disease; **COPD**, chronic obstructive pulmonary disease; **CVA**, cerebral vascular accident; **DIC**, disseminated intravascular coagulation, **DM**, diabetes mellitus, **ESRD**, end-stage renal disease; **HTN**, hypertension; **MI**, myocardial infarction; **PCA**, postconceptural age; PS, physical status; **TIA**, transient ischemic attack

5.2 Subject Exclusion Criteria

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

- Primary diagnosis is something other than a rotator cuff tear
- History (in last 2 years) of shoulder fracture involving the humeral head on affected side
- Previous rotator cuff surgery on affected side
- Isolated subscapularis &/or teres minor tear on affected side
- Acute rotator cuff tear caused by a severe trauma (see TABLE 2: Trauma Classification)
- Shoulder used as a weight-bearing joint
- Contraindication to MRI (claustrophobia, pacemaker, pregnancy, shoulder implant, etc.)
- Glenohumeral osteoarthritis on xrays/MRI, as determined by recruiting MD
- Grade 4 fatty infiltration of rotator cuff (any tendons)

- Candidate for reverse shoulder arthroplasty or total shoulder arthroplasty at baseline
- Non-English speaking (questionnaires only validated in English)
- Severe problems with maintaining follow-up expected (such as but not limited to history of substance abuse, homelessness/incarceration, dementia, brain injury, and psychotic disorders)

Patients receiving workers' compensation are not excluded from the trial.

TABLE 2: Trauma Classification (adapted from Mackay, et. al., 2007)

Low Velocity Trauma	Severe Trauma
Falls from standing height or less	Falls from greater than standing height (e.g., falls while standing on a ladder, chair, porch, table, steps, or other raised surface)
Minimal trauma other than a fall (e.g., turning over in bed)	Motor vehicle crashes
Moderate trauma other than a fall (e.g., collisions with objects or another person during normal activities)	Struck by vehicle or other fast-moving projectile (e.g., bullet, baseball, etc.)
	Assault (i.e., injuries intentionally inflicted by another person)

5.3 Strategies for Recruitment and Retention

Study participants will be recruited through the clinics of designated recruiting physicians at each site. Recruitment will take place in community clinics and academic medical centers (see Appendix for list of recruiting sites). Potential recruits may be

identified through other mechanisms (e.g. primary care provider or non-operative provider referral, patient self-referral after hearing about the study, advertising, etc.) and referred to the clinics of recruiting physicians for evaluation. Patients in these clinics will be screened to determine eligibility and, if eligible, approached for enrollment in the study. Patients may also be contacted prior to their clinic visit to make them aware of the study.

5.3.1 Recruitment / Consent Videos

Patients will typically be shown two short, standardized videos (although these are not required, and staff may present this information verbally):

1) Recruitment Video – This video provides information about the trial (purpose and design), what is involved (length and procedures), and participant compensation.

2) Consent Video – This video provides information about risks and benefits, withdrawal/removal from the study, and information that will be collected.

Use of these videos can help ensure consistency of information presented to study candidates across all sites. The recruitment video has been designed to educate participants about the purpose of the trial and what it involves as well as the importance of randomized assignment and following through with their assigned treatment for 6 months.

The RAs and/or recruiting physician will also introduce the study to the patient via sample standardized scripts and be available to answer questions that the patient may have. In the event that the patient does not wish to watch the videos but wants to participate in the study, the RA may substitute a verbal discussion of the content using the video scripts as a guide.

5.3.2 Crossover

Subjects may cross over from one treatment to another at any point during the trial. Crossovers are usually from the non-operative to the operative arm (although a few patients randomized to the operative arm may not have surgery and have only physical therapy). It takes about 6 months for non-operative physical therapy to be effective. Hence, at the time of recruitment, subjects will be encouraged to stay in their randomized treatment arm for at least 6 months. However, subjects may cross over at any time point if they choose to do so and will still remain in the study.

If a subject crosses over within 6 months following randomization or does not pursue either treatment within 12 months after randomization it will be considered a protocol deviation.

5.3.3 Compensation

Subjects will be compensated for the time and inconvenience of participating in the study. They will be paid:

- $100 for the baseline enrollment visit,
- $50 for each follow-up questionnaire completed (at 3mo, 6mo, 12mo for the main study, and annually in years 2-10 for the exploratory sub-study), and
- $100 for a return visit & MRI for the exploratory sub-study (once, approximately 2-10 years after treatment for the sub-study).

Main Study				Exploratory Sub-Study									
Base-line Visit	3 Mo	6 Mo	12 Mo	2 Yr	3 Yr	4 Yr	5 Yr	6 Yr	7 Yr	8 Yr	9 Yr	10 Yr	Return Visit & MRI*
$ 100	$50	$50	$50	$50	$50	$50	$50	$50	$50	$50	$50	$50	$100

*If applicable

5.3.4 Long-term Participation Strategies

Several strategies will be used to promote continued participation.

- **Complete Contact Information** - Both primary and secondary addresses, phone numbers, and emails will be collected for subjects at baseline as well as on all follow-up questionnaires. If subjects live at an alternate address for part of the year, it will be noted which months are spent at each address.
- **Multiple Means of Contact** – Subjects will be contacted by phone, email, mail, or text as needed. Subjects can specify their preferred means of contact. Alternate means of contact may be used if initial attempts to reach the subject via their preferred means are unsuccessful.
- **Secondary Contact Person** – The name, relationship, address, phone, and email of a secondary contact person will be collected at baseline as well as on all follow-up questionnaires. This person may be contacted if all other attempts to reach the subject fail.

- **Option of Paper or Electronic Questionnaires** – Subjects may choose to complete follow-up questionnaires either on paper or electronically (via tablet or computer) per their preference.

- **Follow-Up Reminders & PI calls** – Subjects who do not complete/return follow-up questionnaires within the expected timeframe will receive follow up reminders. If questionnaires are not completed/returned after at least three reminders by study personnel, subjects may receive a call from the study PI or site PI.

5.3.5 Sharing Results with Participants

Results of the study will be made available via clinicaltrials.gov and on the study website: *www.shoulderstudy.org/studies/arc-trial*.

5.4 Treatment Assignment Procedures

Enrolled participants will be assigned to treatment with approximately equal numbers of subjects randomized to operative and non-operative treatment. Subjects will be randomized ONLY after eligibility has been confirmed and informed consent has been obtained.

Strata information is entered in the database and the research assistant manually initiates randomization, which is automatically generated by the REDCap randomization module. The database has been programmed so that randomization is only possible if all necessary information has been entered and all eligibility criteria have been documented as met.

5.4.1 Randomization Procedures

Randomization will be stratified by site, age class (< 65 years; ≥ 65 years), and tear size class (> 0 < 2 cm; ≥ 2 ≤ 4 cm) and blocked within strata using a random sequence of differing block sizes (i.e., 2, 4 and 6). Accordingly, the maximum treatment assignment imbalance at any site is 3 participants. Randomization strings for each site will be unique, randomly generated, and administered in real time using a randomization module within REDCap.

The study principal investigator, trial project manager, site investigator, and other designated study personnel will receive automatically generated emails when a participant is randomized.

Randomization assignments will be accessible 24 hours a day, 7 days a week via REDCap. If REDCap is unavailable locally for any reason, site personnel will call a

study coordinator at a coordinating center to complete randomization. If REDCap is down globally, randomization will not take place until the system is back up, or the subject affected will not be randomized.

Additional placeholder sites have been included in the randomization table, so that new sites or replacement sites may easily be added to the randomization module in REDCap (if needed) once the study is under way.

5.4.2 Masking Procedures

Intervention arms will not be masked, as this is a non-blinded study.

5.5 Subject Withdrawal

Subjects may withdraw from the study voluntarily or be terminated by the principal investigator.

5.5.1 Reasons for Withdrawal

Subjects are free to withdraw from participation in the study at any time upon request.

An investigator may terminate a subject's participation in the study if:

- Any serious adverse event (SAE) or other medical condition or situation occurs such that the subject cannot continue or continued participation in the study would not be in the best interest of the subject.
- The subject is deceased.
- The subject does not complete any follow-up questionnaires in the first year (Lost to follow-up).
- The subject does not complete annual follow-up questionnaires two years in a row for the exploratory sub-study (Lost to follow-up).
- Prior to randomization, a consented subject is found to not meet eligibility criteria (Screen-fail).
- The study ends earlier than anticipated.

5.5.2 Handling of Subject Withdrawals or Subject Discontinuation of Study Intervention

Subjects who are withdrawn from the study, either through voluntary discontinuation, for failure to complete study questionnaires, or by decision of the principal investigator for reasons enumerated above, will be recorded as terminated. They will be sent a letter confirming their early termination from the study and will no longer be followed. They will not be sent any further follow-up questionnaires or brought back for a follow-up visit & MRI (if applicable).

If a subject is withdrawn due to an SAE or other medical condition that precludes their continuation in the study, the study or site PI will call the subject to discuss and ensure appropriate medical treatment or follow up is arranged.

5.6 Premature Termination or Suspension of Study

The study may be suspended or prematurely terminated if there is sufficient reason or cause. Per the Data & Safety Monitoring Committee (DSMC) charter, the DSMC will monitor progress of the trial and determine any actions related to suspension or termination of the trial. (See Supplemental Materials)

Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the principal investigator will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

6 STUDY INTERVENTION

6.1 Study Procedural Intervention(s) Description

Patients will be randomized to either an operative or non-operative treatment regimen. Non-operative and operative interventions performed for this study are consistent with routine clinical standards of care for rotator cuff tears.

6.1.1 Non-operative Intervention

Subjects randomized to the non-operative arm of the study will be asked to follow a standardized non-operative rehabilitation program. They will not undergo rotator cuff surgery (unless subjects cross over).

Non-operative Rehabilitation Regimen: Subjects randomized to the non-operative arm of the study will follow a prescribed (approximately 3-month) physical therapy and home exercise program to strengthen and stabilize the shoulder muscles. A standardized, non-operative rehabilitation protocol (see Supplemental Materials) has been developed for this trial with extensive input from our team of clinicians, researchers, and expert consultants. Subjects may continue physical therapy beyond 3 months as prescribed/deemed appropriate by their treating clinicians.

6.1.2 Operative Intervention

Subjects randomized to the operative arm of the study will undergo arthroscopic surgery to debride or repair the rotator cuff tear and then follow a standardized post-operative rehabilitation program.

