DEFENSE HEALTH AGENCY
MADIGAN ARMY MEDICAL CENTER
9040 JACKSON AVENUE
TACOMA, WASHINGTON 98431-1100

MCHJ-MOE-C 10 February 2023

MEMORANDUM FOR LTC Jeremy Schroeder, Principal Investigator at Madigan Army Medical Center

SUBJECT: Madigan Army Medical Center Institutional Review Board Expedited Review and Approval of Research Protocol Modification for "Investigation of the Effectiveness of Shockwave Therapy, Photobiomodulation, and Physical Therapy in the Management of Non-insertional Achilles Tendinopathy" Protocol #223011

1. The subject protocol has been reviewed for compliance with applicable human subject protection regulations by the Madigan Institutional Review Board (IRB).

2. The following documents were reviewed by the IRB Chair:

Submission Components			
Form Name		Version	Outcome
EIRB Modification Form		Version 1.0	Acknowledged
EIRB Protocol Template		Version 1.4	Approved
Study Document			
Title	Version #	Version Date	Outcome
Metzger_Elizabeth_CITI_OUSD_GCP FDA_Report_2026 01 26	Version 1.0	null	Acknowledged
COI - Cin	Version 1.0	null	Acknowledged
COI - McKee	Version 1.0	null	Acknowledged
COI - Stormer	Version 1.0	null	Acknowledged
COI - Hager	Version 1.0	null	Acknowledged
223011 Study Poster ERC 10Feb23	Version 1.0	null	Approved
MAMC Roles & Responsibilities	Version 1.4	null	Acknowledged
Appendix H Follow-Up Data Collection CRF	Version 1.1	null	Approved
Appendix D Baseline Data Collection CRF	Version 1.3	null	Approved
Appendix C Demographics CRF	Version 1.1	null	Approved
Appendix A Inclusion Exclusion CRF	Version 1.2	null	Approved
223011 Study Flyer Rev ERC 10Feb23	Version 1.3	null	Approved

3. This protocol modification includes a revised protocol, Appendices A, C, D and H, study flyer and Roles and Responsibilities document, a new study recruitment poster, a request to add Nelson Hager, MD, Jonathan Stormer as Sub-Investigators, Samantha McKee and Honey Cin as Study Coordinators, adding Robert Rossi, Geoffery Gabler and Nana-King Karikari as Study Coordinators who now have EIRB access and to remove Sub-Investigator CPT Chalee Yimyam.

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Changes include updating the protocol to the new template adding the use of a study poster for recruitment and administrative and editorial corrections.

4. One (1) revised study recruitment flyer and one (1) study recruitment poster (stamped Approved 10 February 2023) have been issued. It is your responsibility to log into EIRB and print these versions of your flyer and poster for your use. Please note that only the IRB stamped version of this flyer and poster may be used in accordance with the IRB approved protocol and the advertising plan approved by the Public Affairs Officer, Madigan Army Medical Center.

5. The IRB Chair approved the protocol modification in accordance with 32 CFR 219.110(b)(1)(ii) effective 10 February 2023.

6. As a result of this protocol modification your study may require a revised Data Sharing Agreement (DSA) in accordance with DoDM 6025.18 and DoDI 8580.02. You must send the following documents to the Defense Health Agency (DHA) Privacy & Civil Liberties Office (PCLO) at dha.ncr.j-6.mbx.dsa-mail@health.mil to determine if a revised DSA is required.

a. IRB Approval Letter (this letter)
b. EIRB Protocol v1.4

7. If at any time you have questions about your responsibilities as Principal Investigator, please contact the Madigan IRB office at 253-968-3524 for additional information.

Signature applied by Walter James Sowden on 02/08/2023 11:39:59 PM CST

WALTER J. SOWDEN, PhD
LTC, MS
Chair, Institutional Review Board
Madigan Army Medical Center

EIRB Protocol Template (Version 1.4)

1.0 General Information

***Please enter the full title of your study:**

Investigation of the Effectiveness of Shockwave Therapy, Photobiomodulation, and Physical Therapy in the Management of Non-insertional Achilles Tendinopathy

***Please enter the Protocol Number you would like to use to reference the protocol:**

Photomedicine Project 10: SWT, PBMT, PT for Achilles Tendinopathy
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

Is this a multi-site study (i.e. Each site has their own Principal Investigator)?

Yes

Does this protocol involve the use of animals?

○ Yes ◉ No

2.0 Add Site(s)

2.1 List sites associated with this study:

Primary Dept?	Department Name
◆	**P and R** - Madigan Army Medical Center (MAMC)

3.0 Assign project personnel access to the project

3.1 *Please add a Principal Investigator for the study:

Schroeder, Jeremy Daniel, DO LTC

Select if applicable

☐ Student ☐ Site Chair
☐ Resident ☐ Fellow

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Galvin, Joseph William, D.O. LTC
Associate Investigator
Grogan, Scott Patrick, DO, MBA LTC

Associate Investigator
HAGER, NELSON ALLEN
Associate Investigator
Konitzer, Lisa Nicole
Associate Investigator
Persinger, John Edward
Associate Investigator
Stormer, Jonathan David
Associate Investigator

B) Research Support Staff

Cin, Honey Lal Sui
Research Coordinator
GABLER, GEOFFREY MARK
Research Coordinator
Karikari, Nana-King Ahwoi
Research Coordinator
Lucio, Whitley B
Research Coordinator
MCKEE, Samantha Jade
Research Coordinator
Metzger, Elizabeth C
Research Coordinator
Ory, Rian Lyndzie, MS
Research Coordinator
Rossi, Robert M, MPH
Research Coordinator

3.3 *Please add a Protocol Contact:

Cin, Honey Lal Sui
GABLER, GEOFFREY MARK
HAGER, NELSON ALLEN
Karikari, Nana-King Ahwoi
Lucio, Whitley B
MCKEE, Samantha Jade
Metzger, Elizabeth C
Ory, Rian Lyndzie, MS
Rossi, Robert M, MPH
Schroeder, Jeremy Daniel, DO LTC
Stormer, Jonathan David

The Protocol Contact(s) will receive all important system notifications along with the Principal Investigator. (i.e. The protocol contact(s) are typically either the Protocol Coordinator or the Principal Investigator themselves).

3.4 If applicable, please select the Designated Site Approval(s):

Add the name of the individual authorized to approve and sign off on this protocol from your Site (e.g. the Site Chair).

4.0

Project Information

4.1 * What department(s) will be associated with this protocol?

- [ ] Family Medicine
- [ ] Orthopedics
- [ ] Podiatry
- [ ] Physical Therapy
- [ ] Physical Medicine & Rehab

4.2 * Is the IRB of record for this study an IRB/HRPP that does NOT use EIRB? If Yes, complete the application according to the IRB/HRPP Determination.

If your Projects or Protocols are under the oversight of another IRB that does use EIRB, stop this submission and contact the core site and request an invitation as a performing site.

If your Project or Protocol is now being submitted for the first time to an IRB that does use EIRB, continue with this application and answer the questions to be reviewed by the IRB.

Answering yes means the board of record is an IRB that does NOT use EIRB.

- ○ Yes
- ◉ No

4.3 * Is this protocol research, expanded access, or humanitarian use device?

- ◉ Yes
- ○ No

4.4 * What type of protocol is this?

- [ ] Behavioral Research
- [x] Biomedical Research
- [x] Clinical trial (FDA regulated)
- [ ] Educational Research
- [ ] Expanded Access
- [ ] Humanitarian Use Device (HUD)
- [ ] Psychosocial Research
- [ ] Oral History
- [ ] Other

4.5 Are you conducting this project in pursuit of a personal degree?

- ○ Yes
- ◉ No

4.7 * Is this human subjects research? (As defined by 32 CFR 219) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
(i) Obtains information or biospecimens through intervention or interaction with the individual, and

uses, studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.

(•) Yes ( ) No

4.8 * Do you believe this human subjects research is exempt from IRB review?

( ) Yes (•) No

5.0 Personnel Details

5.1 Does the Principal Investigator have a Permanent Change of Station (PCS) Date or Estimated Institutional Departure Date (EIDD)?

( ) Yes (•) No

5.2 List any Research Team members without EIRB access that are not previously entered in the protocol:

No records have been added

5.3 Are any Contractors or Subcontractors involved in this study? If yes, please list them and describe their role.

(•) Yes ( ) No

Name: (Last, First, M.I.)	Phone Number:	Email Address:	Associated Institution:
Hager, Nelson Role on Protocol: Associate Investigator	425-218-1833	nelson.hager.ctr@usuhs.edu	The Geneva Foundation / MAMC
Persinger, John Role on Protocol: Associate Investigator	253-350-5075	jpersinger@genevausa.org	The Geneva Foundation / MAMC
Gabler, Geoffrey Role on Protocol: Research Physical Therapist and	360-269-3443	ggabler@genevausa.org	The Geneva Foundation / MAMC

Clinical Laser Safety Officer (CLSO)			
Name: (Last, First, M.I.) Rossi, Robert Role on Protocol: Research Coordinator	Phone Number: 551-404-1923	Email Address: rrossi@genevausa.org	Associated Institution: The Geneva Foundation / MAMC
Name: (Last, First, M.I.) Cin, Honey Role on Protocol: Research Coordinator	Phone Number: 425-761-5507	Email Address: hcin@genevausa.org	Associated Institution: The Geneva Foundation / MAMC
Name: (Last, First, M.I.) McKee, Samantha Role on Protocol: Research Assistant II	Phone Number: 229-412-4567	Email Address: smckee@genevausa.org	Associated Institution: The Geneva Foundation / MAMC
Name: (Last, First, M.I.) Karikari, Nana-king Role on Protocol: Research Assistant	Phone Number: 253-228-7347	Email Address: nkarikari@genevausa.org	Associated Institution: The Geneva Foundation / MAMC
Name: (Last, First, M.I.) Ory, Rian L. Role on Protocol: MIRROR Regulatory Affairs Manager	Phone Number: 909-904-5034	Email Address: rian.ory.ctr@usuhs.edu	Associated Institution: The Geneva Foundation / USUHS / MAMC
Name: (Last, First, M.I.) Lucio, Whitley B. Role on Protocol:	Phone Number: 202-375-8831	Email Address: whitley.lucio.	Associated Institution: The Geneva

MIRROR Sr. Regulatory Affairs & Data Manager		ctr@usuhs.edu	Foundation / USUHS
Name: (Last, First, M.I.) Metzger, Elizabeth Role on Protocol: MIRROR Scientific Program Manager	Phone Number: 252-562-2419	Email Address: emetzger@genevausa.org	Associated Institution: The Geneva Foundation / USUHS

5.4 Will you have a Research Monitor for this study?

- ○ Yes
- ◉ No
- ○ N/A

6.0 Data/Specimens

6.1 Does the study involve the use of existing data or specimens only (no interaction with human subjects)?

○ Yes ◉ No

7.0 Funding and Disclosures

7.1 Source of Funding:

Funding Source	Funding Type	Amount
: Other Award Number HU00011920056	: Research Development Testing and Evaluation (RDT&E) funds Photomedicine	880567

Total amount of funding:

880567

7.2 Do you or any other Investigator(s) have a disclosure of a personal interest or financial nature significant with sponsor(s), product(s), instrument(s) and/or company(ies) involved in this study?

○ Yes ◉ No

All personnel engaged in research must complete and attach a Conflict of Interest (COI) form.

