CARILION CLINIC
Institutional Review Board

NEW APPROVAL

PI: Ralph Brown, MD
CC - Carilion New River Valley Medical Center

Re: IRB Approval for Protocol #IRB-22-1780, Clinical Evaluation of a Device for Treatment of Lymphedema of the Upper Extremity

Approval Date: **03/05/2024**
Expiration Date: **02/21/2025**

The Carilion Clinic Institutional Review Board (IRB) has **fully approved** the above referenced study via the fully convened committee for one year (**reviewed on 2/22/2024**). This approval is limited to the activities conducted by the research team members as described in the approved version of the IRB Application (**Version 1.4**). Modifications may not be initiated without prior IRB review and approval except where necessary to eliminate apparent immediate hazards to human participants.

Please note the study expiration date above. All research activities must cease the day before the Expiration Date if the study has not been reapproved by the IRB.

If this study is expected to extend beyond one year, please submit a continuing review request at least 45 days prior to the expiration date. HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk but not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the Expiration Date. Once research activities have been completed, including analysis of all identifiable data, submit a Closure form at least 30 days prior to the Expiration Date. Please retain copies of all records pertaining to this study for a minimum of six (6) years from study closure.

This IRB determined that the study met the criteria for a Non-Significant Risk Device study.

Clinicaltrials.gov: The study meets requirements to be registered on Clinicaltrials.gov. Please ensure you are familiar with all the requirements of Section 801 of the Food and Drug Administration Amendments Act (https://clinicaltrials.gov/ct2/manage-recs/fdaaa), as there are consequences for not registering, including potential fines. You must register this clinical trial prior to enrollment of the first participant. Please contact research@carilionclinic.org for assistance with the ClinicalTrials.gov Protocol Registration and Results System (PRS).

OBTAINING INFORMED CONSENT: Delegated research team members are responsible for obtaining **written** informed consent in the manner approved by the IRB.

- When obtaining **CONSENT** from subjects, **the consent document must contain the Carilion Clinic IRB approval date in the footer of the document**. Please always access the consent form from within the PRIS3M system to ensure the most recently approved version is being used. Please document the consent process within the research record after obtaining consent from subjects.
- **As part of this approval, the IRB has issued a consent document(s) that includes the approval date**. The consent document does not include an expiration date. The approval for the consent document will last the life of the study, or until it is amended; whichever comes first. It is the responsibility of the principal investigator and the research study team to monitor the expiration date of the study for continuing review purposes. It is the responsibility of the principal investigator and the research study team to ensure that no participant is enrolled if the expiration date for the study's IRB continuing review has been exceeded.

- **Electronic consent (eConsent)** has been approved for this study. Please provide both the IRB stamped eConsent and standard consent to HART with a copy of this letter in order for HART to begin the eConsent build in REDCap.
- The Carilion IRB has granted a partial waiver of the requirement of informed consent **for recruitment purposes only** as outlined in 45 CFR 46.116(d). A partial waiver of consent for recruitment purposes permits researchers to obtain information or biospecimens to screen, recruit, or determine eligibility and interest of prospective subjects for a research study without informed consent. This is applicable if (1) the information is obtained through oral or written communication with the subject or the subject's legally authorized representative, or (2) identifiable private information or identifiable biospecimens are obtained by accessing records or stored identifiable biospecimens.

HIPAA WAIVER:

- The Carilion IRB has granted a partial Waiver of Authorization to use and access protected health information for the above-mentioned study for recruitment purposes only.

In conducting this study, you are required to follow the requirements described in INVESTIGATOR GUIDANCE: Investigator Obligations (HRP-800), **found at the end of this letter** and located on the Carilion Clinic IRB website at https://www.carilionclinic.org/irb/policies, including reporting requirements for Unanticipated Problems and privacy breaches.

Please note that this letter conveys IRB approval only and **does not grant Conflict of Interest clearance**. It is the Principal Investigator and research team members' responsibilities to ensure they have completed an Annual COI Disclosure or Transactional Disclosure and CITI COI training. Any potential or perceived conflict or any changes that result in a potential conflict must be disclosed to the Office of Integrity and Compliance within 30 days. Disclosure and conflict management, if applicable, must occur before any employee is permitted to engage in any human subjects research activities. The COI policy can be reviewed at https://www.carilionclinic.org/IRB-OIC-Research-COI-Policy.