Surgery: The subject's attending surgeon will perform an arthroscopic rotator cuff surgery based on the evidence-based surgical protocol (see Supplemental Materials) developed for this trial. This protocol has been developed to maximize the potential for rotator cuff tear repair healing and to reduce the variables that could affect surgical outcomes. Surgeons may perform additional/alternative surgical procedures intraoperatively as deemed necessary (e.g., SLAP repair, debridement only, arthroscopic to open procedure).

Information will be collected on the specific surgical techniques used, such as number of anchors and type of repair (e.g., single row, double row, transosseous, or transtendinous). Any concomitant procedures such as subacromial decompression and acromioclavicular joint resection will also be noted. (See Appendix, Surgery Report Form.)

Post-Operative Rehabilitation Regimen: Following surgery, subjects will be asked to follow a prescribed (approximately 4-month) physical therapy and home exercise program to strengthen and stabilize the shoulder muscles. A standardized, post-operative rehabilitation protocol (see Supplemental Materials) has been developed for this trial with extensive input from our team of clinicians, researchers, and expert consultants. Subjects may continue physical therapy beyond 4 months as prescribed/deemed appropriate by their treating clinicians.

In cases where additional/ alternative surgical procedures were performed, modifications to the post-op protocol are allowable, as medically appropriate.

The post-operative rehabilitation regimen is similar to the one that will be followed for non-operative rehabilitation. The main difference between the two intervention arms is the rotator cuff surgery.

6.2 Concomitant Medications/Treatments

Subjects will be able to take analgesic medications or have shoulder injections, since it would not be ethical to restrict the use of these interventions. Use of non-surgical co-interventions will be recorded in follow-up questionnaires completed by the subject.

6.3 Administration of Procedural Intervention

Interventions will be standardized to the extent this is possible. Standardized protocols have been developed for surgery, as well as for both non-operative and post-operative rehabilitation regimens, and will be disseminated to treating clinicians.

6.3.1 Surgery

Study surgeons at each recruiting site will perform rotator cuff surgery for those subjects in the operative arm of the study recruited from their site. Surgery should be scheduled to occur within 8 weeks after randomization to the operative treatment arm. If surgery occurs later than 8 weeks after randomization, it will be considered a protocol deviation.

6.3.2 Physical Therapy

Local physical therapists will administer the post-operative and non-operative rehabilitation regimens for subjects in both arms of the study. Site personnel will assist in referring subjects to a physical therapist at a location that is convenient for them. Subjects may also utilize any physical therapist of their choice.

Physical therapy should begin within 8 weeks after randomization to the non-operative treatment arm or within 8 weeks following surgery, if in the operative arm. If physical therapy begins later than this time period after either assignment to the non-operative arm or undergoing surgery, it will be considered a protocol deviation. The post-operative protocol calls for physical therapy to begin ideally within 1-week post-surgery, but a later start is not considered a protocol deviation (it is only a protocol deviation if PT is not started within 8 weeks post-surgery).

Non-Operative Physical Therapy: The duration of the non-operative physical therapy program will be approximately 3 months, with subjects attending physical therapy 1-2 times a week on average, for a total of approximately 12-24 visits.

The treatment stages of the non-operative rehabilitation protocol are goal/performance based. Non-operative subjects who make rapid progress may be advanced to the next stage of the rehabilitation treatment protocol if they meet the criteria to do so and may be discharged from physical therapy earlier than 3 months as appropriate.

Post-operative Physical Therapy: The duration of the post-operative physical therapy program will be approximately 4 months, with subjects attending physical therapy 1-2 times a week on average, for a total of approximately 16-32 visits.

The treatment stages of the post-operative rehabilitation protocol are pegged to specific timeframes following surgery. Subjects in the operative arm who meet treatment goals for a given stage early should NOT be advanced to the next stage ahead of schedule, in order to allow proper healing of their shoulder post-op. Rather, the interval between physical therapy visits should be increased as appropriate. Exceptions to this may be made as appropriate for operative patients who receive alternate or additional surgical procedures (e.g., debridement only, SLAP repair, etc.).

The actual number and frequency of physical therapy visits will vary over the course of treatment and by subject, based on individual progress and needs. Physical therapy visits may be conducted on telehealth platforms, as needed. Any modifications of the protocol made due to the limitations of telehealth will be documented on the physical therapy report forms (CRFs-06.1, 06.2).

6.3.3 Home Exercise Program

Subjects themselves will be responsible for attending scheduled physical therapy treatments and adhering to the home exercise program as prescribed by their physical therapist until discharged from physical therapy.

To be considered compliant with the rehabilitation regimen for either arm of the study, subjects are expected to attend physical therapy &/or complete their home program exercises a total of at least three times each week. The three times can be any combination of the two (e.g., 2 physical therapy visits + 1 day of home exercises, 1 physical therapy visit + 2 days of home exercises, and so on).

6.4 Procedures for Training of Clinicians on Procedural Intervention

6.4.1 Treating Surgeons

All study surgeons will be briefed on the standardized surgical protocol that has been developed with physician input and will follow the surgical protocol.

6.4.2 Treating Physical Therapists

To ensure that treating physical therapists – many of whom will be otherwise unacquainted with the study – are aware of the subject's participation in and the requirements of the study, each recruiting site will have a designated Lead Physical Therapist. His/her job will be to contact the treating physical therapist for all subjects recruited from their site as soon as possible after treating physical therapist contact information is obtained, ideally within approximately 2-3 weeks *after randomization* (for the non-operative arm) or within approximately 2-3 weeks *after surgery* (for the operative arm).

The site Lead Physical Therapist will ensure that the treating physical therapist receives a copy of the appropriate rehabilitation protocol (operative or non-operative), will explain the details of the study, will stress the importance of protocol adherence, and will answer any questions the treating physical therapist has regarding the treatment protocol. Treating physical therapists will be encouraged to call their Lead Physical Therapist at any time they have a question or concern during the course of treatment.

6.4.3 Subjects

Subjects will be provided with a Rotator Cuff Home Exercise Program (see Appendix) that contains various exercises which may be assigned to them during their home exercise program. They will be instructed to bring this brochure with them to each physical therapy visit so that their physical therapist can update the assignment of exercises and the set/reps, frequency, etc. for each exercise at each visit. Exercises that no longer need to be performed will be crossed off as finished/discharged. Proper use of the patient exercise brochure will help to ensure that subjects know exactly which exercises they should be doing (in what amount

and with what frequency) at any given time and will promote compliance with the home program.

6.4.4 Research Staff

Research staff will not administer treatment interventions but will be trained by their site physical therapist and provided written instructions on how to perform a physical exam in clinic to measure the strength of both shoulders for each subject (using a dynamometer). In some cases, a physician may designate a staff member (e.g., a Physician's Assistant or qualified delegate) to perform the range of motion portion of the physical exam.

6.5 Assessment of Clinician and/or Subject Compliance with Study Procedural Intervention

A systematic effort will be made to obtain relevant information regarding clinician and/or subject compliance with study interventions through the means outlined below. However, failure to obtain this information after follow-up attempts will not be considered a protocol deviation.

6.5.1 Treating Surgeons

Following rotator cuff surgery, surgeons will complete a Surgery Report Form (CRF-05, see Appendix) detailing the type of tear, the repair/procedures performed, number of anchors used, tendon quality and retraction, etc. A copy of the surgical note from the subject's medical record will be submitted as well. An effort will be made to also collect this information for crossover patients when possible/feasible.

In the rare case that the shoulder surgery is performed by a surgeon not affiliated with the ARC trial, the surgical note will be obtained, if possible, and the surgeon will complete the Surgery Report Form, if feasible. The Surgery Report Form may also be completed by the ARC recruiting physician who enrolled the patient or Site PI to the extent possible based on the treating surgeon's note.

6.5.2 Treating Physical Therapists

Typically, treating physical therapists will complete a Prospective Physical Therapist Report Form (CRF-06.1, see Appendix) twice over the course of the subject's rehabilitation program – The first report will be sent approximately one month after the patient is randomized (for non-operative patients) or one month after surgery (for operative patients). The second will be sent approximately two months later, at the three-month benchmark. If a patient has not started physical therapy by the one-month mark (or contact info for the treating physical therapist was not available at

that time), an additional report will be sent at the 6-month mark. The report form will capture information about the subject's physical therapy start and end dates and which exercises are being/have been performed with the subject. Subjects will sign an authorization form allowing treating physical therapists to share this information with the study research team. If any problems or issues of concern are identified at any report time point, the site Lead Physical Therapist may contact the treating physical therapist in order to address them.

For crossover patients, an effort will be made to obtain physical therapy treatment information for the crossover treatment arm when possible/feasible. This may include retrospective collection of available data (e.g., if PT treatment is already complete or nearly so) and/or prospective data collection similar to that for the assigned treatment arm (e.g., if PT treatment is still in the early stages). A Crossover Physical Therapist Report Form (CRF-06.2, see Appendix) will be used for crossover PT treatment data collection.

6.5.3 Subjects

Subjects will complete a Physical Therapy Diary (CRF-04, see Appendix) – on paper or via the MyCap smartphone app - to record on which days they attended physical therapy (PT) &/or performed their home exercise program (HEP). Diary tracking will begin on the date of the subject's first physical therapy visit after either randomization (for the non-operative treatment group) or rotator cuff surgery (for the operative group) and will officially end when the subject is discharged from physical therapy.

On follow-up questionnaires, subjects will report the date of their shoulder surgery (if applicable) and answer questions regarding their physical rehabilitation program (e.g., start & end dates of PT, average frequency of PT attendance and of performance of HEP).

For crossover patients, an effort to obtain subject PT info will be made when possible/feasible by providing a PT Diary for tracking physical therapy & home exercises for the crossover treatment arm.

6.5.4 MRI Review by Study Radiologist

The study radiologist will review the MRI images and, if available, x-rays of all randomized subjects from all recruiting sites to verify the presence and size of a rotator cuff tear for each subject's affected shoulder and will complete an MRI Review Form (CRF-07, see Appendix) for each subject.

If a subject is found to have no rotator cuff tear or a tear larger than 4cm, or if the radiologist identifies anything of concern other than a rotator cuff tear (e.g., acute

fracture, tumor, etc.), the study PI is to be notified immediately. If an area of concern is identified, the study PI will notify the treating/recruiting physician. If the subject does not have a rotator cuff tear, or has a tear larger than 4cm, a re-check (by the study radiologist) that will override the original read will be requested to verify that the initial reading is accurate. Regardless of the results of the MRI review, the subject will not be withdrawn and will continue to be followed for the duration of the study.