8.0 Study Locations

8.1 Is this a collaborative or multi-site study? (e.g., are there any other institutions involved?)

(•) Yes ( ) No

8.2 Study Facilities and Locations:

Institution	Site Name	Site Role	FWA or DoD Assurance Number	Assurance Expiration Date	Is there an agreement?	IRB Reviewing for Site
Army	MAMC	Lead site	FWA00003277	09/13/2024	: IAIR	: RHC - P IRB
Army	FBCH	Performance site	FWA00017754	06/10/2024	: IAIR	: RHC - P IRB
P&R	USUHS	Coordinating center	FWA00001628	09/14/2024	: IAIR	: RHC - P IRB

Other:

Other Institution Site	Site Role	FWA or DoD Assurance Number	FWA or DoD Expiration Date	Is there an agreement?	IRB Reviewing for Site
No records have been added					

8.3 Are there international sites?

Attach international approval documents, if applicable, when prompted. Note: Ensure local research context has been considered

( ) Yes (•) No

8.4 Is this an OCONUS (Outside Continental United States) study?

( ) Yes (•) No

Select the area of responsibility:

Have you obtained permission from that area of responsibility? (This is a requirement prior to study approval)

( ) Yes ( ) No

9.0

Study Details

9.1 Key Words:

Provide up to 5 key words that identify the broad topic(s) of your study

Achilles Tendinopathy, Photobiomodulation, Shockwave, ESWT, Photomedicine, Military

9.2 Background and Significance:

Include a literature review that describes in detail the rationale for conducting the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the research questions and/or study hypotheses. This section establishes the relevance of the study and explains the applicability of its findings

Non-insertional Achilles Tendinopathy (AT) is a common overuse injury in adults who are both athletes and nonactive.[1] Tendinopathy occurs when there is either a failed healing response or the failure of normal turnover or remodeling response, and results in pain and limited movement.[2] AT contributes to between 6.2% and 9.5% of running injuries.[3] It's been estimated in some studies that burden of AT may reach 52% lifetime prevalence in runners.[4] In the military, lower-extremity injuries due to overuse, (e.g., AT) are the most common category of injuries, with the highest rates of these injuries occurring in the Army.[5]

The most common treatment of choice for AT is exercise loading programs, however eccentric strengthening (ECC) may only improve symptoms in approximately 60% of patients.[1] Laser-induced photobiomodulation (PBM) has been shown to increase cell proliferation and metabolism, which may aid in the repair and remodeling process.[2,6] Studies have found that PBM was effective in the treatment of AT, but it was more effective when paired with exercise sessions.[2,6]

Extracorporeal shockwave therapy (ESWT or SWT) is a process in which energy is delivered to the muscles or tendons for pain relief.[7] A recent network meta-analysis showed that ESWT is effective in treating AT when combined with ECC.[1] Moreover, a recent narrative review presented ESWT as an effective treatment for specific tendinopathies, including AT.[8] Notably PBMT was not able to be compared in the analysis due to no published studies meeting criteria for inclusion. There is also limited information available on the best energy settings to be used in treating AT and the impacts on short term recovery;[1] therefore more research needs to be done into the impact of ESWT on treating AT.

Photobiomodulation therapy (PBMT) and ESWT are effective tendinopathy treatments, and a study on the treatment of other tendons in the body - lateral epicondylitis (tennis elbow) - showed improvement in both the PBMT and the ESWT arms, with ESWT showing a significant difference in increasing handgrip strength.[9] Studies such as this are promising that ESWT and PBMT will be effective in treating other tendon injuries such as AT, however, these treatment methods have not been evaluated in comparison or combination with each other. Promising results from these studies combined with the previous unclarity in the best treatment for AT justifies the need for more research.

This combination of treatment (SWT + PBMT) may provide improved healing over siloed modalities. ESWT works by creating microtears that in turn stimulate the body's inflammatory response and healing cascade.[7] PBMT could then increase this cascade further by increasing the cellular function, particularly when the body is in an inflamed state, such as the state after ESWT.[2,6] Thus, this treatment combination should be explored.

The sub-section of AT amongst Active-Duty (AD) personnel has had very limited research and given the high prevalence, should be addressed. Therefore, our study will compare four different treatment arms utilizing traditional physical therapy (PT), PT plus shockwave therapy (SWT), PT plus PBMT, and PT plus SWT and PBMT. Both self-reported questionnaires and measured outcomes will be used to assess the most effective treatment for AT.

9.3 Objectives/Specific Aims/Research Questions:

Describe the purpose and objective(s) of the study, specific aims, and/or research questions /hypotheses

The primary aim is to evaluate the effects of standard PT compared to PT with SWT, PT with PBMT, and PT with a combination of SWT and PBMT in the management of AT. *We hypothesize servicemembers in each treatment allocation will see improvement in functional outcomes, pain and measures of Achilles tendon structure compared to baseline measures. As SWT and PBMT may change structural properties and modulate pain in tendinopathy, we anticipate greater measures in activity function for participants assigned to SWT and PBMT over PT as sole treatment.*

The secondary outcome will be to evaluate cross-over response. After the initial 3-month randomized control trial, participants who are not satisfied with results will be able to select a different treatment arm for the remaining 3 months of the study.

9.4 Study Design:

Describe study design in one to two sentences (e.g., prospective, use of existing records/data /specimens, observational, cross-sectional, interventional, randomized, placebo-controlled, cohort, etc.). Specify the phase – Phase I, II, III, or IV – for FDA-regulated investigational drug research

A Randomized Control Trial with Elective Cross-Over Design

9.5 Target Population:

Describe the population to whom the study findings will be generalized

Active-Duty Service Members (ADSMs) and the active civilian runner population

9.6 Benefit to the DoD:

State how this study will impact or be of benefit to the Department of Defense

AT is a common overuse running injury among ADSMs that can impact their combat readiness throughout their military career. Current rehabilitation treatment plans include ECC, but its success rate is limited leaving approximately 40% without full relief of pain and symptoms and decreased activity levels. The use of SWT, PBMT, or both SWT and PBMT along with physical therapy on ADSM with AT, may improve their recovery time. Faster healing translates to quicker return to higher level activities, return to duty (RTD), and ultimately mission ready status.

10.0 Study Procedures, Data Management, and Privacy

10.1 Study Procedures:

Describe step-by-step how the study will be conducted from beginning to end

The study procedures will take place in the Physical Therapy, Sports and Exercise Medicine, and Orthopaedic and Podiatry Clinics.

Recruitment, Pre-Screening (before consent), Study Introduction & Informed Consent: Potential participants will be identified via four methods:

1. Under the provisions of an approved Partial HIPAA Waiver Application for this study, local study team members will review medical records of patients coming in to the Sports Medicine, Physical Therapy, Orthopedic, Podiatry, and Physical Medicine & Rehabilitation (PM&R) clinics for suspected/confirmed AT in order to identify prospective research

participants and to seek their authorization to participate/use their protected health information for this research study. The study team will receive approval from the potential participant's provider prior to approaching for possible study participation.
2. Direct referral from local healthcare providers in the local Sports Medicine, Family Medicine, Orthopedic and Podiatry, Physical Therapy, Holistic Health and Fitness (H2F), and Physical Medicine & Rehabilitation (PM&R) clinics.
3. Patients may self-refer to participate in the study. Interested potential participants will be able to contact a member of the study team via email. Potential participants who contact the study team directly will be instructed to seek care with Physical Therapy or their primary care manager for a physical exam and diagnosis of AT, or confirmation of a previous AT diagnosis. The Physical Therapy Clinic is a direct access clinic that does not require a referral.
4. Study advertisements will be posted within the following locations, and copies will be provided to clinic staff:
    - Internal Medicine
    - Aviation Medicine
    - H2F
    - McChord Clinic
    - Winder Clinic
    - Okubo SCMH
    - Allen Soldier -Center Medical Home
    - SRU
    - Puyallup Community Medical Home
    - South Sound Community Medical Home
    - Armed Forces Wellness Center
    - Intrepid Spirit Center
    - Madigan Medical Mall
    - Pharmacy waiting areas, if possible
    - Physical Therapy
    - Podiatry
    - Sports Medicine
    - THOR3
    - Physical Medicine and Rehabilitation
    - Coffee bar
    - Dining Facility entrance
    - Intranet screen saver page
    - 2/75 Ranger Clinic

If a potential participant expresses interest in learning more about the research study, a member of the research staff will briefly introduce the study, express the voluntary nature of participation, assess interest in participating, and screen the potential participant for eligibility. Eligibility will be determined in person using the Inclusion/Exclusion Case Report Form (CRF) (Appendix A).

If the potential participant meets eligibility criteria as determined by the Inclusion/Exclusion CRF and expresses interest in participating, an authorized study team member will initiate the formal consent discussion and, if applicable, obtain informed consent.

Pre-screening conversations may also take place remotely, should a participant contact the study team, using the Screening Script (Appendix O). Potential participants who meet initial eligibility per the Screening Script and express interest in participating will be asked to come to clinic to complete an Inclusion/Exclusion CRF to confirm final eligibility with an authorized study team member prior to providing informed consent as outlined in the respective section below.

Participants are enrolled once the consent process is completed.

Baseline Data Collection/Week 1 Visit 1 (post-consent):
Post-consent, secondary exclusion of pregnancy will be determined by a hCG test for women, which will be conducted by the lab, and completed prior to randomization.

Questionnaires: Prior to receiving their assigned study treatment, participants will provide their contact information (Appendix B Intake CRF) and complete demographic (Appendix C Demographics CRF) and study specific measures (Appendix D Baseline Data Collection CRF).

Ultrasound: A study team member will assess ultrasound measures at baseline for both limbs. Measures of interest include cross-sectional area, width and degree of thickening within the tendon at site of maximal circumference and maximal pain, relative neovascularity, and elastography. A trained study team member will conduct the ultrasound.

The participant will be prone with his/her feet overlying the edge of the bed with a pillow under the anterior ankle for comfort. The team member will scan initially in the longitudinal plane to identify the region of pathology near the avascular zone. The full interrogation should start at the gastroc-soleus junction and proceed distally to the Achilles insertion. Other pathology such as insertional tendinopathic changes, retrocalcaneal bursal changes, aponeurosis pathology, and Achilles tendon tears will be annotated if present. An ultrasound system capable of operating frequencies above 12 MHz will be used for the evaluation. Following the initial grey scale evaluation, color doppler with microvascular flow will be utilized in the area of interest to assess the relative level of hyperemia and neovascularity. The color doppler evaluation should be conducted in both orthogonal planes (transverse and longitudinal) at the area of maximal thickness/width. The relative level of neovascularization will be rated from grade 0: no visible vessels, grade 2: 3 to 5 vessels within the region of interest (ROI), grade 3: vessel's in up to 30% of the ROI. Following the color doppler evaluation, the elastography evaluation should be conducted in two orthogonal planes at the area of maximal thickness/width, IAW manufacture guidance on elastography image collections.

The participant will be identified on the ultrasound system using only the assigned participant ID. This information will be included on the Baseline Data Collection CRF (Appendix D).These images will also be uploaded to the TeleRay data platform. More information in Managing Data Sections 10.14-10.15.

Function: Quantitative function in heel raises to fatigue will be measured at baseline on both limbs. Ankle strength will be graded (0 to 5). We will also ask the participants to complete 20 single-leg hops on both legs and rate their pain using Defense and Veteran Pain Rating Scale (DVPRS) basic (i.e., DVPRS basic will be completed for both the right and left leg). Ankle-dorsiflexion and plantar flexion range of motion (ROM), both active and passive, will be measured using a goniometer. This information will be included on the Baseline Data Collection CRF (Appendix D).

A study team member will also acquire measurements of the participant's back of the knee and bottom of the leg, including the Achilles Tendon, to calculate the appropriate PBMT dose. (See Appendix N for PBM dosing information). These measurements will be included on the Baseline Data Collection CRF (Appendix D). The study team member will also indicate the participant's Fitzpatrick Skin Phototype for PBM treatment on Appendix D.