Please note that this letter conveys IRB approval only and does not grant institutional approval.
If your research involves any Carilion Clinic facilities, then separate arrangements must be made with the appropriate hospital or medical staff department or committees, along with the Carilion Clinic Department of Research & Development.

Participant Compensation: Please contact the Research and Development Office at research@carilionclinic.org if you need to discuss setting up the payment method to your research participants. The Principal Investigator is ultimately responsible to assure proper accounting of payments made to subjects for fiscal accountability and federal tax purposes and to maintain privacy of the human subject.

Research Data Management and Storage: Please contact HART at hart@carilionclinic.org for data management and storage implementation questions.

Carilion Clinic operates under Federal-Wide Assurance FWA00000392.

The Carilion Clinic Institutional Review Board would like to thank you for the opportunity to review this protocol. Please contact Eric Wines at 540-224-5885 or irb@carilionclinic.org if you have any questions regarding this letter.

HRP-800: INVESTIGATOR GUIDANCE: Investigator Obligations

1. PURPOSE

1.1 This guidance describes the obligations of Principal Investigators conducting <Human Research> overseen by Carilion Clinic's local IRB.
1.2 For research overseen by an IRB other than Carilion Clinic's local IRB, investigators should follow the requirements of that IRB.

2. GUIDANCE

2.1 Do not begin research until you have the IRB approval letter and obtained all other required approvals, such as R&D authorization, biosafety approval, and approvals of departments or divisions that require approval of the use of their resources.

2.1.1 If there are any questions about whether you are conducting research involving human subjects, submit form Human Subjects Research Determination and wait for the IRB's determination before commencing the study.

2.2 Personally conduct or supervise the research.

2.3 Protect the rights, safety, and welfare of subjects involved in the research.

2.4 Conduct the research in accordance with the relevant current protocol approved by the IRB, and comply with all requirements and determinations of the IRB, as well as Federal, state, and local laws and regulations, and be guided by the principles contained in the Belmont Report.

2.5 Ensure the research protocol is consistent with the proposal for funding for extramural or intramural support

2.6 Employ sound study design in accordance with the standards of your discipline and design studies in a manner that minimizes risks to subjects.

2.7 Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time and oversight of all research team members, appropriately qualified research team members, equipment, and space.

2.8 Education and training requirements are described in SOG 7.1 IRB Education and Training: INVESTIGATOR AND KEY STUDY PERSONNEL TRAINING.

2.9 Unless the IRB affirmatively approved a protocol to include the following populations, such subjects may not be enrolled:

2.9.1 Adults unable to consent
2.9.2 Children
2.9.3 Neonates of uncertain viability
2.9.4 Nonviable neonates
2.9.5 Pregnant women
2.9.6 Prisoners
2.9.7 Individuals unable to speak English

2.10 When consent, parental permission, or assent are required by the IRB, ensure that they are obtained utilizing the IRB stamped form and documented in accordance with the relevant current protocol as approved by the IRB prior to any study procedures bring performed.

2.11 Submit proposed modifications to the IRB prior to their implementation.

2.11.1Do not make modifications to the research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.

2.12 Submit Continuing Review or Annual Check-in, as described in the approval letter, in the time frame requested by the IRB.

2.13 Submit a study closure to end the IRB's oversight;

2.13.1 When **all** the following apply:

2.13.1.1 The protocol is permanently closed to enrollment;
2.13.1.2 All subjects have completed all protocol related interventions and interactions;
2.13.1.3 No additional identifiable private information about the subjects is being obtained;
2.13.1.4 Analysis of private identifiable information is completed.

2.13.2 When a study has expired or been administratively closed due to a continuing review not being submitted before expiration

2.14 If research approval expires, immediately stop all research activities including analysis of identifiable data, and do not resume the research study until the Continuing Review has been approved by the IRB.

2.15 Promptly report to the IRB the information items listed in HRP-071 Prompt Reporting Requirements to the IRB and SOG 6.4 Non-Compliance.