7 STUDY SCHEDULE

7.1 Pre-Screening (Prior to Clinic Visit)

Potential subjects may be pre-screened prior to their clinic visit via a review of the clinic schedules of participating study physicians or, in some cases, of referring non-operative providers. Those who meet the study age range, present with a shoulder complaint, and are not returning for a post-op visit will be identified as potentially eligible. Sites may wait until patients have had an MRI of their shoulder before including them in pre-screening. (Subject Locator, similar institutionally approved, software applications, or EMR filters at recruiting sites, may be used to facilitate the process of identifying potential participants.) If no obvious exclusionary factors are found in a review of available medical records, identified subjects will be screened in clinic by study MDs to determine study eligibility.

Where allowed per participating institution policy, research personnel may also contact prospective subjects prior to their scheduled clinic visit to make them aware of the study and provide preliminary information in advance of their upcoming visit.

Self-referred subjects who learn of the study through advertising, clinicaltrials.gov, etc. may be pre-screened via electronic survey and/or call with study personnel prior to being seen in clinic for evaluation by a study physician.

PCPs or non-operative specialty providers (such as sports medicine physicians and physiatrists) may refer patients to the clinics of participating study physicians as appropriate for further evaluation.

Activities:

- Review clinic schedules to identify potentially eligible subjects
- PCP/non-op provider referrals to study physicians (as appropriate)
- Review available medical records for any obvious exclusionary factors
- Create a paper or electronic Clinic Screening Form (CRF-00) for potentially eligible subjects with no known exclusionary factors
- Deliver/send Clinic Screening Form (CRF-00) to examining physician prior to potential subject’s clinic visit
- Enter preliminary screening information into REDCap Screening Log

- Contact prospective subjects prior to visit to inform them of the study as appropriate (only if allowed per institutional policy)

- Pre-screen interested patients who contact the study team about study participation and refer for clinic scheduling as appropriate.

7.2 Screening (During Clinic Visit)

Potentially eligible subjects will be evaluated in clinic based on the physician's clinical examination, clinical MRI results, and screening questions that address the study inclusion and exclusion criteria using the Clinic Screening Form (CRF-00, see Appendix).

Activities:

- Clinic Screening Form (CRF-00) completed by physician for potentially eligible subjects to determine eligibility
- Complete Screening Log records for ineligible subjects

7.3 Enrollment/Baseline

Subjects who meet all eligibility criteria per the Clinic Screening Form (CRF-00) will be approached for participation in the trial. The study physician will briefly introduce the study. If the patient is interested in learning more, a trained research assistant will present the study using a sample script and standardized recruitment and consent videos. Subjects who consent to participate in the trial and be randomized will sign a written or electronic consent form and be given a baseline questionnaire to complete– either on paper or electronically (per the subject's preference). Study staff may also perform a brief physical exam to measure and record the subject's strength and range of motion in both arms. If the subject is enrolled remotely, all or part of the physical exam may not be administered.

Study staff will review the completed questionnaire for completeness and confirm the subject's willingness to be randomized. If eligible for the study, the subject will then be randomized to treatment via the REDCap randomization module and either scheduled for surgery or referred for physical therapy as appropriate.

Subjects will also receive a study packet with information about the trial, a copy of their signed consent form, a physical therapy protocol for their assigned arm of the study to give to their treating physical therapist, a patient exercise brochure to use in completing their home exercise program, and a physical therapy diary for tracking their

rehabilitation program. Subjects who elect to complete their physical therapy diary via smartphone app will be assisted by study staff to install and set up the MyCap app.

Subjects who want more time to consider participation in the study will be provided contact information for the site RA in case they decide to participate or have further questions. If they later choose to participate, they would be enrolled remotely. Site RAs will follow up with patients after approximately one week, if the patient has not yet reached out to either decline or express interest in the study.

In cases where a subject lives far away or it is not feasible to return in person to receive their MRI results, a physician may choose instead to call and discuss the subject's MRI results with them over the phone. Subjects who are eligible may be contacted to discuss enrollment in the trial and will have the option to be enrolled remotely. If the subject is remotely enrolled, all or part of the physical exam may not be administered.

Potential subjects who meet all eligibility criteria (including MRI confirmation of tear):

NOTE: Some/ all of these procedures may occur remotely as needed based on clinic policies, restrictions/constraints on the conduct of research activities, or subject preference.

- Approach/contact patient and provide information about the trial
- Obtain and document consent from subjects who agree to participate
- Have subject complete authorization form allowing treating physical therapist to share information about PT Treatment (see Appendix)
- Administer physical exam (obtain ROM & strength measurements) for both shoulders & complete Physical Exam Form (CRF-02, see Appendix). Physician or delegate completes Part A (ROM) and RA completes Part B (strength).
    - Physical Exam Part A (ROM) may be completed based on measurements taken as part of the routine clinic exam. If so, a copy of the clinic note should be obtained as source documentation.
    - NOTE: Physical Exams A (ROM) and/or B (strength) might not be performed if subject is enrolled remotely or due to research restrictions and/or clinic policies/constraints. Such deviations are acceptable in such cases.
- Administer baseline questionnaire (CRF-03.1, see Appendix) & review for completeness when done

- Complete enrollment portion of CRF-01 Patient Study Info Overview (electronic CRF)
- Re-confirm subject's willingness to be randomized
- Randomize subject to treatment via REDCap randomization module
    - If subject assigned to operative treatment arm, refer subject to be scheduled for surgery
    - If subject assigned to non-operative treatment arm, refer subject for physical therapy
- Provide subject appropriate PT protocol for assigned treatment arm (to give to treating physical therapist), patient PT brochure, & PT Diary – Part I (CRF-04.1, see Appendix)
- If subject elects to complete PT diary via smartphone, assist subject with installation and setup of MyCap app and provide instructions for use.
- If subject requests more time to consider participation in study, provide contact info for RA and instruct subject to call and schedule return visit to complete enrollment procedures if he/she decides to participate. (RA may follow up with subject approximately one week later to ask if they have made a decision.)

The REDCap Screening Log is to be completed for each subject once they are found to be ineligible, have declined to participate, or are consented for the study. Screened subjects with pending MRIs should be tracked until MRI results are known and eligibility can be determined.

7.4 Follow-Up

7.4.1 Follow-Up Questionnaires (± approximately 4-6 weeks from follow-up time point)

Subjects enrolled in the study and randomized to treatment will be sent follow-up questionnaires at the following approximate intervals:

- 3 months after randomization
- 6 months after randomization
- 12 months after randomization

- Annually thereafter for years 2-10 (for the exploratory sub-study)

Questionnaires can be completed on paper or electronically, per the subject's preference.

The target window for completion of follow-up questionnaires is -4 weeks/+6 weeks from the ideal follow-up time point, based on date of randomization. For example, if a subject was randomized to treatment on June 1st, the ideal date for completion of his/her 3-month follow up questionnaire would be Sept 1st (+3 months); the lower window would be August 1st (ideal date minus 1 month) and the upper window would be Oct 14th (ideal date + 6 weeks). Questionnaires will be sent out no earlier than the lower window date.

A concerted, systematic effort will be made to obtain completed questionnaires by the target upper window date (including approximately 3 contacts by research staff, a PI contact, and/or contact from site PI/ recruiting physician/ site staff, if needed). However, it will not be considered a protocol deviation if a patient questionnaire is completed after the upper window date or not completed at all.

At ALL Follow-Up Time Points:

- Send questionnaires (by mail or electronically) to subjects shortly after their lower window date
- If completed on paper, review and enter data into REDCap
- If completed electronically, review answers provided in REDCap
- If important data is missing or is ambiguous/contradictory, contact subject to resolve and document appropriately
- If questionnaire not completed/returned within 1-2 weeks, follow up with subject per follow-up procedures specified in MOOP

At 3-month, 6-month, & 12-month Follow-Up Time Points:

- Review SAE/AE section of questionnaire
    - If subject reports SAE/AE on follow-up questionnaire:
        1) Contact patient and/or study site for additional information as appropriate
        2) Complete event report in REDCap

- Monitor changes to assigned treatment (e.g.,crossover) or failure to obtain study treatments, as reported via the Surgery/Trauma Update &/or Treatment sections of the questionnaires:
    - If subject reports information indicating crossover or no treatment:
        1) Verify information provided with patient &/or site research staff
        2) Record as a protocol deviation, if applicable (e.g., if assigned treatment not started within 8 weeks after randomization)
        3) Record as “crossover” in the patient’s research record, if applicable (e.g., if crosses over within 6 months after randomization)

At 12-month Follow-up Time Point Only:

- Perform a review of subject’s record to see if either surgery and/or physical therapy treatment has been reported by or for subject.
    - If no record of either treatment, verify with patient &/or site research staff, as appropriate
    - If no treatment received within 12 months after randomization, record in research record as protocol deviation

7.4.2 Physical Therapy Diary (for duration of prescribed physical therapy program)

Subjects who choose to complete their physical therapy diary on paper will typically submit the completed PT diary (CRF 04, see Appendix) in two installments, at the time of their 3-month and 6-month follow-up questionnaires, respectively. A first installment will be given to them at enrollment. A second installment will be sent to them at the time of their 3-month questionnaire. Patients for whom treatment start is delayed &/or who cross over to the other treatment arm may be sent additional copies of the diary, as appropriate. Collection of PT diaries may occur at up to three time points (3, 6, and 12 months) to help ensure that the full duration of their physical therapy program is captured.

Subjects who choose to complete their physical therapy diary via smartphone will enter their information daily until discharged from physical therapy. Verification that this information has been submitted via the app will occur at the time the 3-month, 6-month, and (if needed) 12-month follow-up questionnaires are sent out, with periodic monitoring in between to catch any technical issues. A systematic effort will be made

to obtain physical therapy compliance data from subjects via the PT diary. However, failure to obtain this information after reasonable follow-up attempts will not be considered a protocol deviation. PT information is also collected from the subject on the follow-up questionnaires during the first year of study participation and from the treating physical therapist(s) via Physical Therapist Report forms.

7.5 Follow-Up Visit & MRI (2-10 years after treatment for exploratory sub-study)

On one occasion, approximately 2-10 years after randomization to treatment, subjects may be asked to return for a follow up visit and MRI for the exploratory sub-study. During the visit, a physical exam may be performed again to measure range of motion (ROM) and strength in both shoulders.

Subjects may also undergo a research MRI similar to the clinical MRI performed prior to enrollment in the trial.