Randomization:
Participants will be randomly assigned to one of 4 study groups (PT only, PT + SWT, PT + PBMT, or PT + PBMT + SWT) using a computer-generated randomization model prepared by the study biostatistician.

Study treatments (PT only, PT + SWT, PT + PBMT, PT + SWT + PBMT):
This study has been split into two parts. Part 1 is the initial randomized control trial, and Part 2 is when the participants can select the treatment they want to receive if they are dissatisfied with their initial treatment. Participants cannot/will not be blinded to the treatment arm that they receive due to the obvious differences in the treatments.

Part 1
All participants may complete a PT program as standard of care (SoC) treatment addressing individual strength, mobility, and flexibility deficits in both proximal (e.g., spine and hip girdle) along with distal (thigh, leg and foot/ankle) muscle groups. The provider may also use other modalities to address distal issues. The PT treatment received as SoC is not a study-specific research procedure; however, physical therapy care provided will be tracked by a chart review (Appendix G).

If a participant has not been placed on profile at the time of consent, a profile may be written by the study medical provider to ensure limitation of activities, as medically appropriate.

In order to standardize the loading program for study participants, we will provide all participants with an at-home exercise program designed by Dr. Karin Silbernagel for progressive Achilles tendon loading.[10] This will be completed alongside the standard of care PT they are receiving. Activities including running will be allowed as tolerated following published guidelines by Dr. Silbernagel.[11,12,13] This treatment protocol consists of four phases that last 12 weeks to 6 months. The first phase includes a circulation exercise and various forms of toe raises. Phase two increases the intensity of the various toe raise exercises, and in phases three and four plyometric activities are added. Participants are expected to exercise every day for the first 12 weeks and then can decrease to 2-3 times per week thereafter, up to 6-months. The at-home exercise program instructions are outlined in participant handout Appendix J Silbernagel Guidelines.

All participants will also follow the University of Delaware Return to Sport protocol for returning to running (Appendix K).

All activities, including home exercises and running, pain, and pain medications taken, will be recorded by the participant daily in a log (Appendix E).

If a study participant has bilateral AT, the leg with the most severe symptoms [determined by the Victorian Institute of Sports Assessment – Achilles (VISA-A) in the Data Collection CRF; more information regarding the VISA-A in Section 10.2] will be chosen as the primary data point for the study. However, both legs will be treated consistently according to the treatment group the participant was randomized into.

Physical Therapy (PT) Only Arm

Participants in the PT only arm will follow the PT program outlined above. Twice a week for three weeks, a team member will check-in with the participants to ensure physical therapy exercise adherence, and response to treatment. During the second check-in of the week, the study team member will also ensure the participant is keeping their activity/medication/pain log; the study team member will also deliver the DVPRS with supplemental questions. (See Appendix F for Check-in Data Collection CRF). These check-ins may occur virtually or in-person.

In Part 1, the *physical therapy only* arm requires 8 visits. The participants will complete 2 check-in visits each week (remote or in person), for three weeks. Follow-up data will be collected at 6 weeks (virtual or in-person) and at 3 months (in-person).

PT + Shockwave Therapy (SWT) Arm:

The *physical therapy + shockwave therapy* arm will receive SWT once a week for three weeks in addition to the PT treatment described above. Twice a week, for three weeks, a team member will check-in with the participants to ensure physical therapy exercise adherence, and response to treatment. During the second check-in of the week, the study team member will also ensure the participant is keeping their activity/medication/pain log; the study team member will also deliver the DVPRS with supplemental questions. (See Appendix F for Check-in Data Collection CRF). The first check-in of the week will occur in-person after the SWT, if, however, this is not feasible, it may be conducted virtually; the second check-in of the week may occur virtually or in-person.

In total, participants will receive one SWT treatment each week (in person) and complete two check-ins each week (remote or in person), for three weeks. The SWT will take approximately 5-20 minutes.

A medical provider will conduct SWT on study participants, using the OrthoPlus Ultra 100 /radial D-Actor. (See OrthoPulse Radial Edition Application Brochure and OrthoPlus Ultra 100 Operations Manual). This Extracorporeal Pressure Activation Treatment (EPAT) device will be used at a radial shockwave of 3000 counts treatment settings of 15 Hz minimum 2 bars with a focus applicator head at mid-portion of Achilles using clinical focusing technique, and 3000 counts at 15 Hz minimum 2.5 bars using broad oscillator to myotendinous region and over symptomatic areas of gastrocnemius and soleus, treatment will be applied distally to proximally to facilitate lymphatic return adjusting treatment air pressure and amount of force applied by applicator head by patient comfort. The maximum setting for each treatment applicator will be 4 bars of air pressure, and the first 500 counts using each applicator will be applied at 1.5 bars to help desensitize the tissue prior to increasing energy settings. The settings used for each participant will be recorded and followed in a similar approach to treatment.

A CuraMedix representative will provide training to the study team for this machine.

In Part 1, participants in this group will have 8 visits: 3 combined SWT and check-ins post-treatment (in person), 3 check-in only visits (remote or in person), 6-week follow-up (virtual or in-person), and 3 month follow-up (in person).

PT + Photobiomodulation Therapy (PBMT) Arm:

The *physical therapy + photobiomodulation therapy* arm will receive PBMT twice a week, for three weeks, in addition to the PT treatment described above.

A member of the study team will measure the treatment area according to a standard protocol (Appendix N PBM Dose Calculations), to calculate and determine the treatment time, approximately 5-20 minutes. PBMT will be delivered at 25W.

The PBMT will be provided by a trained study team member. Training for the PBMT will be conducted by a LightForce representative. PBMT will be delivered using the LightForce® XPi 25W device with the Smart Hand Piece technology, provided by LiteCure, LLC/DJO (New Castle, DE) which has a built-in accelerometer in the hand piece that controls the speed of light delivery to the treatment area. The LightForce® XPi therapy laser is an FDA cleared device for the treatment of pain. The trained team members will use the Smart Hand Piece technology, which achieves effective treatments and improves dosing accuracy by assessing the operator's speed and providing real-time visual (red – amber – green light) and sensory feedback. The Smart Hand Piece is calibrated to shut-off when moving too slowly, and warn the operator when moving too fast by vibrating. (See LightForce Brochure). The therapy is delivered through a flexible optical fiber threaded through the hand piece, which contains a rolling glass massage ball. PBMT will be delivered at 10 J/cm^2 and applied in a serpentine pattern to the calf from the fold in the back of the knee to the bottom of the leg including distal Achilles tendon and calcaneus. The setting for treatment will be adjusted for skin pigmentation using the Fitzpatrick Scale and values recorded for each participant.

After each PBMT visit (twice a week, for three weeks), a team member will check-in with the participants to ensure physical therapy exercise adherence, and response to treatment. During the second check-in of the week, the study team member will also ensure the participant is keeping their activity/medication/pain log; the study team member will also deliver the DVPRS with supplemental questions. When/if needed, check-ins may occur virtually. (See Appendix F for Check-in Data Collection CRF).

In Part 1, participants will receive PBMT twice each week, for three weeks. The PBMT treatment arm requires 8 visits: 6 combined PBMT and check-ins (in person), 6-week follow-up (virtual or in-person), and 3-month follow-up (in person).

PT + SWT and PBMT Arm

The *physical therapy + shockwave therapy + photobiomodulation therapy* arm will receive both SWT and PBMT treatments in addition to PT treatment described above. The SWT and PBMT will be performed by a trained study team member. Participants will receive PBMT twice each week and SWT one time each week, for three weeks. The SWT visit may be combined with a PBMT visit in the same week. Up to two times each week after a treatment visit (for three weeks), a team member will check-in with the participants to ensure physical therapy exercise adherence, and response to treatment. During the second check-in of the week, the study team member will also ensure the participant is keeping their activity/medication/pain log; the study team member will also deliver the DVPRS with supplemental questions. When /if needed, these check-ins may occur virtually. (See Appendix F for check-in data collection CRF).

In Part 1, the PT+ SWT + PBMT treatment arm requires 8 visits: 3 for PBMT alone with check-ins (in person), 3 for PBMT & SWT with check-ins (in person), 6-week follow-up (virtual or in-person), and 3-month follow-up (in person).

Part 2

At the 3-month follow-up, participants who are not satisfied with their current treatment response will be given the option to choose any one of the remaining treatment arms. Participants will also have the option to decline further treatment. Any biological female of child bearing age and capacity that opts to receive treatment with SWT and/or PBMT will be required to complete a urine hCG test prior to receiving treatment in Part 2 of the study.

For all groups in Part 2, the number of non-PT study treatment visits the participants will need to complete will be dependent on which treatment arm the participant selects; however, regardless of what treatment the participant chooses, if any, the participant will be required to complete at least one in-person visit at the 6-month follow-up.

Follow-Up Data Collection:

Regardless of study arm assignment, all participants will be asked to log their activity, pain, and medication intake (Appendix E), daily for 12 weeks. This log will be collected/checked weekly for the first 3 weeks and then at the 6-week and 3-month follow-up visits.

Check-ins (remote or in person, as applicable/convenient) will be conducted twice a week for the first three weeks. Any issues with treatment will be recorded on Appendix F Weekly Check-In CRF. In addition, once a week, for the first 3 weeks, the DVPRS with supplemental questions will be administered.

A chart review will be completed at 3 months to ensure that all PT visit information is recorded in study documentation (Appendix G). A medical record review will be completed to obtain this information. A study visit is not required on behalf of the participant.

A self-report battery will be obtained for each Achilles tendon, regardless of treatment, using Appendix H Follow-Up Data Collection CRF, which will be administered at 3-weeks, 6-weeks, 3-months, and 6-months post-intervention start.

Participants will complete the ultrasound imaging, heel raise test, ankle strength and ROM, hopping test, and be asked to complete a patient satisfaction and expectation survey at the 3-month and 6-month timepoints.

Participants will be evaluated for adverse events at each follow-up time point and any complications will be documented.

Data may be captured in person or remotely (e.g., entered directly into REDCap using a personalized coded link with no log-in required, verbally over the phone with a study team member, etc.). Reminder phone calls, texts, and/or emails will be sent to participants at their preferred contact method indicated on the Intake Form (Appendix B).

Please see the Study Flow Diagram (Appendix L) for a visual representation of the study procedures.

Missed Appointments and Study Removal:
If a participant misses a scheduled appointment, they will be contacted to reschedule in order to maintain the treatment plan of their assigned study treatment group. In the event that a participant misses an appointment, study staff will make one attempt to reschedule each day on three separate days (for three total attempts to reschedule). If the participant cannot be reached or does not respond/reschedule, they will be removed from the study due to non-compliance.

10.2 Data Collection:

Describe all the data variables, information to be collected, the source of the data, and how the data will be operationally measured.

Questionnaires:

- The Demographics CRF (Appendix C) and the Data Collection CRF (Appendix D) will be used to will be used to obtain demographic information, Fitzpatrick Skin Phototype, and foot, ankle, and calf measurements for PBMT dosage calculation. The Fitzpatrick Skin Prototype is a rating of susceptibility to skin damage from ultraviolet (UV) radiation.
- Symptoms severity specific to Achilles will be Victorian Institute of Sports Assessment – Achilles **(VISA-A)**
    - The VISA-A is currently the only valid and reliable measure to assess function and pain in AT (validity, $P<0.01$; test-re-test reliability, $r = 0.98$)
- Patient-Reported Outcomes Measurement Information System **(PROMIS-29)** will be used to capture other aspects of non-disease specific measures of health-related domains (physical, mental and social health).
- The University of Wisconsin Running Injury and Recovery Index **(UWRI)**will measure aspects unique to returning to running.
- Defense and Veteran's Pain Rating Scale **(DVPRS)**will capture pain; basic applied after hop test and supplemental provided at each visit.
- Lower Extremity Functional Scale **(LEFS)** will capture functional status.
- To quantify patient choice and motivation for treatment, an unvalidated survey will be obtained to determine patient goals of enrollment in study and reason for selecting a different intervention, and patient satisfaction with treatment.