2.16 Follow Carilion Clinic's requirements to disclose financial interests.

2.16.1 Disclose conflicts of interest for all study team members on submission of an initial review.

2.16.2 Disclose changes to your conflicts of interest.
2.16.2.1 On submission of continuing review
2.16.2.2 Within 30 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest that would have required disclosure on initial review

2.17 Retain research records for the greater of:
2.17.1 At least three years after completion of the research.
2.17.2 If the study involves Protected Health Information, research records must be maintained for a minimum of six years after the completion of the research.
2.17.3 For drug studies conducted under an IND, two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified.
2.17.4 For device studies conducted under an IDE or abbreviated IDE, two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.
2.17.5 The retention period required by the sponsor
2.17.6 The retention period required by local, state, or international law.
2.17.7 The retention period required by a site that is not part of Carilion Clinic.

2.18 Contact the Research & Development Department regarding the need for a contract and letter of indemnification if your study involves any funding or resources from an outside source, or if you will be sharing data outside of Carilion Clinic prior to publication. If it is determined that either a contract or letter of indemnification is needed, subjects cannot be enrolled until these documents are complete.

2.19 Maintain confidentiality of all information gained during the conduct of research at Carilion Clinic, including but not limited to information about patients, employees, physicians, and students.

2.20 Do not accept or provide payments to professionals in exchange for referrals of potential subjects ("finder's fees").

2.21 Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments") without prior IRB approval.

2.22 Notify the IRB immediately if involved in any regulatory or misconduct litigation or investigation by the FDA, or if you are debarred by the US FDA from involvement in clinical research studies.

2.23 If unable to perform the duties as outlined above for an extended period of time, you will close the study or transfer the duties of PI to the sub-investigator or to another qualified individual.

Carilion IRB Application (Version 1.4)

1.0 General Information

*Please enter the full title of your study (#[%irb_number%]):		
Clinical Evaluation of a Device for Treatment of Lymphedema of the Upper Extremity		
***Please enter an abbreviated study title or key words you would like to use to reference the study:**		
Upper extremity lymphedema * This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.		

2.0 Add departments

2.1 Add the departments of all Key Study Personnel that will be involved with the design, conduct, or reporting on this project:

Is Primary?	Department Name
	CC - Carilion - Other
	CC - External - VTCSOM
	CC - External- Virginia Tech Blacksburg

3.0 ■ Assign key study personnel(KSP) access to the study

3.1 * Please add a Principal Investigator for the study:

Name	Role	Training Record
Brown, Ralph Jr, MD	**Principal Investigator**	View Training Record

3.2 Please add the Research Staff, if applicable:

A) Additional Investigators

Name	Role	Training Record
Molotkova, Evgeniya, MD Candidate	**Sub-Investigator**	View Training Record
Muelenaer, Andre	**Sub-Investigator**	View Training Record
Newberry, Tara	**Sub-Investigator**	View Training Record

B) Research Support Staff

Name	Role	Training Record

Fielder, Annette	**Other**	View Training Record
Spivey, Cara	**Research Coordinator**	View Training Record

3.3 *Please add a Study Contact:

Name	Role	Training Record
Molotkova, Evgeniya, MD Candidate	**Study Contact**	View Training Record
Spivey, Cara	**Study Contact**	View Training Record

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

4.0 Key Study Personnel (KSP) Info

4.1 Provide the following information below for each Carilion Clinic research team member: You will be asked to provide information about members of the research team that are outside Carilion at a later time.

Click "add another entry" to respond to this item.

****CITI Training in Human Subjects Research Biomedical Researchers and GCP (for FDA-regulated and NIH-funded) will be verified for each team member before the application will be reviewed by the IRB. Detailed instructions for Carilion's CITI training requirements can be found at https://www.carilionclinic.org/irb/education . Please ask all team members to ensure their Carilion email address is added to their CITI account profile so that their CITI training is pulled into this system. This feed occurs on a nightly basis.***

Entry 1

Research team member name:	Molotkova, Evgeniya, MD Candidate
Degree:	BS
Status:	VTCSOM Medical Student **If other, specify:**
Email address:	emolotkova3@vt.edu
Phone number:	6784353316
Alternate phone number (optional):	
Affiliation:	VTCSOM **If other, specify:**
Research Duties (check all that apply):	☐ PI: Ultimately responsible for the study including conduct by all study team members ☑ Identification of potential subjects