- Schedule subject to have research MRI
- While subject on site for MRI, may perform physical exam (ROM & strength measurements) for both shoulders & complete Physical Exam Form (CRF-02, see Appendix)

8 STUDY PROCEDURES / EVALUATIONS

Study procedures and evaluations will consist of subject- and clinician-reported outcomes and observations as well as imaging to document structural features of the shoulder/rotator cuff.

8.1 Study Procedures/Evaluations

- **Pre-Screening –** Review of clinical schedule & available medical records conducted by site RA to identify potentially eligible subjects for study. Electronic/phone pre-screening of interested patients who inquire about study participation.

- **Clinical Screening** – Assessment of medical factors related to eligibility for study obtained via interview and observation by physician during clinical examination and recorded on Clinic Screening Form (CRF-00, see Appendix).

- **Physical Examination –** Measurement of strength (using a dynamometer) by site RA and range of motion (using a visual diagram) of both shoulders by physician or trained designee. Performed once at enrollment/baseline (for the primary study) and possibly again 2-10 years after treatment (for the exploratory sub-study). Recorded on Physical Examination Form (CRF-02, see Appendix). At enrollment, physical exam Part A (ROM) may be completed based on measurements taken as part of the routine clinic exam, and physical exams A (ROM) and/or B (strength) might not be performed due to remote enrollment, research restrictions, or clinic policies/constraints.

- **Baseline & Follow-Up Questionnaires -** Patient questionnaires (CRF-03.1, 03.2, 03.3, 03.4, see Appendix) that ask about pain and movement, shoulder symptoms, daily and recreational activities, general and emotional health, and what treatments have been used to help the subject's shoulder. Completed by the subject at baseline and each designated follow-up time point (3mo, 6mo, 12mo, and annually thereafter for years 2-10).

- **Physical Therapy Diary** – Patient-reported record (CRF-04.1, 04.2, see Appendix) of which days the subject attended physical therapy &/or completed their home exercise program during their prescribed rehabilitation program (post-op or non-op). Collected at 3-month, 6-month, & 12-month follow-up timepoints,

as appropriate. Subjects may also opt to complete the diary via smartphone using the installed MyCap app.

- **Surgery Report** – Post-surgery report form (CRF-05, see Appendix) completed by treating surgeon after performing rotator cuff surgery (or may be completed by ARC site PI/ recruiting physician, if surgery was performed by a non-ARC surgeon), noting intra-operative observations of tear size, location, and shape; tendon quality and retraction; and cuff repair performed.

- **Physical Therapist Report** – Physical Therapy report form (CRF-06, see Appendix) completed by treating physical therapist, noting start/end dates and frequency of physical therapy attendance by subject and physical therapist's compliance with the prescribed protocol. Completed once at 1 month and again at 3 months after surgery (for subjects in the operative arm) or 3 months after randomization (for subjects in the non-operative arm), respectively. If the subject's treatment start is delayed (or treating physical therapist info is not available) at 1-month time point, a report will also be sent at 6 months.

- **MRI Reading** – MRI Reading Form (CRF-07, see Appendix) completed by study radiologist following an independent review of subject's MRI images and x-rays (if available), noting size, location, and degree of tear; status of biceps tendon, muscle atrophy, tendon retraction and fatty infiltration; as well as presence of arthritis, lesions, and other pathologies. Performed for initial MRI (at enrollment/baseline) and follow-up MRI (at 2-10 years after treatment, if applicable), and may be performed on a routine clinical care MRI, if subject has subsequent MRI during study period.

  Follow-Up MRI - Research MRI of shoulder (without contrast) performed at 2-10 years after treatment for the exploratory sub-study to assess structural changes such as tear size and fatty infiltration of the rotator cuff muscle over time since treatment. In some cases, patients may receive a subsequent clinical MRI or other shoulder imaging during the study period as part of their standard clinical care. In such cases, these MRIs and imaging studies may be collected and reviewed, if possible.

9 ASSESSMENT OF SAFETY

9.1 Specification of Safety Parameters

The operative and non-operative treatments in this trial are standards of usual care. The Adverse Events (AEs) and Serious Adverse Events (SAEs) are therefore those inherent to standard of care treatments. Safety parameters will be recorded in our online data capture system (REDCap). These parameters include the date of occurrence of AE/SAE, a detailed description of the nature of the event, assessment, follow up, and the resolution of the AE/SAE, as appropriate to the event. The safety procedures will be performed for our primary study/trial that ends at one (1) year of follow up and not for the exploratory sub-study. Further details are provided in the sections below.

9.1.1 Unanticipated Problems

Unanticipated problems include breach of confidentiality or loss of data. Safeguards to prevent this include storage of data in locked file cabinets, use of password protected REDCap databases, use of courier service with tracking for transfer of MRI discs with PHI to the data coordinating center, and restricting access to data by authorized study personnel only.

9.1.2 Adverse Events (AEs)

AEs for this trial include:

- Post-operative infection
- Post-operative bleeding
- Nerve injury
- Blood clot/ DVT
- Complications due to anesthesia
- Adhesive capsulitis (frozen shoulder)

9.1.3 Serious Adverse Events (SAEs)

SAEs for this trial include:

- Death
- Event requiring hospitalization (in-patient admission) related to treatment

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

All reportable events will be recorded in the study record with start dates occurring any time after informed consent is obtained until 7 days (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation for the main study (i.e.,1 year of follow-up after randomization). Subjects will be asked about the occurrence of AE/SAEs on each follow-up questionnaire in the first year. Unsolicited AE/SAEs may also be submitted directly in REDCap by study personnel. Event reports started by sites will be monitored by authorized study personnel to ensure that the events are ultimately submitted for review by the study PI/ authorized study personnel and reported to the IRB as appropriate.

Serious events related to study treatment will be followed for outcome information, as appropriate, until resolution or stabilization. Unanticipated problems will be recorded in the data collection system throughout the study as discovered.

9.3 Characteristics of an Adverse Event

9.3.1 Relationship to Study Intervention

Study PI will assess relationship to study intervention. To assess relationship of an event to study intervention, the following guidelines will be used:

1. Related (Possible, Probable, Definite)
    a. The event is known to occur with the study intervention.
    b. There is a temporal relationship between the intervention and event onset.
    c. The event abates when the intervention is discontinued.
    d. The event reappears upon a re-challenge with the intervention.
2. Not Related (Unlikely, Not Related)
    a. There is no temporal relationship between the intervention and event onset.
    b. An alternate etiology has been established.

9.3.2 Expectedness of Event

The Study PI will be responsible for determining whether an adverse event is expected or unexpected. An adverse event will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information for the intervention.

9.3.3 Seriousness of Event

- The study PI will determine the seriousness of an adverse event. Per the FDA, an event is serious if it results in ANY of the following outcomes:Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/ incapacity
- A congenital anomaly/ birth defect

9.4 Reporting Procedures

9.4.1 Related SAEs & Safety Issues

The following will be reported to the IRB, the funding agency, and the DSMC within 10 calendar days of the PI becoming aware of the event:

- Any serious adverse event that in the investigator's opinion was unanticipated or unexpected, involved risk to participants or others, and was possibly related to the research procedures
- Any noncompliance with the IRB-approved protocol that increased risk or affected the participant's rights, safety, or welfare.

9.4.2 AEs & Anticipated Unrelated SAEs

AEs and anticipated or unrelated SAEs will be handled in a less urgent manner but will be reported to the DSMC, IRB, and funding agency. All individual AE and Safety reports will be maintained by the investigator and a summary (not individual reports) of all adverse events that have occurred within the last approval period that are associated with the study, whether related or non-related, will be submitted to the

IRB at the time of continuing review. These reports will also be submitted to the DSMC) during the yearly DSMC meetings and the funding agency in the final progress report.

Adverse events may include a participant's death as a result of a longtime illness (non-related), a breach in confidentiality, or any complaint of a participant unless the risk involved is serious (in which case, the event is reported as an unanticipated problem involving risk to participants or others or as a serious adverse event at the time of occurrence).

9.4.3 Unanticipated Problems

Incidents or events that meet the OHRP criteria for unanticipated problems will be recorded in an event report form. The following information will be included when reporting an adverse event, or any other incident, experience, or outcome as an unanticipated problem to the IRB:

- appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- a detailed description of the adverse event, incident, experience, or outcome;
- an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

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

- Unanticipated problems that are serious adverse events will be reported to the IRB and the funding agency within 10 calendar days of the investigator becoming aware of the event.
- Any other unanticipated problem will be reported to the IRB, the funding agency, and the DSMC in a less urgent manner during annual continuing review and DSMC meetings.

9.5 Halting Rules

While the comparison of treatment arms is novel, the actual therapy in each treatment arms is not. All procedures are standardized, and potential adverse events are well understood. The surgery is an outpatient procedure with very low risk. Nonetheless, a continuous monitoring rule for monitoring SAE has been developed for the DSMC to ensure the SAE rate does not exceed 10%[14].

10 STUDY OVERSIGHT

The study oversight committees will be active for the primary study/trial and dissolve at the end of the primary study. They will not be active for the exploratory sub-study.

10.1 Data and Safety Monitoring Committee (DSMC)

In addition to the study PI's responsibility for oversight, study oversight will be under the direction of a Data and Safety Monitoring Committee (DSMC) composed of members with expertise in orthopedic surgery, physical therapy, musculoskeletal research, and biostatistics as well a lay community member. The DSMC will operate under the rules of a charter that will be approved at the organizational meeting of the DSMC. The DSMC for this study is convened for the primary study (and not the exploratory sub-study).

The DSMC will meet annually, or more frequently at their discretion, to assess safety and efficacy data, study progress, and data integrity for the study. If safety concerns arise, more frequent meetings may be held. At the end of each meeting the DSMC will make a formal recommendation regarding the continuation of the study.

10.2 Scientific Advisory Board

A Scientific Advisory Board of international experts from various disciplines relevant to this trial will meet once per year along with investigators from all sites to review progress, potential trial challenges, discuss methodology issues, and ensure that the study's work reflects evolving clinical science.

10.3 Study Steering Committee

The Steering Committee will be comprised of the study principal investigator (who will serve as Chair), individual site principal investigators, and other members selected for their content expertise as advisors to the Steering Committee. The Steering Committee will meet approximately quarterly to closely monitor trial operations, ensure adequate study accrual, protocol compliance, timely data entry, ensure implementation of the recommendations of the DSMC, and general study integrity.

10.4 Stakeholder Advisory Board

A Stakeholder Advisory Board comprised of a diverse group of individuals with an interest in rotator cuff tears, including patients, their caregivers, and insurance and medical industry representatives, will advise in the development of study materials and the conduct of the study as it relates to study participants. The Stakeholder Advisory Board will meet approximately every other month to review the progress of the trial.