Ultrasound: Ultrasound measures will be assessed at baseline, 3 months and 6 months. Measures of interest include cross-sectional area, width and degree of thickening within the tendon at site of maximal circumference and maximal pain, relative neovascularity, and elastography.

Function: Quantitative function in heel raises to fatigue, and ankle strength and ROM, will be measured at baseline, 3 months and 6 months on both limbs. We will also ask the participants to complete 20 hops and rate their pain using the Defense and Veteran's Pain Rating Scale (DVPRS).

Return to activity: We will be asking participants to record their return to activity, tracking the date, exercise and pain level and medication use using the training diary.

A chart review will be conducted at the end of 3 months to capture all PT visits.

Check-ins will be conducted to ensure at home exercise adherence and address any rehabilitation issues; weekly the DVPRS with supplemental questions will be delivered (Appendix F).

Study Visits for all treatment arms:
An overview of the questionnaires and measurements that will be taken at various time points, regardless of treatment arm, are described in the Data Collection Schedule (see Appendix T).

10.3 At any point in the study, will you request, use, or access health information in any form, including verbal, hard copy and electronic?

- (•) Yes
- ( ) No

10.4 Review the definitions below and respond to the following two questions. If you are not sure of the answers, email DHA.PrivacyBoard@mail.mil for assistance. The *Military Health System (MHS)* is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force *MHS workforce members* are employees, volunteers, trainees, and other persons whose conduct, in the performance of work for the MHS, is under the direct control of the MHS, whether or not they are paid by the MHS. *MHS business associates* are persons or entities that provide a service to the MHS and require protected health information (PHI) to provide the service.

Are you an MHS workforce member?

- (•) Yes, I am an MHS workforce member
- ( ) No, I am not an MHS workforce member

Are you an MHS business associate?

- ( ) Yes, I am an MHS business associate
- (•) No, I am not an MHS business associate

10.5 Have you consulted with an MHS data expert to determine the data elements required for your study?

Consulting with a data expert often saves time later in the compliance process because the data expert can advise on the data available in the numerous MHS information systems, the quality of that data and the methods for encrypting and collapsing data. To schedule a consult with an MHS data expert, send an email to: (**DHA.PrivacyBoard@mail.mil**)

- ( ) Yes, then complete the questions below according to the data consult
- (•) No, then complete the questions below according to the best of your knowledge

10.6 Indicate how you will request data from the MHS. Select all that apply.

- [x] Talking with MHS health care providers or MHS health plans about specific research

participants

- [ ] Obtaining MHS hard copy records specific to research participants
- [x] Obtaining data from an MHS information system(s)

10.7 If you are obtaining data from an MHS information system(s), indicate whether you plan to receive a data extract or whether you plan to access an MHS information system directly to create a data set.

A data extract is when the MHS or a contractor provides the data set directly to the researcher. When receiving a data set through data extract, the researcher may indicate whether the data elements should be provided as is, encrypted or collapsed. In contrast to a data extract, access to an information system means that the researcher may directly access an MHS information system and create a data set for the research study

- [ ] Data Extract
- [x] Access

10.8 Do you intend to request de-identified data from the MHS in your research study?

There are different two methods for de-identifying data pursuant to HIPAA:
1) Safe Harbor Method: Removing all of the identifiers listed in Table 1 below, provided that the researcher does not have actual knowledge that the remaining data can be used alone or in combination with other information to identify the individual who is the subject of the information
2) Statistical Method: An expert, with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable, determines that the data is not individually identifiable

- ( ) Yes
- (•) No

10.9 Indicate the MHS information system(s) from which you will seek to obtain data

If you do not know which system(s) contains the data elements you need, refer to the Guide for DoD Researchers on Using MHS Data or request guidance from an MHS data expert at: **DHA.PrivacyBoard@mail.mil**.

Below is a list of commonly used MHS systems. If the system from which you seek to obtain data is not listed below, list the name of the system in the "Other MHS Systems" category below
PHI Systems:

MHS Information System	Requesting Data
: AHLTA	: Yes
: CHCS	: Yes

PII-Only Systems:

MHS Information System	Requesting Data
No records have been added	

De-Identified Data & Other Systems:

Information System	Requesting Data
Other MHS System (May include PII and/or PHI) List other system here: Genesis	: Yes

10.10 Do you intend to merge or otherwise associate the requested data with data from any sources outside of the MHS, including other DoD systems that are not part of the MHS?

- ○ Yes, will merge data
- ◉ No, will not merge data

10.11 Indicate the data elements about research participants or relatives, employers, or household members of the research participants that you will request from MHS hard copies or from MHS information systems.
If you will merge data, also indicate non-MHS data elements about research participants or relatives, employers, or household members of the research participants that you will have access to in any form or medium.

Direct and Indirect Identifiable Data Elements	DHA Hard Copies	DHA Data Elements to be Accessed	DHA Data Elements Verbal	Extracted DHA Digital Data	Downloaded DHA Digital Data	Non-DHA Hard Copies or Digital
1. Names	☐	☑	☐	☐	☐	☐
2. Postal address with only town, city, state, and zip code	☐	☐	☐	☐	☐	☐
3. Postal address with all geographic subdivisions smaller than state, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of Census: 1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and 2)	☐	☑	☐	☐	☐	☐

the initial three digits of a zip code from all such geographic units containing 20,000 or fewer people is changed to 000						
4. Dates including all elements (except year) directly related to an individual, including birthdate, admission date, discharge date, and date of death	☐	☑	☐	☐	☐	☐
5. Ages over 89 and all elements of dates (including year) indicative of such age, unless you will only request a single category of "age 90 or older"	☐	☐	☐	☐	☐	☐
6. Telephone Numbers	☐	☑	☐	☐	☐	☐
7. Fax Numbers	☐	☐	☐	☐	☐	☐
8. Email Addresses	☐	☑	☐	☐	☐	☐
9. Social Security Numbers	☐	☐	☐	☐	☐	☐
10. Medical Record Numbers (MRN)	☐	☐	☐	☐	☐	☐

(including record ID)						
11. Health Plan Beneficiary Numbers (including DEERS ID, Electronic Data Interchange Personal Identifier (EDIPI) or Number (EDIPN))	☐	☐	☐	☐	☐	☐
12. Account Numbers	☐	☐	☐	☐	☐	☐
13. Certificate /License Numbers	☐	☐	☐	☐	☐	☐
14. Vehicle identifiers and serial numbers, including license plate numbers	☐	☐	☐	☐	☐	☐
15. Device identifiers and serial numbers	☐	☐	☐	☐	☐	☐
16. Web Universal Resource Locators (URLs)	☐	☐	☐	☐	☐	☐
17. Internet Protocol (IP) address numbers	☐	☐	☐	☐	☐	☐
18. Biometric identifiers, including finger and voice prints	☐	☐	☐	☐	☐	☐
19. Full-face photographic images and						

any comparable images	☐	☐	☐	☐	☐	☐
20. Any other unique identifying number, characteristic, or code (including non-military provider IDs)	☐	☑	☐	☐	☐	☐
21. Free Text Fields	☐	☐	☐	☐	☐	☐

If you are obtaining SSNs, provide a justification as to why and explain why a substitute cannot be used.

Due to guidelines stated within DoDI 1000.30, Reduction of SSN Use within DoD, the reduction or elimination of SSN usage must occur wherever possible. If SSNs are required to complete the project, the PI must provide a justification and explanation as to why a substitution cannot be used.
For example:

- If alternatives to SSN (e.g., EDIPNs or pseudo person IDs) are sufficient in other instances, will those alternatives to SSN usage be sufficient to respond to Congressional inquiries and /or Senior DoD stakeholders inquiries?
- Are alternatives to SSN used first?
- Are those alternatives to SSN insufficient to combine data from multiple data sources? Is the issue that some individuals do not possess alternatives ID numbers and SSN is the only way to identify them?

N/A

a. Will you receive or obtain health information?

> ***Note:*** *If you indicate you are not receiving health information, the answer must be consistent with the DHA data source. For a non-health information data request, if you are a non-MHS employee or non-MHS business associate, you may not access an information system that has PHI or LDS. For both MHS and Non-MHS employees and MHS business associates, you may* ***NOT*** *include data elements in the above table on: 1) lines 10 or 11, 2) line 21 if the free text field comes from a PHI or LDS system, and 3) lines 12, 13, or 18 if the account numbers, certificate and license numbers, biometric data, or any other data elements are health information created or received by an MHS health care provider, health plan, or business associate in relation to the physical or mental health or condition of an individual or payment for health care.*

◉ Yes, I will receive or obtain health information
○ No, I will not receive or obtain health information

b. If no data elements were checked in the above table, is it possible that the requested DHA data is or will be identifiable because of any unique data elements, triangulation, or small cell size?

☑ Data elements were checked in the above table, STOP HERE.

NOTE: *A unique data element includes any unique features that alone are not identifiable but that could be used to identify an individual within the context of other information, such as any type of code (such as diagnosis or procedural), rank of general or admiral, gender, or race.*

Triangulation means using different data elements that when combined can be used to identify an individual, such as including the above lists of unique data elements in a data set. Determining whether an individual is identifiable through triangulation requires consideration of all data elements in combination. Within the military, the use of rank and/or diagnosis code, procedural codes, or any other code that changes on a predictable basis, increases the possibility of identification. Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Department of Defense Manual 6025.13, Medical Quality Assurance and Clinical Quality Management in the Military Health System MHS, provides that the threshold for de-identifying data within the MHS requires a cell size of three, but also states that the de-identification standards must meet the DoD implementation of the HIPAA Privacy Rule. Centers for Medicare and Medicaid also gives guidance on small cell size stating that no data cell less than 11 may be published or displayed. However, the Office for Civil Rights' OCR, which is the official regulatory office for the HIPAA Privacy Rule, provides that OCR does not designate a universal value for small cell size in accordance with the de-identification standard; instead, the cell size should be set at a level that is appropriate to mitigate risk of identification by the anticipated recipient of the data set. This means that a cell size of 3 or 11 may not meet the HIPAA Privacy Rule requirements if the cell size level does not appropriately mitigate risk of identification by the anticipated recipient of the data set.

Note: If dates are altered as a means of de-identifying the data, diagnosis and procedural codes need to be rolled-up or collapsed. If dates are provided "as time between events," the roll-up is not necessary.

- ☐ Yes, the DHA data will become identifiable
- ☐ No, the DHA data will not become identifiable

10.12 Do you believe it is possible for the MHS data to become identifiable because of triangulation, a small cell size, or any unique data element(s)?

Triangulation means using different data elements that are not themselves identifiable but that when combined can be used to identify an individual. For example, triangulation would use rank and race together to determine the identity of an individual with a particular health condition.

Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Guidance for acceptable cell size is available from the Centers for Medicare and Medicaid Services. For example, the rank category of four star generals with a particular diagnosis may be less than 30, so the rank category may need to be expanded to include lower ranks.

A unique data element includes any unique features that are not explicitly enumerated in the categories of data in rows 1 – 20 of the table above (in Section 10.10), but that could be used to identify an individual. Unique data elements include characteristics that are not themselves identifying, such as the rank of general or admiral, or a race or gender, but within the context of other information could be identifiable.