- [x] Contacting potential subjects
- [x] Screening of subjects, including assessing eligibility criteria
- [x] Obtain Informed Consent
- [ ] Randomization
- [x] Conduct of study procedures that result in research data
- [x] Prepare or dispense study drug/device
- [ ] Research specimen collection/shipping
- [x] Adverse Event documenting and reporting
- [x] Data entry
- [ ] Data Analysis - Identifiable
- [x] Data Analysis - De-identified
- [x] Regulatory document maintenance
- [ ] Other (specify):

Entry 2

Research team member name:	Muelenaer, Andre
Degree:	MD
Status:	Physician **If other, specify:**
Email address:	andrem1@vt.edu
Phone number:	
Alternate phone number (optional):	
Affiliation:	VT **If other, specify:**
Research Duties (check all that apply):	☐ PI: Ultimately responsible for the study including conduct by all study team members ☐ Identification of potential subjects ☐ Contacting potential subjects ☐ Screening of subjects, including assessing eligibility criteria ☐ Obtain Informed Consent ☐ Randomization ☐ Conduct of study procedures that result in research data ☑ Prepare or dispense study drug/device ☐ Research specimen collection/shipping ☐ Adverse Event documenting and reporting ☐ Data entry ☐ Data Analysis - Identifiable ☑ Data Analysis - De-identified ☐ Regulatory document maintenance ☑ Other (specify): Training research staff, physical contact with subjects in case of an emergency

Entry 3

Research team member name:	Newberry, Tara
Degree:	
Status:	Carilion Staff/Employee **If other, specify:**
Email address:	tanewberry@carilionclinic.org
Phone number:	
Alternate phone number (optional):	
Affiliation:	Carilion Clinic **If other, specify:**
Research Duties (check all that apply):	☐ PI: Ultimately responsible for the study including conduct by all study team members ☐ Identification of potential subjects ☐ Contacting potential subjects ☐ Screening of subjects, including assessing eligibility criteria ☐ Obtain Informed Consent ☐ Randomization ☐ Conduct of study procedures that result in research data ☑ Prepare or dispense study drug/device ☐ Research specimen collection/shipping ☐ Adverse Event documenting and reporting ☐ Data entry ☐ Data Analysis - Identifiable ☑ Data Analysis - De-identified ☐ Regulatory document maintenance ☑ Other (specify): Training research staff, physical contact with subjects in case of an emergency

Entry 4

Research team member name:	Spivey, Cara
Degree:	MS
Status:	Other: **If other, specify:** Clinical Research Coordinator
Email address:	crspivey@carilionclinic.org

Phone number:	
Alternate phone number (optional):	
Affiliation:	Carilion Clinic **If other, specify:**
Research Duties (check all that apply):	☐ PI: Ultimately responsible for the study including conduct by all study team members ☑ Identification of potential subjects ☑ Contacting potential subjects ☑ Screening of subjects, including assessing eligibility criteria ☑ Obtain Informed Consent ☐ Randomization ☑ Conduct of study procedures that result in research data ☑ Prepare or dispense study drug/device ☐ Research specimen collection/shipping ☑ Adverse Event documenting and reporting ☑ Data entry ☑ Data Analysis - Identifiable ☑ Data Analysis - De-identified ☑ Regulatory document maintenance ☑ Other (specify): Study contact

Entry 5

Research team member name:	Brown, Ralph Jr, MD
Degree:	MD
Status:	Physician **If other, specify:**
Email address:	rdbrown@carilionclinic.org
Phone number:	
Alternate phone number (optional):	
Affiliation:	Carilion Clinic **If other, specify:**
Research Duties (check all that apply):	☑ PI: Ultimately responsible for the study including conduct by all study team members ☑ Identification of potential subjects ☑ Contacting potential subjects ☑ Screening of subjects, including assessing eligibility criteria ☑ Obtain Informed Consent