11 CLINICAL SITE MONITORING

Internal clinical site monitoring will be conducted to ensure that the rights of human subjects are protected, that the study is implemented in accordance with the protocol and/or other operating procedures, and that the quality and integrity of study data and data collection methods are maintained. Monitoring for this study will be performed by data manager and trial project manager under the supervision of the study PI who will review data and documentation regularly and visit sites as needed. A monitoring report generated from data within the study REDCap databases will be created and used to track and monitor data completion and study activities. These monitoring activities will be performed for the primary study.

11.1 Screening/Enrollment Monitoring Reports

The screening, enrollment and study data for each site will be reviewed regularly by the trial project manager and study PI to ensure that potentially eligible study participants are being screened, approached and consented as appropriate and study-related documents and images are submitted in accordance with the study protocol and Manual of Operating Procedures (MOOP). During the main study, study data analysts will prepare a monthly report of requested information drawn from study records in REDCap.

11.2 Site Monitoring Calls

All sites will participate in regular site calls with the trial project manager to provide study updates and review data from Screening, Enrollment & Data reports. Call participants, notes regarding what was discussed, and any actions to be taken will be recorded and reviewed periodically by the study PI. Issues of immediate concern will be brought to the attention of the study PI as they are identified.

11.3 Site Visits

If issues or questions of concern pertaining to site operations arise during the course of the study, the study PI &/or other authorized study personnel may visit the site in person to observe how site procedures are being implemented and determine appropriate remedies, if needed.

Sites may also be visited within the first year of recruitment to ensure everything is operating correctly and to address any operational questions or challenges, as deemed appropriate by the study PI.

12 STATISTICAL CONSIDERATIONS

12.1 Study Hypotheses

Aim 1: To compare pain and function in patients undergoing operative versus non-operative treatment of atraumatic rotator cuff tears at 12 months of follow-up.

Hypothesis 1: Patients undergoing operative treatment will have significantly greater improvement in pain reduction and function (measured by SPADI)[12] as compared with those treated non-operatively at 12 months of follow-up.

Aim 2: To assess effects of rotator cuff tear size and age on comparative outcomes (measured by SPADI) in operative versus non-operative treatments for atraumatic rotator cuff tears.

Hypothesis 2a: Surgery will be more effective than non-operative treatment in cuff tears of increasing size.
Hypothesis 2b: Surgery will be more effective than non-operative treatment of rotator cuff tears with decreasing age.

12.2 Final Analysis Plan

Overview: We are planning a trial where patients will be randomly assigned in equal proportion to operative or non-operative care.

Primary Endpoint: The primary outcome measure is SPADI, and the primary endpoint is the change in SPADI at 12 months relative to baseline. SPADI is measured on a scale of zero to 100, with lower scores for better outcomes. SPADI is a reliable and valid measure of shoulder function[15-20].

Secondary Endpoint(s): ASES-SF[13], cross-sectionally and longitudinally over time.

Analysis Population: We define the intent-to-treat (ITT) population as the group of patients randomized to a treatment arm regardless of any other consideration.

12.2.1 Primary Analysis

The primary analysis will be conducted on the intent-to-treat (ITT) population as defined above. The distribution of 12-month change in SPADI, stratified by treatment arm, will be summarized graphically with histograms, boxplots, and plots of CDFs as appropriate. Our primary analysis for testing the 3 specific hypothesis in section 12.1 will be conducted in the context of a mixed model. That model is,

$$y_{ij} = \beta_0 + \beta_1 I_{\{TRT_i=Op\}} + \beta_2 t_{ij} + \beta_3 I_{\{TRT_i=Op\}} t_{ij} + \beta_4(tearsize_i) + \beta_5(age_i) + \beta_6(I_{\{TRT_i=Op\}} * tearsize_i) + \beta_7(I_{\{TRT_i=Op\}} * age_i) + u_i + e_{ij}$$

where y_{ij} represents the change in SPADI from baseline for participant $i = 1, \dots, n$ at time j= 3, 6, 12 months who was assigned to management arm TRT_i ($I_{\{TRT_i=Op\}} = 1$ if participant i is on the Operative arm and 0 otherwise) . β_0 is the intercept, β_3 is differential change in SPADI score over time due to treatment (i.e., the treatment effect over time; assumed linear here but it will be modeled flexibly as needed), β_4 and β_5 are the effects of tear size and age at the beginning of treatment, and β_6 and β_7 are the tear size and age interactions with treatment that potentially will help identify those patients most likely benefit from therapy. The first 8 terms represent fixed effects. The last 2 terms represent a patient specific random intercept to model the effects of study site and residual error, respectively. The estimate of interest from this longitudinal model is the predicted differential in 12-month SPADI change ($\Delta\Delta SPADI_{12}$; 1st Δ is for treatment change, 2nd Δ is for 12-month change), which is typically estimated as a contrast or difference in predicted 12-month SPADI change.

A directly parallel analysis will also be conducted, where y_{ij} represents SPADI for participant $i = 1, \dots, n$ at time j= 3, 6, 12 months with baseline SPADI as a covariate. In the first model, analyses might lead to a statement such as “Pain and function improved over 12 months in the operative (non-operative) care group 11 points more on average compared to patients treated with non-operative (operative) therapy. In the second model, analyses may lead to a statement such as, “At 12 months, mean SPADI scores were 11 points lower in the non-operative (or operative) group.”

A restricted cubic spline may be fit for continuous covariates to allow for nonlinearity. Further, we will examine different parameterizations of “time” to appropriately capture longitudinal trends (e.g., we might use a time-squared term or let time be categorical). To account for site-to-site variation, the model will include either a fixed effect or random effect for sites (not shown here). The choice between a fixed and

random effect often generates debate[21]. While our general preference is to use a random effect, and that is our stated plan here, we realize that with multiple sites the resulting random effect estimates could be unstable due to imbalance in the number of recruitments, especially if there are pronounced aggregate covariate dissimilarities across sites. In such a case, we will use a fixed effect for site. For completeness, we will report the unadjusted estimates for $\Delta\Delta$SPADI$_{12}$ that results when Z_i is removed from the model. Note that in a randomized study the purpose of covariate adjustment in a regression model is to obtain unbiased estimates of effects accounting for the enormous variation typical of longitudinal studies.

Heterogeneity of Treatment Effects Analysis:

This analysis, part of the mixed model longitudinal data detailed above, will assess the interaction of age (years at randomization) and tear size (cm) with treatment on ΔSPADI$_{12}$. The covariate set for the adjusted mixed models is defined in section 12.2.1. Table 1 depicts an example of a binary covariate interaction with treatment with a contrast effect size at the MCID = 10 – 15 – 30 + 50=15. The standard general contrast variance assuming common variance among groups and equal cell size $= \sigma^2[\sum_{i=1}^{k}(\frac{C_i^2}{n_i})$. These elements form the basis for the interaction sample sizes in figure 4.

Table 1. Example Table of Average 12-Month Change in SPADI from Baseline where the Interaction Effect is the MCID

Treatment	Group 1	Group 2
Non-operative	10	15
Operative	30	50

12.2.2 Secondary Analyses

Secondary analyses will be based a more general model denoted,

$$y_{ij} = \beta_0 + \beta_1 I_{\{TRT_i=Op\}} + \beta_2 t_{ij} + \beta_3 I_{\{TRT_i=Op\}} t_{ij} + \gamma Z_i + u_i + e_{ij}$$

where y_{ij} represents the change in ASES-SF (or any other outcome metric) from baseline for participant $i = 1, \ldots, n$ at time j= 3, 6, 12 months who was assigned to management arm TRT_i ($I_{\{TRT_i=Op\}} = 1$ if participant i is on the Operative arm and 0 otherwise) and who has a k-dimensional vector of covariates Z_i (e.g., gender, mental health inventory, fatty infiltration, etc.) with effect parameters γ_k. β_0 is the intercept, and β_3 is differential change in ASES score over time due to treatment (i.e., the treatment effect over time; assumed linear here but it will be modeled

flexibly as needed). As in section 12.2.1, the last 2 terms represent a patient specific random intercept and residual error, respectively. The estimate of interest from this longitudinal model is the predicted differential in 12-month ASES-SF change ($\Delta\Delta$ASES-SF$_{12}$; 1st Δ is for treatment change, 2nd Δ is for 12-month change), which is typically estimated as a contrast or difference in predicted 12 month ASES-SF change.

Similar to the setting described in section 12.2.2 directly parallel analyses will also be conducted, where y_{ij} represents ASES-SF (or other secondary outcomes) for participant $i = 1, \ldots, n$ at time j= 3, 6, 12 months with baseline ASES-SF as a covariate. Differential inference between these two sets of models was described above.

12.3 Sample Size Considerations

12.3.1 Primary Aim

A longitudinal mixed model will be used to compare the 12-month change in SPADI between treatment arms. The operating characteristics of this plan depend on the marginal distribution of ΔSPADI$_{12}$, the assumed true distributional shift, and observed covariate patterns. Figure 3 displays the marginal distribution of ΔSPADI$_{12}$ for patients by treatment group. These distributions were derived from preliminary data taken from an ongoing prospective, non- randomized cohort of patient with degenerative rotator cuff tears receiving either non-operative or operative intervention. The mean ΔSPADI$_{12}$ was -16.7 (SD=24.2; n=72) overall. Current estimates for non-operative therapy are -12.3 (SD=21.55; n=45) and -40.6 (SD=19.14; n=27).

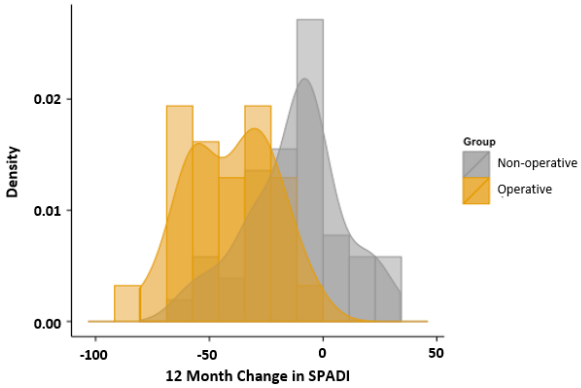


Figure 3. Distributions of 12-month change in SPADI by treatment group.