- ○ Yes, I believe there is a reasonable possibility the MHS data will become identifiable
- ◉ No, I believe there is no reasonable possibility the MHS data will become identifiable

10.13 Have you completed and uploaded an appropriate HIPAA document (i.e. HIPAA Authorization will be obtained or Waiver/alteration of HIPAA Authorization is being requested)?

- ◉ Yes
- ○ No
- ○ N/A

If yes, please check which one.

- ○ HIPAA Authorization
- ◉ HIPAA Waiver (Full or Partial)
- ○ Other (please provide copies when uploading Other Study Documents)

10.14 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for this Study:

Include in this section the plan for acquiring data (both electronic and hard copy), access during the study, data/specimen storage and length of time stored, shipment/transmission, and the plan for storage and final disposition at the conclusion of the study. Describe any data agreements in place for accessing data within and/or outside of your institution (e.g., Data Sharing Agreement, Data Use Agreement, Business Agreements, etc.)

Data Capture Methods:
The local study team will collect study data directly from the study participant (including in person, via mail or email, or over the phone), from their attending provider(s), clinical evaluations or, where applicable, from the participant's medical record (i.e., relevant medical and treatment history and relevant clinical notes) and record it on study Case Report Forms (CRFs). (See Appendices A-I).

The completed CRFs will serve as source documents for this study. Other source documents include relevant clinical notes, imaging, and/or test results which, if applicable, will be redacted and stored in the participant's research file.

Participants may also enter their coded data directly into REDCap using a personalized survey link (no log-in required). In these cases, the completed REDCap questionnaire(s) will be printed and added to the participant's research record as a source document.

Electronic Data Entry:
Following each research visit, a local study team member will review any completed paper CRFs for accuracy and completeness and then enter the collected non-personally identifiable data from the paper CRFs into REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD) server and maintained by the Uniformed Services University Information Technology (USU IT).

Please see Appendix R for additional information on REDCap.

Ultrasound images will also be uploaded to TeleRay, more information is outlined below.

Data Storage & Access:
With the exception of the Informed Consent Form, HIPAA Authorization, Intake CRF, and electronic Master List, all research data (both paper and electronic) will be identified using a unique study ID only, and not by the participant's name, date of birth, DoD ID, or other protected identifier.

Paper research forms and source documents will be stored in a locked cabinet inside of a locked room within the Sports Medicine Clinic at Madigan.

Ultrasound images will be uploaded to TeleRay. Teleray ensures that all accounts stored in Microsoft Azure's self-healing network with advance security protocols enabled and is only located in the USA Secure Connection: The sessions established are secure (with secured tokens that are regenerated). Random AES keys are generated by clients at the beginning of the media connection and, to increase security, additional keys are generated periodically throughout the session. TeleRay employs Transport Layer Security (TLS) to encrypt video data. The core protocols used are Secure Real-time Transport Protocol (SRTP) for media traffic encryption and Datagram Transport Layer Security (DTLS)-SRTP for key negotiation, both of which are defined by the Internet Engineering Task Force (IETF). The endpoints use Advanced Encryption Standard (AES) cipher with 256-bit keys to encrypt audio and video, and Hash-based Message Authentication Code- Secure Hash Algorithm 1 (HMAC-SHA1) to verify data integrity. No PHI/PII will be entered into TeleRay. Access to the coded data uploaded to TeleRay will be controlled and managed by the local MAMC research team.

The coded electronic research data for this study will be stored in REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD) server and maintained by the Uniformed Services University Information Technology (USU IT). No PHI/PII will be entered into REDCap.

This coded electronic research data will be accessible by authorized staff from Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR) which is based out of the Department of Physical Medicine & Rehabilitation (PM&R) at the Uniformed Services University (USU) and is serving as the data coordinating center for this research study. Access to the electronic coded research data will be governed strictly on an individual-by-individual basis

within REDCap. Individual data access as well as privileges will be clearly delegated, audited, and monitored by MIRROR/USU. Staff from MIRROR/USU will not have access to the paper research records or any identifiable research data.

The local study team will maintain a separate electronic master list which matches unique study IDs with participant identifying information. The electronic master list will be stored separately from the coded electronic research data in a secure, password protected document on a computer and network that requires CAC access and will only be accessible by local research staff.

All research data and forms (both paper and electronic) will only be accessible by authorized study staff, authorized staff from MIRROR/USU (coded data entered into REDCap and TeleRay only, as described above), the IRB of record, the local research office (if applicable), and applicable governmental agencies as part of their duties and in accordance with federal law. These duties include making sure that research participants are protected.

Informed Consent Forms and HIPAA Authorizations will be maintained for a period of 6 years following study closure and then securely shredded. Paper research forms will be maintained for a period of 5 years following study closure and then securely shredded. The master list connecting unique study ID to participant identifiers will be destroyed at study closure. The electronic coded research data will be maintained indefinitely as described below in protocol section 10.15.

De-identified data will be shared with Spaulding Rehabilitation Network/Massachusetts General Hospital implementing a parallel study at a civilian hospital.

Appropriate data sharing agreements in place.

Is this a data repository?

(•) Yes ( ) No

If Yes, provide name of the Repository.

USU OCIO REDCap; TeleRay

Who will have access to the Repository?

Study investigators, study team members, and MIRROR Core team members, as appropriate.

What data type will be stored in the Repository?

- [ ] PHI
- [ ] LDS
- [x] De-identified Data

10.15 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for Future Research:

If the study involves collecting, storing, or banking human specimens, data, or documents (either by the Investigator or through an established repository) for FUTURE research, address. How the specimens/data will be used, where and how data/specimens will be stored (including shipping procedures, storage plan, etc.), whether and how consent will be obtained, procedures that will fulfill subjects' request as stated in the consent, whether subjects may withdraw their data/specimens from storage, whether and how subjects may be recontacted for future research and given the option to decline, whether there will be genetic testing on the specimens, who will have access to the data/specimens, and the linkage, the length of time that data/specimens will be stored and conditions under which data/specimens will be destroyed.

Long Term Data Storage & Access:
The de-identified electronic dataset will be maintained by MIRROR/USU and the study team indefinitely, or as long as it is practical to maintain.

The de-identified data uploaded to TeleRay will be maintained by the local research team indefinitely, or as long as it is practical to maintain, and while funding is allotted for this service.

De-identified electronic research data will be securely transmitted from local study teams to the MIRROR /USU via REDCap, TeleRay, or the DoD SAFE application (or other comparable safe data

sharing system implemented by the local site and/or the US Army/DHA). REDCap utilizes Secure Sockets Layer (SSL) in addition to other safeguards on its web server to maintain secure communication with end-users (see Appendix R). DoD SAFE uses a TLS (Transport Layer Security) protocol when files are uploaded and downloaded. TeleRay employs Transport Layer Security (TLS) to encrypt video data. The core protocols used are SRTP for media traffic encryption and DTLS-SRTP for key negotiation, both of which are defined by the IETF. The endpoints use AES cipher with 256-bit keys to encrypt audio and video, and HMAC-SHA1 to verify data integrity.

Once received, the electronic de-identified research data will be stored within an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD)-compliant server.

Access to the de-identified research data will be governed strictly on an individual-by-individual basis within the secure electronic data capture and management system. Individual data access as well as privileges will be clearly delegated, audited, and monitored by MIRROR/USU. Any future research using retained data will require a research protocol to be approved by an Institutional Review Board or other authorized official responsible for protecting human subjects of research.

Any future research using retained data will require a research protocol to be approved by an Institutional Review Board or other authorized official responsible for protecting human subjects of research.

Consent for Future Use:
The Informed Consent Form for this research study states that de-identified research data will be shared with MIRROR/USU and maintained indefinitely for possible use in future research. By consenting to participate in this research study, participants agree to allow us to maintain their de-identified research data indefinitely for possible use in future research.

Participants will not be given the option to opt out of us retaining their de-identified research data indefinitely for possible future use. The consent form states, "If you do not want your deidentified data collected as part of this research study to be kept for use in future research studies, you should not sign this consent form."

Data Withdrawal from Storage:
Participants may request to have their data (including ultrasound images) withdrawn at any time before their personal identifiers have been removed. Once their data has been de-identified, it will be impossible for the researchers to locate their specific study data.

Is this a data repository?

○ Yes ○ No

If Yes, provide the name of the Repository

USU OCIO REDCap; TeleRay

Who will have access to the Repository?

Study investigators, study team members, and MIRROR Core team members, as appropriate.

What data type will be stored in the Repository?

☐ PHI
☐ LDS
☑ De-identified Data

11.0 Statistical/Data Analysis Plan

11.1 Statistical Considerations:

List the statistical methods to be used to address the primary and secondary objectives, specific aims, and/or research hypotheses. Explain how missing data and outliers will be handled in the analysis. The analysis plan should be consistent with the study objectives. Include any sub-group analyses (e.g., gender or age group). Specify statistical methods and variables for each analysis. Describe how confounding variables will be controlled in the data analysis

Descriptive statistics will report location and scale in terms of mean and standard deviation for normally distributed variables, median and interquartile intervals for ordinal metric variables, and in terms of proportion and size for categorical variables.

Outliers will be removed if determined to be erroneous based on relevant clinical expertise. Data will be analyzed on a complete-case intention-to-treat (ITT) basis. Confounding will be principally controlled by randomization. In order to increase the precision of our estimates, we may also statistically adjust for patient demographics and relevant clinical variables if warranted based on statistical best practices.

Methods to be used for the Primary Aim: Time-to-event analyses (return to activity) will use survival analysis. All other outcome measures (including our primary outcome measure (VISA-A) and other aforementioned secondary outcome measures such as functional testing, ultrasound measures, etc.) will be analyzed using generalized additive models predicting change in each outcome measure by treatment group at 3 months. Sensitivity analyses for non-time-to-event outcome measures will be performed to evaluate trends by treatment group and will use longitudinal hierarchical/multilevel models incorporating random effects to account for repeated measures.

Methods to be used for the Secondary Aim: Due to the lack of washout period between initial and cross-over periods, as well as the removal of patient blinding (patients may choose the specific treatment they wish to receive during this final 3-month period), cross-over response will be analyzed as an exploratory aim versus an inferential aim. Due to the exploratory nature of this aim, additional or adjusted analyses may be performed to best explore and evaluate the data collected. Generalized additive models will be used to explore cross-over results and a limited set of measures will be explored (patient satisfaction, functional tests, ultrasound measures).

Multilevel models will incorporate random effects to account for repeated measures, using distribution families and link functions appropriate for the outcomes of interest, determined using QQ plots analyzed for best model fit. All statistical analyses will be performed using the R Programming language.

11.2 Sample Size:

We are requesting to enroll 160 total participants (40 per initial treatment arm) after adjusting for screen failures and attrition for a final sample of at least 112 (28 per initial treatment arm). 35 patients in each initial treatment group (140 patients total) will achieve 90% power to detect an effect size of 16 points. 30 patients in each initial treatment group (120 patients total) will achieve 90% power to detect an effect size of 17 points. 25 patients in each initial treatment group (100 patients total) will achieve 90% power to detect an effect size of 18 points. Effect size for the purpose of power calculations was defined as the difference between VISA-A at 3 months between PT only and PT + Additional Treatment (assumptions were based on PT + PBMT due to availability of comparable historical research), with statistical significance defined as $\alpha = 0.05$.