- [ ] Randomization
- [x] Conduct of study procedures that result in research data
- [x] Prepare or dispense study drug/device
- [ ] Research specimen collection/shipping
- [x] Adverse Event documenting and reporting
- [x] Data entry
- [ ] Data Analysis - Identifiable
- [x] Data Analysis - De-identified
- [x] Regulatory document maintenance
- [ ] Other (specify):

Entry 6

Research team member name:	Fielder, Annette
Degree:	
Status:	Carilion Staff/Employee **If other, specify:** Occupational Therapist
Email address:	alfielder@carilionclinic.org
Phone number:	
Alternate phone number (optional):	
Affiliation:	Carilion Clinic **If other, specify:**
Research Duties (check all that apply):	

- [ ] PI: Ultimately responsible for the study including conduct by all study team members
- [x] Identification of potential subjects
- [x] Contacting potential subjects
- [x] Screening of subjects, including assessing eligibility criteria
- [x] Obtain Informed Consent
- [ ] Randomization
- [x] Conduct of study procedures that result in research data
- [x] Prepare or dispense study drug/device
- [ ] Research specimen collection/shipping
- [x] Adverse Event documenting and reporting
- [x] Data entry
- [ ] Data Analysis - Identifiable
- [x] Data Analysis - De-identified
- [ ] Regulatory document maintenance
- [ ] Other (specify):

5.0 Application Type

5.1 Select the application type:

- (●) Human Subject Research Study
- ( ) Determination of Human Subjects Research (including QA/QI Determination)
- ( ) Establishing a prospective Data or Specimens Research Repository
- ( ) Humanitarian Use Device (non-research use)
- ( ) Expanded Access or Compassionate Use
- ( ) Single Patient Emergency Use
- ( ) Preparatory to Research Application
- ( ) IRB Grant Review ONLY for preliminary approval if required by funder
- ( ) Requesting Carilion Clinic RELY on another IRB of Record (WIRB, CIRB, VT, UVA, Advarra etc.)
- ( ) Conversion of a paper application due for Continuing Review or Annual Check-In

Please ensure the PI has completed and submitted the R&D Application Department Level Review Form (eCRAF), and that the PI's Department Chair or signatory has signed off on the R&D Department Level Review eCRAF Form BEFORE you proceed any further with this IRB application. Please read the below bullet points carefully and acknowledge your understanding.

- **The R&D Application Department Level Review eCRAF Form must be submitted by the PI and signed off by Department Chair or signatory through RedCap BEFORE you may proceed with this IRB application.**
- **The R&D Application Department Level Review eCRAF Form serves a major function for section and department level review and may result in this study not being permitted due to resources, scientific validity, or other reasons.**
- **You must submit a copy of the signed R&D Application Department Level Review eCRAF Form with this IRB application in the supplemental document section.**
- **Failure to complete the steps in the above order will result in a significant delay in the IRB's review of this study.**

(●) Acknowledged

6.0 Funding Information and Outside Services

6.1 Select the applicable funding source(s).

- [ ] None (no money, equipment, supplies, and/or services will be provided by external source)
- [ ] No monetary funding BUT equipment, supplies, and/or services will be provided
- [ ] Federal Government
- [ ] Foundation or Non-profit
- [ ] Industry/Commercial Sponsor
- [ ] State or Local Government
- [ ] Investigator or Departmental/Unit Funds
- [ ] Carilion RAP Grant
- [x] Other

Please specify:

VTCSOM Research Domain funding

6.2 Select services from all areas outside of the Research Team members' affiliations that are necessary to conduct the work.

Research and Development (R&D) will contact you to arrange a Feasibility Meeting based on your responses below. This will ensure roles, responsibilities, and costs associated with this project are understood by all parties. Final sign-off from leadership in the additional service areas, as well as contracts, may be required.