12.3.2 Effect Size and Alternative Hypotheses

We provide sample size estimates for MCID effect sizes of 10 to 25 by intervals of 5. MCID for SPADI and ASES is between 8 and 26.9. Thus, using an effect size estimate of 10 is a very conservative approach. A MCID of 15-20 is also on the conservative spectrum. In

Aim 1 we test the null hypothesis that ΔSPADI12 for patients treated operatively versus non-operatively is equal. As shown below, a sample size of 180 provides outstanding power to detect a 10-unit difference between treatment arms in 12-month SPADI change from baseline. For Aim 2, our projected maximum sample size of 180 patients provides 80% power to detect an interaction of 20 SPADI units.

12.3.3 Sample Size Projections

A sample size of 180 participants (90 per treatment group) provides excellent power (a two-sided Type I Error of 0.05 was used). Figure 4 illustrates the power for four different tests of ΔΔSPADI12. In both panels the cyan, black, blue and red lines show the power for a simple t-test of 12-month SPADI change scores between treatment groups for effect sizes between groups of 10 (aim 1), 15-20 (aim 2), and 25 SPADI units. These curves are based on the estimated standard deviation from the preliminary data: (black) t-test on available data, (red) mixed model on complete case data, (blue) multiply imputed mixed model. The upper panel denotes power settings for the main effect comparison of non-operative versus operative care. The lower panel to detect the same minimally clinically meaningful changes in binary subgroups across treatment groups (e.g., age by treatment interactions).

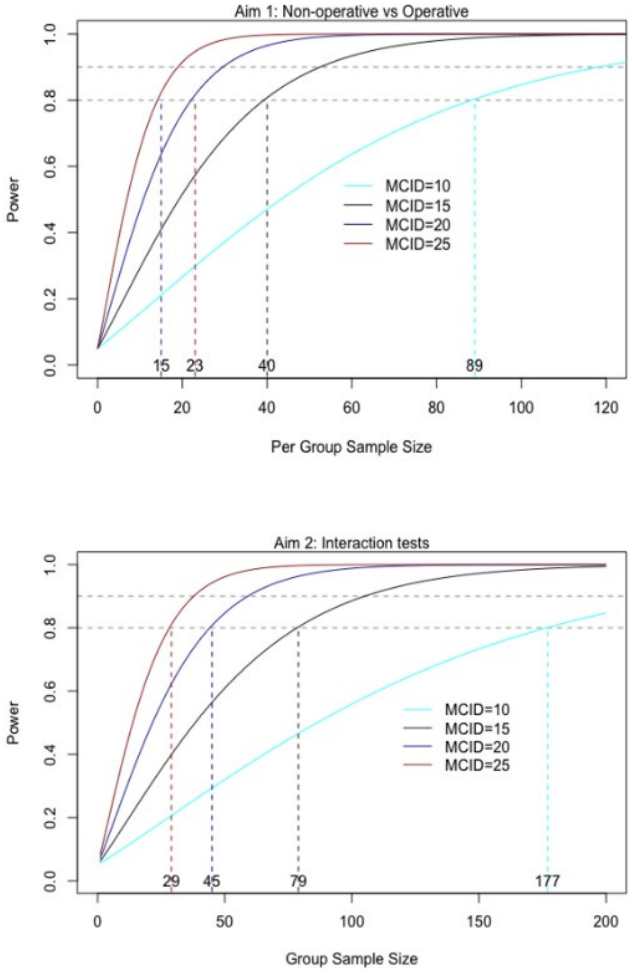


Figure 4. Power curves. Upper panel for Aim 1 primary treatment comparison. Lower panel for Aim 2 interactions.

Power for aim 1 to detect an MCID of 10 or larger is 80% at 89 patients per group (178 total) and 90% for an MCID of 15 at 54 patients per group (108 total). For the subgroup/patient heterogeneity analyses, 80% power to detect a 2-way interaction as small as the MCID=20 is achieved with 45 patients per group (total n=180). We will also attempt to recruit additional patients beyond the target of

180 in our allocated recruitment period to account for loss to follow-up and crossovers.

These projections are conservative. Firstly, a mixed model modelling significant covariates sequesters variance from the residual variance, thus increasing power for fixed effects tests. Further, analyses of our preliminary data revealed an intraclass correlation coefficient (ICC) for institution was 0.04 (essentially zero) and largely inconsequential given the longitudinal correlation in SPADI measurements. If necessary, our approach permits the sequestering of site-to-site variability from residual error, increasing power for detecting fixed effects in the data. The summation of Anderson-Darling scores over pre and post SPADI normality of SPADI in our historical data suggest improvement in normality is achieved using the natural log transformation. A similar approach will used to assess the best transformation of the data a priori to analyses

12.3.4 Safety Review

A continuous monitoring rule for monitoring SAE has been developed for the DSMC to ensure the SAE rate does not exceed 10%.

12.3.5 Efficacy Review

There is no planned interim analysis of study efficacy outcomes, as all interventions are standard of care.

12.4 Sensitivity Analyses

Sensitivity Analyses: We will not rely only on Gaussian parametric modeling, as our primary mixed effects model will be cross-checked using a proportional odds regression comparing treatment effects after adjusting for baseline SPADI, study site, age, tear size, fatty infiltration, and their interactions[28-30]. We will conduct full information analysis and no levels will be combined. Thus, for k unique SPADI change scores, there will be k-1 levels. In model development, descriptive statistics and graphical displays of outcomes and predictor variables will be examined. Under this category we also note our plans the sequential modeling under MCAR, MAR, and MNAR missing data analyses described below. We will also perform a sensitivity analysis of the time from baseline to a 10/15 point (MCID) change in SPADI using Cox regression, and the binary outcome of achieving a 10-25 point change in SPADI (success) versus failure using logistic regression. We will repeat sensitivity analyses for secondary outcomes.

12.5 Exploratory Sub-Study

The analysis for the exploratory sub-study will be performed similar to that for Aims 1 and 2 for the main study with additional time points.

13 SOURCE DOCUMENTS & ACCESS TO SOURCE DATA/DOCUMENTS

Study staff will maintain appropriate medical and research records for this study, in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of subjects. Study staff will permit authorized representatives of the funder and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity.

13.1 Source Documents

This study will utilize the following source documents:

- Patient medical records, including clinic notes & surgery notes
- X-ray/MRI images
- Case Report Forms (paper &/or electronic)
    - Clinic Screening Form (CRF-00, see Appendix), for patients recruited for the study
    - Patient Study Info Overview Form (CRF-01, see Appendix)
    - Physical Exam Form, Part A & B (CRF-02, see Appendix)
    - Patient Questionnaires:
        - Baseline Questionnaire (CRF-03.1, see Appendix)
        - 3/6 Month Follow-Up Questionnaire (CRF-03.2, see Appendix)
        - 12 Month Follow-Up Questionnaire (CRF-03.3, see Appendix)
        - Annual Follow-Up Questionnaires for exploratory sub-study (CRF-03.4, see Appendix)
    - Physical Therapy Diary (CRF-04, see Appendix), or MyCap App Physical Therapy Diary (if data reported electronically)
    - Surgery Report Form (CRF-05, see Appendix)
    - Physical Therapist Report Form (CRF-06, see Appendix)
        - Prospective PT Report Form (CRF-06.1)

- Crossover PT Report Form (CRF-06.2)

- MRI Review Form (CRF-07, see Appendix)

CRFs will be considered source documents when they document direct reports by the subject and/or direct observations by clinicians or study personnel. The exception to this is the Clinic Screening Forms for ineligible patients or eligible patients who decline to participate. These forms will be used as worksheets only and, once the information about why the patient was not eligible or declined has been entered into the Screening Log, will not be retained.

13.2 Maintenance of and Access to Source Documents

Individual sites will have access to the medical records and CRFs (paper or electronic versions) for the subjects recruited from their site. Only designated study personnel or personnel authorized to perform follow-up and monitoring will have electronic access to CRFs for all subjects. Data Access Groups (DAGs) will be created in REDCap to control access to subject data and electronic source documents collected there.

13.2.1 Clinical Screening Forms

- A Clinic Screening Form (CRF-00, see Appendix) will be initiated for potentially eligible patients whose available medical records do not indicate the presence of exclusionary factors. Forms and the screening log may include basic appointment and demographic info (including zip code) but no personally identifiable information (such as name, DOB, etc.).

- The form will be given to the physician prior to or during the clinical exam for use in evaluating the subject's eligibility for the study. Clinic Screening Forms may be completed on paper or electronically.

- For subjects determined to be ineligible or who decline to participate, information from the Clinic Screening Form will be entered into the screening database, including the reason for ineligibility &/or non-enrollment. These paper documents will not be retained.

- For subjects whose MRI results are pending, a partially completed clinic screening form may be kept in a locked file until final eligibility can be determined.

- For subjects who are eligible for the trial and consent to participate, information from the clinic screening form confirming their eligibility will be

entered into the subject database prior to randomization and, if completed on paper, a copy of the form scanned and uploaded to REDCap. Hard copies of paper forms will be retained locally on site in the subject's file in a locked cabinet.

13.2.2 Consent Forms

- A copy of the signed consent form will be provided to the subject, either in clinic or by mail or email, as appropriate.
- If consent was obtained on paper, the original hard copy of the signed consent form will be kept on file at the recruiting site in a locked cabinet (accessible only to the authorized site study personnel)
- A scanned copy of the original signed paper consent form (certified as a true and complete reproduction of the original by site personnel) will be uploaded into the subject's record in REDCap (accessible only to the authorized recruiting site and coordinating center study personnel)
- If consent was obtained via e-Consent, the electronic version completed and signed in REDCap or other approved e-Consent platform shall be considered the original source document. A copy of the completed e-consent form will be provided to the subject.

13.2.3 Paper Case Report Forms

- This includes case report forms originally completed on paper (with the exception of Clinic Screening Forms for ineligible or declining patients).
- The original hard copy will be kept on file in a locked cabinet at the site where it was originally completed/collected (accessible only to authorized local site study personnel)
- A scanned copy (certified as a true and complete reproduction of the original by site personnel) will be uploaded into the subject's record in REDCap (accessible only to authorized recruiting site and coordinating center study personnel)

13.2.4 Electronic Case Report Forms

- This includes any case report forms completed via electronic survey or entered directly into MyCap or REDCap by subjects, clinicians, or study personnel.

- Electronic data originally captured via direct data entry by the reporting source will be stored in the subject's REDCap record.

- If necessary, for data review,/ verification or regulatory purposes, a copy of the corresponding electronic form's data may be downloaded and printed or saved to a secure server (accessible only to authorized study personnel). Any printed copies will be stored in the subject's file in a locked cabinet. Downloaded or printed forms may be deleted or properly destroyed if no longer needed for review or verification purposes.