11.3 Total number of subjects requested (including records and specimens):

160

11.4 If you are recruiting by study arm, please identify the arms of the study and how many subjects will be enrolled in each arm

Across all performance sites, up to 160 participants will be randomized 1:1:1:1 to the four initial treatment arms (40 participants per arm)

11.5 Please provide a justification for your sample size

Power was calculated using repeated Monte Carlo Markov Chain simulations predicting 3-month VISA-A between treatment arms, and sourced assumptions of mean and spread from Tumilty et al (2016). MCID was considered to be a 6.5 point difference in VISA-A[14].

11.6 Data Analysis Plan: Complete description: Background, Objectives, Design, Step by Step how the project is going to be done, Data analysis plan:

Outliers will be removed if determined to be erroneous based on relevant clinical expertise. Data will be analyzed on a complete-case intention-to-treat (ITT) basis. Confounding will be principally controlled by randomization. In order to increase the precision of our estimates, we may also statistically adjust for patient demographics and relevant clinical variables.

Methods to be used for the Primary Aim: Time-to-event analyses (return to activity) will use survival analysis. All other outcome measures (including our primary outcome measure (VISA-A) and other aforementioned secondary outcome measures) will be analyzed using generalized additive models predicting change in each outcome measure by treatment group at 3 months. Sensitivity analyses for non-time-to-event outcome measures will be performed to evaluate trends by treatment group and will use longitudinal hierarchical/multilevel models incorporating random effects to account for repeated measures. Analyses under the primary aim will use the initial 3-month cohort only.

Methods to be used for the Secondary Aim: Due to the lack of washout period between initial and cross-over periods, as well as the removal of patient blinding (patients may choose the specific treatment they wish to receive during this final 3-month period), cross-over response will be analyzed and treated as an exploratory aim versus an inferential aim. Due to the exploratory nature of this aim, additional or adjusted analyses may be performed to best explore and evaluate the data collected. Generalized additive models will be used and a limited set of measures will be explored (patient satisfaction, functional tests, ultrasound measures).

Hypothesis tests will be two-tailed and statistical significance will be considered at the putative threshold (alpha=0.05). P-values (outside of analysis of primary outcome) will be subject to a false discovery rate adjustment in keeping with best statistical practices. Multilevel models will incorporate random effects to account for repeated measures, using distribution families and link functions appropriate for the outcomes of interest, determined using QQ plots analyzed for best model fit. All statistical analyses will be performed using the R Programming language.

12.0 Participant Information

12.1 Subject Population:

DEERS eligible, adult (between the ages of 18-64, inclusive), active-duty Service members diagnosed with AT.

12.2 Age Range:

Check all the boxes that apply. if the age range of potential subjects (specimens, records) does not match the range(s) selected, please specify in the text box.

- [ ] 0-17
- [x] 18-24
- [x] 25-34
- [x] 35-44
- [x] 45-54
- [x] 55-64
- [ ] 65-74
- [ ] 75+

12.3 Gender:

- [x] Male
- [x] Female
- [ ] Other

12.4 Special categories, check all that apply

- [ ] Minors /Children
- [ ] Students
- [ ] Employees - Civilian
- [ ] Employees - Contractor
- [ ] Resident/trainee
- [ ] Cadets /Midshipmen
- [x] Active Duty Military Personnel
- [ ] Wounded Warriors
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Physically Challenged (Physical challenges include visual and/or auditory impairment)
- [ ] Persons with Impaired Decisional Capacity
- [ ] Prisoners
- [ ] Pregnant Women, Fetuses, and Neonates
- [ ] Non-English Speakers
- [ ] International Research involving Foreign Nationals - Headquarters Review is necessary

You must also consider the requirements of DoDI 3216.02, Enclosure 3, paragraph 7.e.

12.5 Inclusion Criteria:

Order Number	Criteria
1	DEERs Eligible
2	Between ages of 18-64 (inclusive) years old
3	Currently AD in any of the US Armed Forces
4	Clinical diagnosis of mid-portion Achilles tendinopathy (including both unilateral and bilateral) by a healthcare provider based on accepted diagnostic criteria
5	Able to read and understand English language for consent purposes
6	Able to commit to 3-weeks of intervention and 6-months of follow-up

12.6 Exclusion Criteria:

Order Number	Criteria
1	Primary insertional Achilles tendinopathy
2	Platelet Rich Plasma (PRP), corticosteroid injection, or prolotherapy within 3 months
	Received dry needling within the past 4 weeks

3	
4	Previously completed the Silbernagel protocol for Achilles tendinopathy within the past 3 months
5	Received SWT within the past 3 months to their Achilles
6	Tattoo in the area of treatment (due to sensitivity to PBMT)
7	Current use of pacemaker
8	Patients with a known underlying cardiac disease that could be affected by shockwave therapy
9	Patients with neuropathy affecting sensation to pain
10	Current use of medications associated with sensitivity to heat or light (e.g., amiodarone, chlorpromazine, doxycycline, hydrochlorothiazide, nalidixic acid, naproxen, piroxicam, tetracycline, thioridazine, voriconazole)
11	Current or chronic sciatica (lumbosacral radiculopathy) resulting in chronic or intermittent lower extremity pain, numbness, or tingling
12	Achilles tendon tear or prior Achilles tendon surgery
13	Recent lower extremity injury within the last 3 months that required professional medical attention (e.g., ankle sprain, meniscus)
14	Concurrent participation in another research study addressing pain issue
15	Previously enrolled in the study for contralateral (opposite) leg
16	Currently pregnant or plan to become pregnant during intervention period (safety of PBM not established in pregnancy) as determined by hCG urine test
17	Diagnosis of rheumatological disease/connective tissue condition, symptomatic arthritis of foot and ankle, a primary running related injury outside Achilles tendinopathy, other contraindications to PBMT or SWT

13.0 Recruitment and Consent

13.1 Please describe the recruitment process, including how subjects will be identified and selected for the study.

Potential participants will be identified via four methods:

1.Under the provisions of an approved Partial HIPAA Waiver Application for this study, the local study team members will review
medical records of patients coming in to the Sports Medicine, Physical Therapy, Orthopedic, Podiatry, and Physical Medicine & Rehabilitation (PM&R) clinics, for suspected/confirmed AT in order to identify prospective research participants and to seek their authorization to participate/use their protected health information for this research study. The study team will receive approval from the potential participant's provider prior to approaching for possible study participation.

2. Direct referral from local healthcare providers in the local Sports Medicine, Family Medicine, Orthopedic and Podiatry, Physical
Therapy, Holistic Health and Fitness (H2F), and Physical Medicine & Rehabilitation (PM&R) clinics.

3. Patients may self-refer to participate in the study. Interested potential participants will be able to contact a member of the study
team via email. Potential participants who contact the study team directly will be instructed to seek care with the Physical Therapy or their primary care manager for a physical exam and diagnosis of AT, or confirmation of a previous AT diagnosis. The Physical Therapy Clinic is a direct access clinic that does not require a referral.
4. Study advertisements will be posted within the following locations, and copies will be provided to clinic staff:

- Internal Medicine
- Aviation Medicine
- H2F
- McChord Clinic
- Winder Clinic
- Okubo SCMH
- Allen Soldier -Center Medical Home
- SRU
- Puyallup Community Medical Home
- South Sound Community Medical Home
- Armed Forces Wellness Center
- Intrepid Spirit Center
- Madigan Medical Mall
- Pharmacy waiting areas, if possible
- Physical Therapy
- Podiatry
- Sports Medicine
- THOR3
- Physical Medicine and Rehabilitation
- Coffee bar
- Dining Facility entrance
- Intranet screen saver page
- 2/75 Ranger Clinic

Participants who are identified by clinic staff will be provided with information for contacting the study team.

The local research team will keep a separate electronic screening log containing DoD ID number, eligibility status, and date screened. This log will be password protected and stored in a secure folder on a secure drive accessible only by authorized local research staff. This log is needed to avoid any duplicative screening of those that are screen failures or who decline study participation. This reduces burden on potential participants, providers, and study team members and ensures the study team will not screen the same person twice or examine records for eligibility criteria when screen status has already been already established.

13.2 Compensation for Participation:

Participants may receive up to $150 for participation in this research.

Participants will be compensated at the following intervals:

- Completion of 6-week follow-up visit: $50
- Completion of 3-month follow-up visit: $50
- Completion of 6-month follow-up visit: $50

Participants will receive payment in the form of a gift card or Visa-type card equivalent.

Participants will only be paid for applicable research activities that they complete. They will not receive compensation for research activities they do not complete.

In accordance with the DoDI 3216.02, a federal employee (e.g., service member) completing a research activity while *on duty* will not be eligible to receive compensation for their research participation. However, a federal employee completing a research activity while *off duty* will be eligible to receive compensation for their research participation.

In order to receive compensation for participation in this research, a study team member will ask the participant to confirm their leave status in accordance with US Code Title 5, Section 6382. It will be the responsibility of the study participant to provide accurate information regarding their leave status at the appropriate compensation intervals. Upon request, the PI and/or authorized

study team member may provide certification for intermittent leave, or leave on a reduced leave schedule, for planned study medical treatment(s) (in accordance with US Code Title 5, Section 6383).

13.3 Please describe the pre-screening process. If no pre-screening, enter Not Applicable in the text editor

This study has two screening phases: 1) Pre-screening based on initial inclusion/exclusion criteria (before informed consent) and 2) a formal screening phase to determine eligibility for randomization to intervention arm (after informed consent).

Pre-Screening (before consent):
If a potential participant expresses interest in learning more about the research study, a member of the research staff will briefly introduce the study, express the voluntary nature of participation, assess interest in participating, and screen the potential participant for initial eligibility in close collaboration with the patient's attending provider. Pre-screening conversations may also take place remotely using the Screening Script (Appendix O).

Initial eligibility (see Protocol Sections 12.5 *Inclusion Criteria* & 12.6 *Exclusion Criteria*) will be confirmed in-person using an Inclusion/Exclusion CRF (Appendix A). This Inclusion/Exclusion CRF does not record any PII/PHI.

Individuals that do not meet inclusion/exclusion criteria will be encouraged to continue to seek care with their primary care provider and/or direct access at physical therapy.

If the potential participant meets eligibility criteria as determined by the Inclusion/Exclusion CRF and expresses interest in participating in the study, an authorized study team member will initiate the formal consent discussion and, if applicable, obtain informed consent. See protocol section 13.4 for additional information on the consent process.

Formal Screening (post-consent):
As part of the formal screening procedures, all consented participants that are biological females of child-bearing age and capacity will be required to complete a urine hCG pregnancy test. If the pregnancy test is positive, per the inclusion/exclusion criteria, the participant will be formally withdrawn from the study at this point, and will be encouraged to seek care with their primary care physician. If the pregnancy test is negative, the participant will be eligible to be randomized to a study arm and continue with the study procedures.

13.4 Consent Process: Revised Common Rule, Section 219.116: General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.

Are you requesting a waiver or alteration of informed consent?

○ Yes ◉ No

Please explain the consent process:

Consent will be obtained in accordance with principles of Belmont Report and Common Rule guidelines.

The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy of the signed consent form will be given to the participant and the original will be stored in a locked cabinet inside of a locked office within the Sports Medicine Clinic at Madigan. Documentation of consent will be recorded in the participant's medical record. No Legally Authorized Representatives will be utilized.

Formal consent, as represented by the act of signing a dated, IRB approved consent statement for the study will only occur after confirming eligibility using the Inclusion/Exclusion CRF, a thorough review of what is involved in the study, and after all questions have been answered. Potential participants will be provided information regarding all available study treatments and reminded of the expectations placed on them if they enroll, including the blinding and randomization processes.

The potential participant will be given a copy of the informed consent document to read before, during, and/or after discussion of the informed consent with the Research Coordinator, Principal Investigator, Associate Investigator, or other authorized study team member. Sufficient time will be given to the potential participant to understand the study purpose, study procedures, time commitments, potential risks and benefits, and the types of health information that will be accessed, collected, and used by the research team if they agree to participate in the study.