13.2.5 MRI / X-Ray Images

- This includes images available directly within the electronic medical record or electronic copies of these images.

- Copies of the enrolled subject's MRI/X-Ray images used for the purpose of determining/verifying eligibility at recruiting sites will be burned to CD disc, marked with their study ID and mailed via FedEx or other tracked mail service to the coordinating center. Discs received will be secured in a locked cabinet.

- The images will be reviewed by the study radiologist in completing and documenting the MRI review.

- In some cases, patients may receive a follow-up MRI or other shoulder imaging either as part of their standard clinical care or as part of the exploratory sub-study. In both cases, these MRIs and imaging studies may be collected, if possible, and the same procedures as above will be completed.

14 QUALITY CONTROL AND QUALITY ASSURANCE

14.1 Electronic Data Capture (REDCap)

Study data will be collected and managed using REDCap[31] electronic data capture tools[32]. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The system uses a meta-data approach to build the user interface in an automated fashion. Thus, the study team defines the data elements as would occur for any typical trial. The data dictionary is then submitted to the system in a standardized format, and a web-based case report form is created in a fraction of the time and cost of traditional electronic systems.

14.2 Data Security

Components of the REDCap software have 21CFR11 compliance. REDCap servers are housed in a local data center, and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is the preferred medium by Vanderbilt's Privacy Office and Institutional Review Board.

14.3 Data Entry

The Data Coordinating Center(s) and authorized study personnel will use REDCap for data collection/entry, data validation, audit trails, export procedures, and downloading to statistical packages. Data will download into R or SAS (or other appropriate statistical software) for data cleaning and data quality checks. An initial check of data completeness is done via REDCap's logic and range checking that occurs at data entry and is customizable. Before the data is entered into the database, the user is prompted to revise data if the initial check finds problems with the data, certain fields are skipped, values are missing or out of range, etc.

14.4 Staff Training and Tracking

The best approach to ensuring good quality data is to provide training and support to those individuals who collect and enter data. The Data Coordinating Center will work closely with the RAs at each site to ensure they understand and can perform their duties

to the best of their abilities. A “kick-off” meeting is planned prior to start of enrollment at the coordinating center. We will go over basic study procedures as they relate to the physicians, physical therapists, and the RAs, respectively.

Additionally, detailed, written step-by-step instructions/SOPs will be provided for tasks to be performed by site personnel, and live training sessions via teleconference will be scheduled for recruiting physicians, site Lead Physical Therapists, and site RAs prior to the start of enrollment at each site. Training sessions will be recorded where feasible so they can be used to train other personnel who are subsequently added to the study. Training and reference materials will be updated periodically as needed.

Regular site calls will be led by the trial project manager to discuss recruitment and any data/study protocol related issues. RAs and study staff will complete required training in the protection of human subjects and Good Clinical Practice (GCP) requirements.

Separate administrative databases in REDCap may be utilized to track the training of personnel from all sites on the study protocol, operating procedures, study amendments, as well as to document completion of required human subjects protection and Good Clinical Practice (GCP) training.

14.5 Standard Operating Procedures (SOPs)

Standard Operating Procedures (SOPs) will be developed and included in the Manual of Operating Procedures (MOOP) detailing how data should be entered and will be evaluated for accuracy in relation to source documents.

14.6 Data Review

Authorized study personnel will review data as soon as possible after entry and note any incomplete, ambiguous, or conflicting items. The study participant, clinician or study personnel who submitted the data will be contacted to provide or clarify important data that is missing or in question. Surveys completed electronically &/or direct data entry performed by the subject, clinician, or study personnel will be reviewed for completeness and consistency by authorized study staff, and any items requiring attention will be similarly resolved. Once the data review is complete, the record will be locked by coordinating center personnel to prevent further changes.

Reports both within REDCap and created using statistical software will be utilized to identify and monitor missing/inconsistent data in need of attention and/or correction.

14.7 Data Validation and Query Management

Data validation and query management procedures will identify suspicious data through the application of validation rules, generate requests for data review by study sites, and monitor the resolution of these requests. This entails performing more complex checks on the data than done at data entry (e.g., cross-form data validation and querying). Data that fail validations will be flagged with a status of “suspicious,” reviewed by authorized study personnel and clarified by consulting the appropriate source documents.

14.8 Quality Review and Data Auditing

To ensure consistency in data entry, most forms completed on paper will be entered in the primary database by authorized central study personnel.
If there are substantial or repeated data quality issues, this may be cause for suspending site enrollment until the current data is thoroughly cleaned and validated. Decisions on suspension of site enrollment will be made by the study PI. The study PI and Study Principal Statistician will be responsible for oversight and addressing quality assurance issues (correcting procedures that are not in compliance with protocol) and quality control issues (correcting errors in the data entry).

15 ETHICS/PROTECTION OF HUMAN SUBJECTS

15.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

15.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all subject 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 subject is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

Review and approval of the protocol and supporting materials for this multi-site primary study will be conducted by a single, central IRB. The relying IRBs of participating sites will ensure compliance with local laws, institutional policies, and federal regulations at their respective sites.

15.3 Informed Consent Process

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to subjects and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the subject. Consent forms will be IRB-approved, and the subject is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the subject and answer any questions that may arise. The subject will sign the informed consent document prior to any study-related assessments or procedures. Subjects will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to subjects for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline

to participate in this study. The consent process will be documented in the research record.

Each participating institution will be provided with a consent form template. Each institution may revise or add information to designated sections of the consent template to comply with institutional consent and privacy policies &/or local laws but may not remove procedural or risk content from the model consent form.

15.4 Exclusion of Women, Minorities, and Children (Special Populations)

Individuals of any gender or racial/ethnic group within the specified age range may participate in this study. Pregnant women are excluded from this study and women of child-bearing age may be excluded from the research MRI, due to pregnancy being a contraindication to MRI. Non-English speakers are also excluded from this study, as the standardized questionnaires by which primary and secondary outcomes will be measured are only validated in English.

15.5 Subject Confidentiality

Subject confidentiality is strictly held in trust by the investigators, study personnel, and the funder(s) and their agents. This confidentiality is extended to cover medical imaging and tests in addition to any study information relating to subjects.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the research study, or the data will be released to any unauthorized third party.

The study monitor, auditor(s), authorized representatives of the IRB, the funder/sponsor or regulatory agencies may inspect all study documents and records required to be maintained by the investigators, including, but not limited to, medical records (office, clinic, or hospital) for the study subjects. The clinical study sites will permit access to such records.

15.6 Subject Injury

There are no plans to compensate patients who are injured as a result of study participation. Medical care will be provided at/by the recruiting institution in accordance with local institutional policies as specified in the site-specific consent form.

There are no plans for the study funder(s)/sponsor(s) to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for the study funder(s)/sponsor(s) to give subjects money for an injury.

15.7 Communication of Protocol Changes

Important protocol modifications, including procedural updates and document revisions will be communicated to relevant parties (e.g., investigators, study personnel, IRBs, trial participants, trial registries, etc.). Any means specified below, or in combination, may be utilized for this purpose.

- IRB Exchange (IREx) – Site IRBs will be notified of IRB amendments, continuing review, and other IRB-related submission via the IREx online platform that supports the single IRB.
- Numbered Memos & BOX (or similar electronic file storage platform) – Approval of IRB amendments; changes to case report forms (CRFs), recruitment, and other study materials, as well as updates to internal study documents (e.g., roster, SOPs, personnel FAQs, etc.) will be communicated formally via Numbered Memos, and documents needed by sites disseminated via BOX (an online document repository) or other appropriate platform/application
- Clinicaltrials.gov – Changes or updates to the study will be updated on the ClinicalTrials.gov trial registry as appropriate by the trial project manager and approved by the study PI.
- Website/Letter –Website and/or direct communication such as letters or newsletters may be used to update enrolled patients about study changes.

15.8 Conflict of Interest

Conflicts of interest are reported by the DSMC on an annual basis and study investigators will report conflicts of interest as per their institutional policies and/or journal requirements. It is the responsibility of the individual investigators/DSMC members to reveal and update their conflicts of interest.

16 DATA HANDLING AND RECORD KEEPING

The investigators are 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. Any corrections to paper or electronic CRFs should be documented in accordance with specified guidelines and explanatory notes added as appropriate. The investigators will maintain adequate case histories of study subjects, including accurate case report forms (CRFs), and source documentation.

16.1 Data Management Responsibilities

Data collection and accurate documentation are the responsibility of the study personnel under the supervision of the investigator. Scanned copies of all original documents and paper CRFs will be uploaded directly into REDCap and original paper documents and forms stored securely on site at the location they were completed or received. Unanticipated problems and adverse events must be reviewed by the investigator or designee.

16.1.1 Recruiting Sites

Recruiting site personnel are responsible for:

- documenting screening of potentially eligible subjects
- documenting subject eligibility and consent
- administering baseline questionnaires and physical examinations for consented subjects, and assisting with follow-ups if requested by the coordinating center
- entering basic required data into REDCap (Patient Info Overview, Eligibility, etc.) for consented subjects
- randomizing subjects to treatment via REDCap
- sending subjects' MRI/x-ray imaging to the coordinating center
- ensuring completion and submission of surgery reports for subjects randomized to operative treatment, and

- reporting AEs, SAEs, and unanticipated problems to the coordinating center upon becoming aware of them

16.1.2 Coordinating Centers

Coordinating center personnel are responsible for:

- ensuring that copies of original paper documents and CRFs are uploaded to REDCap by recruiting sites
- performing data entry of most CRFs
- collecting subjects' MRI / x-ray imaging and coordinating MRI review by study radiologist
- administering all subject follow-up questionnaires
- collecting subject physical therapy diaries
- sending & collecting physical therapist reports
- ensuring appropriate recording, reporting, and action for AEs, SAEs, and unanticipated problems

16.2 Data Capture Methods

The study will utilize both paper and electronic data capture methods, as subjects will have the option to complete questionnaires and diaries either on paper or online. All research data will be centrally collected and stored in a REDCap electronic data capture system. Some of the data will be entered directly into the system by the subject or reporting clinician or study personnel via electronic means (tablet, computer, or smartphone), while other data will be manually entered by study staff from paper CRFs. Access to the REDCap system is password protected and data access groups (DAGs) will be utilized to limit access as appropriate by site and/or role.