Questions can be raised by the potential participant at any time during the consent discussion and at any time during the conduct of the study. The potential participant will be instructed that their participation is completely voluntary and that they may withdraw from the study at any time without penalty. Their decision to participate or to not participate, or to withdraw from the study after consent, will not affect their access to health care that they are otherwise entitled to and it will not affect their military position.

The authorized study team member present during the consent conversation will confirm that the potential participant has no additional questions before deciding to provide consent.

Every effort will be made to eliminate the perception of authority, which is a particularly important consideration when recruiting active-duty study participants. When applicable, the study investigators will be in scrubs or civilian clothes instead of uniform and will introduce themselves as doctor rather than their military rank. Some potential participants may be patients of the study PI or AI. In these cases, the consent conversation will be initiated by non-physician study staff to prevent any misconception of coercion or undue influence.

Informed consent and HIPAA authorization will be obtained in person.

In the event that there are significant new findings regarding the therapy that may affect participants' willingness to continue in the study, an information sheet will be provided to all current and past participants. The informed consent document will be amended for future participants.

Following completion of informed consent, the results of the Inclusion/Exclusion CRF will be entered into REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a DoD server and maintained by the Uniformed Services University Information Technology (USU IT), and a unique study ID will be generated. This coded study ID will be used on all research data collection forms in place of the participant's name, Department of Defense (DoD) ID, or other protected identifier. No PII will be entered into REDCap. Please see Appendix R for additional information on REDCap.

In order to document screen failures and refusals, the results of the Inclusion/Exclusion CRF may be entered into REDCap even if a patient doesn't consent to participate in the study. The Inclusion/Exclusion CRF does not record any PHI/PII.

13.5 DoDI 3216.02 requires an ombudsman to be present during recruitment briefings when research involves greater than minimal risk and recruitment of Service members occurs in a group setting. If applicable, you may nominate an individual to serve as the ombudsman.

- (●) N/A
- ( ) Propose ombudsman

13.6 Withdrawal from Study Participation:

Explain the process for withdrawal and specify whether or not the subjects will be given the opportunity to withdraw their data their data/specimens in the event they wish to withdraw from the study

Participant Withdrawal:
Participants may withdraw from the study at any time without penalty. Participants will be informed that withdrawal will not affect their access to health care that they are otherwise entitled to and it will not affect their military position.

If a participant withdraws from the study, we may retain and analyze all coded/de-identified data collected up to the time of withdrawal if the data is necessary to maintain the integrity of the study. However, no further data will be collected after the date of withdrawal.

Participants may contact the study research coordinator/assistant or Principal Investigator to formally withdraw from the study. Participants will be advised to follow-up with their personal physician if they choose to withdraw.

Withdrawal Without Participant Consent:
Participants will be withdrawn if they fail to meet the formal screening criteria outlined in protocol section 13.3.

Additionally, a participant may be withdrawn from the study without their consent if remaining in the study might be dangerous or harmful to them. Participation may also be stopped if the military mission requires it, if they lose their right to receive medical care at a military hospital, if the study is canceled, if they fail to adhere to the protocol and/or therapy plan, or if they display inappropriate behavior towards study personnel.

The reason for any withdrawal/removal will be documented.

14.0 Risks and Benefits

14.1 Risks of Harm:

Identify all research-related risks of harm to which the subject will be exposed for each research procedure or intervention as a result of participation in this study. Consider the risks of breach of confidentiality, psychological, legal, social, and economic risks as well as physical risks. Do not describe risks from standard care procedures; only describe risks from procedures done for research purposes

The potential risks directly associated with study-specific activities and procedures are minimal.

Physical Therapy (PT)
Possible risks associated with physical therapy treatment include: worsening of pre-existing conditions, continued and/or increased pain that may limit activities, no improvement in mobility or strength, soreness, or failing during and/or injury from physical therapy exercises and/or performance-based tests.

Research Procedure: Shockwave Therapy (SWT)
The OrthoPlus Ultra 100 is a Class I FDA approved device with minimal risk. It is a low energy device and no severe events have been reported. Reported discomforts of shockwave include bruising, swelling and rarely, tissue damage. Pain response is expected due to device treatment over sites of injury and use of process of clinical focusing; we will monitor each participant and adjust treatment settings to ensure pain is tolerable during the treatment. Participants may stop the SWT at any time.

Research Procedure: Photobiomodulation (PBM) Therapy
The risks associated with PBMT are minimal. PBM treatment is used by a variety of healthcare practitioners for painful clinical conditions. Mild discomfort may be experienced during the treatment, the treatment should not be "hot", but participants should notify the study team member if they feel any uncomfortable warming. Individuals with neuropathies or difficulty distinguishing changes in skin temperature are at higher risk. Potential research-related risks include damage to eye structures and skin, which are both very rare.

Additionally, any time information is collected for a study, there is a small risk of breach of confidentiality.

14.2 Measures to Minimize Risks of Harm (Precautions, safeguards):

For each research procedure or intervention, describe all measures to minimize and/or eliminate risk of harms to subjects and study personnel

The laser device (LightForce XPi) will be processed through MAMC Property and safety checked through Healthcare Technology Management and Sustainment (HTMS) before being used. A member of the research team will serve as a clinical laser safety officer (CLSO) to establish and manage the study-specific laser safety program. The designee will work with the MAMC Laser Safety Officer (LSO) and participate in the MAMC Laser Safety Committee (LSC) meetings quarterly to receive proper training. Along with the LSO and CLSO, the PI will ensure that the treatment space meets all regulatory requirements for utilization of a treatment laser, including appropriate signage and use of laser blocking screens to absorb any potential scatter/refraction of light outside of the treatment area.

Protective eyewear will be worn by all participants and study team members during treatment sessions to avoid damaging their eyes.

In the rare occurrence that participants experience uncomfortable warmth over the treatment area during PBMT, the treatment will be modified or stopped.

In the occurrence that participants experience a high level of pain during SWT, the treatment will be modified or stopped.

In order to protect participant confidentiality, research data will be identified using a unique study ID only, and not by participant name, date of birth, DoD ID, or other similar identifier. All available measures allowed by law will be taken by research staff to protect participant confidentiality. See protocol section 14.3 for additional information.

Check-ins occur frequently to address any adverse events associated with the rehabilitation protocol. All participants will be evaluated for adverse events at each follow-up visit. All adverse events, regardless of severity, will be reported to the Principal Investigator. The Principal Investigator will review all adverse events. Adverse events will also be reported according to the guidelines stated in Protocol Section 16.1.

14.3 Confidentiality Protections (for research records, data and/or specimens):

Describe in detail the plan to maintain confidentiality of the research data, specimens, and records throughout the study and at its conclusion (e.g., destruction, long term storage, or banking). Explain the plan for securing the data (e.g., use of passwords, encryption, secure servers, firewalls, and other appropriate methods). If data will be shared electronically with other team members/collaborators outside the institution, describe the method of transmission and safeguards to maintain confidentiality. Explain whether this study may collect information that State or Federal law requires to be reported to other officials or ethically requires action, e. g., child or spouse abuse

Upon consenting for the study, participants will be assigned a unique study ID. With the exception of the Informed Consent Form, HIPAA Authorization, and electronic Master List, all research data (both paper and electronic) will be identified using this unique study ID only, and not by the participant's name, date of birth, DoD ID, or other protected identifier.

Paper research forms and source documents will be stored in a locked cabinet inside of a locked room within the Sports Medicine Clinic at Madigan, accessible only by local research staff designated and authorized by the Principal Investigator. The paper Intake CRF which records participant contact information, Informed Consent Forms and HIPAA Authorizations will be stored separately from the coded paper research forms in a locked cabinet inside of a locked room within the Sports Medicine Clinic, accessible only by authorized local research staff.

The coded electronic research data for this study will be stored in REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD) server and maintained by the Uniformed Services University Information Technology (USU IT). The local study team will manage the storage and upload of ultrasound in TeleRay, which is an encrypted and access controlled data platform. No PHI/PII will be entered into REDCap or TeleRay. See Appendix R for additional information on REDCap.

The local study team will maintain a separate electronic Master List which matches the unique study IDs with participant identifying information. The electronic Master List will be stored separately from the coded electronic research data in a secure, password-protected electronic document on a computer and network that requires CAC access.

All research data and forms (both paper and electronic) will only be accessible by authorized study staff, the IRB of record, the local research office, and applicable governmental agencies as part of their duties and in accordance with federal law (except as stated in the next paragraph). These duties include making sure that research participants are protected.

Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR), which is based out of the Department of Physical Medicine & Rehabilitation (PM&R) at the Uniformed Services University (USU), is serving as the data coordinating center for this research study. As such, authorized staff from MIRROR/USU will have access to the coded research data that is entered into REDCap. Authorized staff from MIRROR/USU will not have access to the electronic Master List, the paper research records, or any participant PHI/PII. There will be appropriate data sharing agreements in place.

Any research data shared with an approved agency for review will be linked only to the participant's unique study ID and not with the personal identity of the participant (i.e., name, DOB, DoD ID, address, phone number, etc.). If the research data is used in scholarly presentations or journal articles, the investigators will protect the anonymity of individual participants and report only aggregate data (e.g., group means) where appropriate.

Participants will not be individually identified in any publication or presentation of research results.

14.4 Potential Benefits:

Describe any real and potential benefits of the research to the subject and any potential benefits to a specific community or society

If the individuals in the research are considered experimental subjects (per 10 USC 980), and they cannot provide their own consent, the protocol must describe the intent to directly benefit all subjects

We cannot guarantee that participants will benefit from participation in this research study. The aim of this study is to improve recovery of AT, it is expected that all treatment arms will help AT recovery, some treatments potentially quicker that other, more traditional treatment options. This may also provide better/faster treatment pathway(s) for AT in the AD and larger physically active populations.

14.5 Privacy for Subjects:

Describe the measures to protect subject's privacy during recruitment, the consent process, and all research activities, etc.

Recruitment, consent conversations, and follow-up research activities will take place in a private setting (e.g., closed clinic room, investigator's office, etc.) to minimize the potential opportunity to be overheard or inadvertently witnessed. Information being collected will be limited to only the minimum amount of data necessary to accomplish the proposed research.

14.6 Incidental or Unexpected Findings:

Describe the plan to address incidental findings and unexpected findings about individuals from screening to the end of the subject's participation in the research. In cases where the subject could possibly benefit medically or otherwise from the information, state whether or not the results of screening, research participation, research tests, etc., will be shared with subjects or their primary care provider. State whether the researcher is obligated or mandated to report results to appropriate military or civilian authorities and explain the potential impact on the subject

There is the possibility incidental findings could reveal information the participant would not otherwise be aware of. In cases where the participant could possibly benefit medically or otherwise, the participant will be notified and, when appropriate, so will their primary care provider. Research representatives will not share incidental and unexpected findings with anyone else unless required by law.

In cases involving military personnel, information regarding their health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

Although unlikely, incidental findings could impact a participant's future ability to receive health or life insurance, as is the case with all medical care. Incidental findings may also make the participant feel anxious.

15.0 Study Monitoring

15.1 Your study requires either Data and Safety Monitoring Plan (DSMP) or a Data and Safety Monitoring Board (DSMB).

- (•) DSMP
- ( ) DSMB
- ( ) Both
- ( ) Not Applicable

A DSMP should describe the plan to monitor the data to verify that the data are collected and analyzed as specified in the protocol. Include who will conduct the monitoring, what will be monitored, and the frequency of monitoring. It should also include the plan to ensure the safety of subjects

Participant Safety Monitoring Plan:
To ensure the safety of participants the PI will:

1. Monitor the conduct of the protocol per the approved study plan and ensure protection of human participants. This may involve periodic review of medical records and/or research files of enrolled participants.
2. Review and keep abreast of adverse events and protocol deviations that occur during the research.
3. The PI will review and sign adverse event logs/reports, protocol deviation logs/reports, and continuing reviews/annual progress reports.
4. If there is concern about the welfare of enrolled participants, the PI will stop the research study in progress, remove individual participants from a study, and take whatever steps necessary to protect the safety and well-being of research participants until the IRB can assess the situation.
5. Ensure that all study team members keep current required human subjects research trainings which require renewal every 3 years.

If an adverse event or protocol deviation occurs, it will be evaluated by the Principal Investigator and appropriate actions will be taken as outlined in Section 16.0 Reportable Events. In the case of an emergency, first responders will be called. In order to address the challenge of early identification of an increased risk of a known adverse event, all adverse event data will be tracked and evaluated.

On-site physicians will monitor the progress and health of the participants alongside our Principal Investigator. Participants can elect to withdraw from the study at any time. Participants may also be taken out of the study at any point if a research provider (or one of their treating providers)

determines that it is no longer safe for them to continue with the study. If a participant elects to drop out of the study or is withdrawn for safety reasons, they will resume standard of care treatment with their assigned health provider(s).

Data Monitoring Plan:
Data will be collected and stored in both paper CRF and electronic format as described previously in protocol section 10.14 Data Management. In addition to data quality and data validation checks done continually by REDCap for electronic format data, authorized MIRROR staff will perform routine checks of the coded electronic data entered into REDCap and Teleray to ensure that data has been properly input and that data entry is consistent with expected values. The local PI will ensure that paper research forms and the electronic Master List are completed and securely stored in accordance with stated protocol procedures.

Please see protocol Section. 14.3 Confidentiality Protections and 14.5 Privacy for Subjects for additional information regarding how we will protect participant privacy and confidentiality throughout this study.

16.0 Reportable Events

16.1 Reportable Events: Consult with the research office at your institution to ensure requirements are met. Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event.

Consult with the research office at your institution to ensure requirements are met

• Describe plans for reporting expected adverse events. Identify what the expected adverse events will be for this study, describe the likelihood (frequency, severity, reversibility, short-term management and any long-term implications of each expected event)

• Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the research protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event

AEs/SAEs/UPIRTSOs:
The study overall is considered to be minimal risk for study participants, defined as not substantially above what would be encountered in everyday life including provision of routine medical care for the condition of Achilles tendinopathy. Potential risks are preventable by ensuring that appropriate and rigorous screening procedures are in place, and risk mitigation procedures (e.g., wearing appropriate eye protection) are utilized. Based on clinical use of this technology, and reports from other research studies, the risk of expected adverse events is low.

However, all reportable events, regardless of severity, will be reported to the Principal Investigator. The Principal Investigator will review all adverse events and make a determination of severity and relationship to participation in the research study.

All Serious Adverse Events (SAEs) that are unexpected and related, or possibly related, to study participation will be reported to the IRB via telephone or email within 24 hours of discovery and a complete written report via eIRB will follow within 5 business days.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs) will be reported to the IRB via telephone or email within 24 hours of discovery and a complete written report via eIRB will follow within 5 business days.

Unexpected (but not serious) adverse events (AEs) occurring in subjects which, in the opinion of the PI, are related or possibly related to study participation AND places subjects or others at a greater risk of harm that was previously known or recognized in the protocol will be reported to the IRB via telephone or email within 24 hours of discovery and a complete written report via eIRB will follow within 5 business days.

Expected AEs/SAEs and AEs/SAEs that are not related or not possibly related to study participation will be tracked by the local study team using an Adverse Event Tracking Log and reported to the IRB at the time of continuing review or, if applicable, at study closure.

Continuing Review (CR) Progress Reports are generally performed on a 12-month cycle. More frequent
Progress Reports may be required at the discretion of the IRB.

Protocol Deviations:
All protocol deviations, both major and minor, will be reported to the Principal Investigator. The Principal Investigator will review all protocol deviations.

Major protocol deviations, as determined by the Principal Investigator, will be promptly reported to the IRB via telephone or email within 24 hours of discovery and a complete written report will follow within 5 working days.

Minor protocol deviations will be tracked by the local study team using a Protocol Deviation Log and reported to the IRB at the time of continuing review or, if applicable, at study closure. Follow up visits that occur outside of the windows stated in protocol will be considered minor protocol deviations.

17.0 Equipment/non-FDA Regulated Devices

17.1 Does the study involve the use of any unique non-medical devices/equipment?

○ Yes ◉ No

18.0 FDA-Regulated Products

18.1 Will any drugs, dietary supplements, biologics, or devices be utilized in this study?

- ☐ Drugs
- ☐ Dietary Supplements
- ☐ Biologics
- ☑ Devices
- ☐ N/A

18.3 Device Details:

- ☑ Are device(s) in this research being used in accordance to the approved labeling?
- ☐ Are device(s) in this research being used in a manner other than its approved labeling?

When adding a device indicate in the details section of the device if the use is either used in accordance to the approved labeling or in a manner other than it's approved labeling

View Details	Device Name
⊟	LightForce® XPi therapy laser

Manufacturer/Supplier of Device	LiteCure, DJO Global
Where will the Devices Be Stored	In the research area
Will Devices be supplied at no Cost	No

Is this a HUD (HDE)	No
HDE Number	N/A
Who holds the IDE	N/A
IDE details	

⊟ OrthoPlus Ultra 100

Manufacturer/Supplier of Device	CuraMedix
Where will the Devices Be Stored	In the research area
Will Devices be supplied at no Cost	No
Is this a HUD (HDE)	No
HDE Number	N/A
Who holds the IDE	N/A
IDE details	

18.4 Reporting Requirements for FDA-regulated research under IND and IDE:

Describe the process for complying with FDA regulatory requirements for adverse event reporting and adverse device effects reporting to the sponsor

The PI will be responsible for reporting any unanticipated adverse effects and unanticipated problems to the FDA.

18.5 Sponsor (organization/institution/company):

☑ N/A

If applicable, provide sponsor contact information:

19.0 Research Registration Requirements

19.1 ClinicalTrials.gov Registration:

- ○ Registration is not required
- ◉ Registration pending
- ○ Registration complete

19.2 Defense Technical Information Center Registration (Optional):

- ◉ Registration is not required
- ○ Registration pending
- ○ Registration complete

20.0 References and Glossary

20.1 References:

1. Rhim, H. C*., et al*. Comparative Efficacy and tolerability of Nonsurgical Therapies for the Treatment of Midportion Achilles Tendinopathy: A Systematic Review With Network Meta-Analysis. *The Orthopaedic Journal of Sports Medicine* **8** (7), 1-8 (2020)
2. Tumilty, S., et. al. Photobiomodulation and eccentric exercise for Achilles tendinopathy: a randomized control trial. *Lasers in Medical Science* **31**, 127-135 (2016).
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4. Zafar, M. S*., et al.* Basic science and clinical aspects of Achilles tendinopathy*. Sports Med Arthrosc Rev* **17**(3), 190-197 (2009)
5. Jones B. H., *et al.* Medical surveillance of injuries in the U.S. Military descriptive epidemiology and recommendations for improvement. *Am J Prev Med.* **38** (1), S42-60 (2010).
6. Do Santos, S. A., *et al.* Parameters and Effects of Photobiomodulation in Plantar Fasciitis: A Meta-Analysis and Systematic Review. *Photobiomodulation, Photomedicine, and Laser Surgery* **37** (6), 327-335 (2019)
7. CuraMedix, OrthoPulse^{TM} Ultra Operations Manual Part No. 23300.0100, **www. curamedix.com**
8. Burton, I., Combined extracorporeal shockwave therapy and exercise for the treatment of tendinopathy: A narrative review, *Sports Medicine and Health Science,* **4** (1), 2022, 8-17, ISSN 2666-3376, https://doi.org/10.1016/j.smhs.2021.11.002.
9. Celik, D., *et al*. Photobiomodulation Therapy Versus Extracorporeal Shock Wave Therapy in the Treatment of Lateral Epincondylitis. *Photobiomodulation, Photomedicine, and Laser Surgery* **37** (5), 269-275 (2019)
10. Silbernagel, K. G. & Crossley, K. M. A Proposed Return-to-Sport Program for Patients with Midportion Achilles Tendinopathy: Rationale and Implementation. *Journal of Orthopaedic & Sports Physical Therapy* **45(**11), 876-886 (2015)
11. Silbernagel, K. G., *et al*. Continued Sports Activity, Using a Pain-Monitoring Model, During Rehabilitation in Patients with Achilles Tendinopathy: A Randomized Control Trial. *The American Journal of Sports Medicine* **35**(6), 897-906 (2007)
12. *Azevedo, et al.* Biomechanical variables Achilles tendinopathy. *British Journal of Sports Medicine* **43**(4), 288-292 (2009)
13. Franettovich, M.M. *et al*. Neuromotor control of gluteal muscles, *Med. Sci. Sports Exerc*. **4 6**(3), 594-599 (2014)
14. Mccormack, et al. The Minimum Clinically Important Difference On The Visa-A And Lefs For Patients With Insertional Achilles Tendinopathy*. International Journal of Sports Physical Therapy.* 10, 639-644. (2015)

20.2 Abbreviations and Acronyms:

Achilles Tendinopathy (AT)
Active-Duty (AD)
Active-Duty Service Member (ADSM)
Advanced Encryption Standard (AES)
Adverse Event (AE)
Associate Investigator (AI)
Case Report Form (CRF)
Common Access Card (CAC)
Continuing Review (CR)
Datagram Transport Layer Security (DTLS)
Date of Birth (DOB)
Defense and Veteran's Pain Rating Scale (DVPRS)
Defense Health Agency (DHA)
Department of Defense (DoD)
Eccentric strengthening (ECC)
Electronic Medical Record (EMR)
Extracorporeal shockwave therapy (ESWT)
Food and Drug Administration (FDA)
Hash-based Message Authentication Code- Secure Hash Algorithm 1 (HMAC-SHA1)
Health Insurance Portability and Accountability Act (HIPAA)
Holistic Health and Fitness (H2F)
Human Research Protection Office (HPRO)
Institutional Review Board (IRB)
Internet Engineering Task Force (IETF)

Laser Safety Officer (LSO)
Lower Extremity Functional Scale (LEFS)
Megahertz (MHz)
Musculoskeletal Injury (MSI)
Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR)
Patient-Reported Outcomes Measurement Information System (ProMIS-29)
Personally Identifiable Information (PII)
Photobiomodulation (PBM)
Photobiomodulation therapy (PBMT)
Physical Medicine & Rehabilitation (PM&R)
Physical Therapy (PT)
Platelet Rich Plasma (PRP)
Principal Investigator (PI)
Protected Health Information (PHI)
Protocol Deviation (PD)
Range of Motion (ROM)
Research Coordinator (RC)
Research Electronic Data Capture (REDCap)
Return/ing to duty (RTD)
Secure Access File Exchange (SAFE)
Secure Real-time Transport Protocol (SRTP)
Secure Sockets Layer (SSL)
Serious Adverse Event (SAE)
Shockwave therapy (SWT)
Standard of Care (SOC)
The University of Wisconsin Running Injury and Recovery Index (UWRI)
Timepoint (T)
Transport Layer Security (TLS)
Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs)
Uniformed Services University (USU)
Uniformed Services University Information Technology (USU IT)
Victorian Institute of Sports Assessment – Achilles (VISA-A)