Collection of screening, enrollment, and baseline data will be distributed across recruiting sites with limited data entry required locally. Most data entry will be performed centrally at the coordinating center(s) to ensure consistency of data entry. Collection of subject follow up data via questionnaires and physical therapy diaries, as well as of data from physical therapist reports and imaging reviews, will be performed centrally by the coordinating center(s). These functional may be performed when designated to do so.

Collection and processing of enrollment, baseline, and follow up data will be ongoing throughout the course of the study, relative to subject randomization dates and corresponding follow up time points. Collection of treatment information (surgery and physical therapy reports) will occur at designated time points, relative to subject randomization and date of surgery. Collection and processing of MRI / x-ray review data will be batched, occurring on an ongoing basis during subject enrollment and follow-up.

16.3 Types of Data

The types of data to be collected include: screening information (age, demographic data, eligibility, reasons for declining to participate etc.); MRI/x-ray imaging; questionnaire responses from subjects; physical exam measurements; laboratory reports (re: surgery & physical therapy) from treating clinicians and reviewing radiologist; as well as safety data.

16.4 Schedule and Content of Reports

16.4.1 Monthly Screening, Enrollment and Data Report (approximately every month)

Study data analysts will prepare a report approximately each month detailing the screening, enrollment, crossover and dropout rates for all sites as well as information on quality control items such as missing and suspicious data. Data from this report will be reviewed with sites during regular site calls and by the Steering Committee during scheduled calls as needed, so that issues of concern can be identified and addressed in a timely manner.

16.4.2 Interim Progress Reports to PCORI (approximately every 6 months)

Approximately, every 6 months, an Interim Progress Report will be submitted to PCORI providing updates on milestones, key personnel, financial status, accomplishments & challenges, and publications. Any schedule changes to the frequency of this report will be made as per the requirements of the funding agency.

16.4.3 Data Monitoring Reports to DSMC (approximately every 6-12 months)

Prior to each meeting of the DSMC, study data analysts will prepare a Data Monitoring Report focused on the conduct of the study, including pooled enrollment and dropout rates, timeliness (compliance) of data submission, eligibility rates, reason(s) for ineligibility, baseline data, landmark frequency data, and AEs/SAEs.

Any schedule changes to the frequency of this report will be made as per the requirements of the DSMC.

16.4.4 Final Progress Report to PCORI (at conclusion of study)

At the conclusion of the study, a Final Progress Report will be submitted to PCORI which contains the following:

- overview of study findings and impact,
- milestones update,
- recruitment, enrollment, and retention update,
- accomplishments and challenges,
- engagement report,
- financial status update,
- key personnel effort update,
- publications update,
- data sharing,
- future directions,
- progress statement for public use

Changes to the content of this final report may be made depending on the funding agency's requirements.

16.5 Study Records Retention

Study records (paper and electronic) will be maintained for at least three years from the completion of the study and the PCORI contract term date.

16.6 Protocol Deviations and Violations

Broadly speaking, a protocol deviation is any noncompliance with the clinical study protocol and may be on the part of the subject, the investigator, or study staff. As a result of deviations, corrective actions may be developed by the study staff as appropriate and implemented promptly.

All deviations from the protocol must be addressed, as appropriate, in study subject source documents, documented in the study record, and reported to the IRB and funding agency, according to their requirements.

16.6.1 Protocol Deviations

A protocol deviation is an incident involving noncompliance with the protocol, but one that typically does not have a significant effect on the subject's rights, safety, welfare, and/or the integrity of the resultant data. Deviations may result from the action of the participant, investigator, or staff. (VUMC IRB Handbook, 2016)

Examples of protocol deviations may include (not an exhaustive list):

- Signed copy of consent form not given to subject during informed consent process
- Subject does not begin treatment within 2 months following randomization
- Subject does not have assigned treatment/ crosses over within 6 months after randomization
- Subject does not pursue either treatment (surgery or physical therapy) within 12 months after randomization
- Follow-up questionnaire not sent to subject for designated time point

16.6.2 Protocol Violations

A protocol violation is an accidental or unintentional change to the IRB-approved protocol procedures without prior sponsor and IRB approval. Violations, as opposed to simply deviations, generally affect the subject's rights, safety, welfare, and/or the integrity of the resultant data. (VUMC IRB Handbook, 2016)

Examples of protocol violations may include (not an exhaustive list):

- Informed consent obtained after the initiation of study procedures
- Failure to obtain informed consent
- Failure to report a Serious Adverse Event

17 PUBLICATION / DATA SHARING POLICY

17.1 Trial Registry

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ARC trial will be registered with ClinicalTrials.gov prior to enrollment of the first participant. World Health Trial Registry Data Set information will be recorded and maintained in ClinicalTrials.gov.

17.2 Dissemination of Study Results

This study will comply with the *NIH Public Access Policy*, which ensures that the public has access to the published results. 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. PCORI has similar requirements and the preparation of this trial was funded by NIH.

Results will be disseminated through publications, ClinicalTrials.gov, PCORI summary (in layman's terms), and via the study website (*www.shoulderstudy.org/arc-trial/*).

17.3 Publication Guidelines

Criteria for authorship on publications resulting from this trial are described below. An executive committee chaired by the PI (Nitin Jain, MD) will be responsible for developing publication procedures and resolving authorship issues.

The ARC trial will have its primary publication on the effectiveness of surgery versus physical therapy for atraumatic rotator cuff tears. For this/these publications, the participating physicians should have randomized at least 15 patients for the trial to be considered for co-authorship. This requirement may be waived at the discretion of the PI. They would also need to satisfy other criteria set forth by ICJME and each of the journals for authorship. Given the large number of physicians participating in the trial, these names may be consolidated as "The ARC Trial Team." The final decision for granting authorship would be based on relative contributions of team members and will be determined by the study PI (Nitin Jain, MD). Participation in the study conduct as a team member does not guarantee authorship. Authorship on the primary publication also does not guarantee authorship on secondary or subsequent publications. Authorship will be based on the need for expertise and contribution of team members for individual publications, as determined by the PI.

17.4 Final Data Set

Study staff designated by the PI will have access to the final trial dataset.

17.5 Data Sharing

The PI supports sharing of research resources to promote advances towards optimizing outcomes in patients with rotator cuff tears. De-identified datasets will be shared with scientists interested in the topic after approval from the IRB and the PI is obtained. Requests for data must be submitted in writing and must clearly state the intended use and the length of time for data analysis. Each request will be reviewed and will need to be approved by the PI. The PI reserves the right to deny data requests.

17.5.1 IPD Data Sharing

Individual participant data (IPD) and related data dictionaries may be made available to other researchers (at the end of the study). The type(s) of supporting information that may be shared, in addition to the IPD and data dictionaries for the IPD itself are: Study Protocol, Statistical Analysis Plan (SAP), and Informed Consent Form (ICF). Requests for IPD and additional information must be submitted and will be reviewed as outlined above by the PI. The PI reserves the right to deny IPD requests.

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SUPPLEMENTAL MATERIALS

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 IRB amendments.

- Study/Site Roster
- Manual of Operating Procedures (MOOP)
- Standard Operating Procedures (SOP) for Recruiters
- Standard Operating Procedures (SOP) for Site Lead PTs
- Instructions / PT Report Form Completion Guide for Treating Physical Therapists
- Surgical Protocol
- Post-operative Rehabilitation Protocol
- Non-operative Rehabilitation Protocol
- Physical Therapist Cheatsheet
- MRI Protocol
- Dynamometry Protocol
- ARC Study Physician FAQs
- ARC Study Physical Therapist FAQs
- ARC Study Personnel FAQs
- Data and Safety Monitoring Committee (DSMC) Charter

APPENDICES

These documents are officially affiliated with the protocol and will be submitted to the IRB as a part of the protocol. As such, changes to these items require an IRB amendment.

Appendix A:	Schedule of Events
Appendix B:	Inclusion/Exclusion Criteria Reference Card (for MDs, Coordinators/RAs)
Appendix C:	Promotional Materials: • Patient Brochure (trifold) • Clinic Patient Poster • Clinic Staff Poster • Clinical Trials Notification Email
Appendix D:	Recruitment Scripts & Materials: • Pre-Visit Call Sample Script • Pre-Visit Cover Letter • MD Study Intro Script (for discussing trial with patients) • RA Script - Recruitment & Consent • RA Script – Remote Recruitment & Enrollment • Recruitment Video Slides & Script • Consent Video Slides & Script • Follow-up Sample Script for Patient Who Need More Time to Decide • Follow-Up Call Script for Site PI/ Recruiting MD
Appendix E:	Patient Information & Materials: • ARC Study Patient Fact Sheet Template (for subjects) • FAQs for Study Participants • Patient Physical Therapy Brochure • MyCap App Instructions (for subjects) • Study folder (for subjects) • Study Pen • Study Magnet • Study Mug • Patient Thank You Card
Appendix F:	Consent Documents: • Consent Form Template • Info Release Form (to go to treating Physical Therapist)

Appendix G:	Case Report Forms: • Clinic Screening Form (CRF-00) • Patient Study Info Overview (CRF-01) • Physical Exam Form – Part A & B (CRF-02) • Baseline Questionnaire (CRF-03.1) • 3-/6-Month Follow Up Questionnaire (CRF-03.2) – Left & Right versions • 12-Month Follow Up Questionnaire (CRF-03.3) – Left & Right versions • Annual Follow Up Questionnaire, years 2-10 for sub-study (CRF-03.4) – Left & Right versions • Physical Therapy Diary (CRF-04) • Surgery Report Form (CRF-05) • Physical Therapist Report Form – Prospective (CRF-06.1) • Physical Therapist Report Form – Crossover (CRF-06.2) • MRI Review Form (CRF-07)
Appendix H:	Correspondence: • PT Study Intro Letters (for inside PT packet) • Patient Welcome Letter • Questionnaire Cover Letters • Termination Letter • Study Completion Letter
Appendix I	List of current study sites, personnel and other clinical investigators

APPENDIX A: SCHEDULE OF EVENTS

	Main Study				Exploratory Sub-Study									
Procedures	**Baseline**	**3 Month Follow Up**	**6 Month Follow Up**	**12 Month Follow Up**	**2 Year Follow Up**	**3 Year Follow Up**	**4 Year Follow Up**	**5 Year Follow Up**	**6 Year Follow Up**	**7 Year Follow Up**	**8 Year Follow Up**	**9 Year Follow Up**	**10 Year Follow Up**	**Follow Up Visit (2-10 years)**
Physical Exam (ROM & strength)	X													X*
PT Diary		X	X	X*										
Questionnaires	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Research MRI														X*

* If applicable