- [ ] Animals
- [ ] Basic Science Laboratory Services
- [ ] Center for Simulation, Research & Patient Safety (CSRPS)
- [ ] Department of Medicine
- [ ] Department of Pediatrics
- [ ] Department of Psychiatry
- [ ] Department of Surgery
- [ ] Emergency Department
- [ ] Hazardous Materials
- [x] Health Analytics Research Team (HART), including Epic Data Extraction, Statistics Services, Carilion RedCap, Epic Research Access
- [ ] Human Resources
- [ ] Jefferson College
- [ ] Nuclear Medicine
- [ ] Nursing
- [ ] Pathology
- [ ] Pharmacy
- [x] Physical Therapy
- [ ] Radiology
- [ ] Recombinant DNA/RNA
- [ ] Respiratory
- [ ] Solstas Lab
- [ ] Technology Services Group (TSG)
- [ ] Other
- [ ] None

6.3 You have selected that HART services are needed for this research. Specify the resources needed.

- [ ] Epic Data Extract
- [x] Statistics Support (biostatisticians)
- [x] Carilion REDCap (Data management)
- [x] Epic Research Access for Chart Review
- [ ] TriNetX Identifiable Patient List/Data Set
- [x] SPARC Carilion Secure Research Environment

Note: If you have not yet discussed this project with the HART team, please contact them at HART@carilionclinic.org before proceeding any further with this application. This will ensure that your request for this project is feasible.

7.0 Regulatory Compliance

7.1 How many studies is the PI currently responsible for?

1

7.2 Does the PI have protected or dedicated time available to conduct this research?

(•) Yes ( ) No

7.3 Has any member of the research team ever received a FDA 483, "Warning Letter", Notice of Disqualification, or other warning or disciplinary action from an agency or licensing authority?

○ Yes ◉ No

7.4 Has this study been disapproved or terminated by another IRB?

○ Yes ◉ No

8.0 Conflict of Interest

8.1 A Conflict of Interest, per the Carilion Clinic Organizational Policy, is a situation in which an Investigator's and/or their Family Member's financial, professional, or other personal consideration may directly or indirectly affect, or reasonably appear to affect, the Investigator's professional judgement in performing their Institutional Responsibilities. A Conflict of Interest may be actual, apparent, or potential. Any research team member listed on the IRB application is considered to be an Investigator. It is the Principal Investigator' s responsibility to query all Carilion research team members on this study to ensure they have honestly completed their Annual COI Disclosure and that it is current. The Principal Investigator should be notified by the study team member if the study team member has disclosed any related interests. Carilion Clinic's Conflicts of Interest in Research Policy can be found here.

If this study has any external funding or support, have all Carilion research team members filed an Annual COI Disclosure through Carilion Clinic's Office of Organizational Integrity and Compliance via the COI-Smart online disclosure system?

○ Yes
◉ No
○ N/A - this study does not have any external funding or support

An Annual COI disclosure must be completed for ALL Carilion research team members. Please contact the Carilion Clinic Office of Organizational Integrity & Compliance immediately at researchcompliance@carilionclinic.org in order to ensure you can submit a disclosure through COISmart.

If new Carilion study team members are added to this study in the future, you must contact researchcompliance@carilionclinic.org. If the new team member needs to submit an Annual COI disclosure, this must occur before the new team member is permitted to conduct any work on this research study.

Do any Carilion research team members or their family members have a Conflict of Interest or related outside interest with the sponsor/funding agency of this study?

◉ Yes ○ No

Please email researchcompliance@carilionclinic.org and irb@carilionclinic.org immediately to ensure this Conflict of Interest or Outside Interest has been appropriately managed. Please note that the IRB may require additional management conditions for this study.

It is the Principal Investigator and conflicted employee's responsibilities to ensure the conflict or any changes that result in a potential conflict are disclosed to the Office of Integrity and Compliance who will refer it to the Carilion Clinic's Research Conflict of

Interest Commitee for appropriate management when necessary. Disclosure and management must occur before the conflicted employee is permitted to engage in any research activities. Any employee who violates the Conflict of Interest policy is subject to disciplinary actions, up to and including termination.

9.0 Collaboration

9.1 Is this research project a collaboration between Carilion Clinic and another institution (including, but not limited to Fralin Biomedical Research Institute at VTC, VTCSOM, VT, UVA)?

(•) Yes ( ) No

9.2 Please provide the name(s) of the collaborating institution(s) and the name(s) and contact information of the lead PI(s) at that institution.

This research project is a collaboration between Carilion Clinic, VTCSOM, and VT.

VTCSOM:
- Evgeniya Molotkova (BS, emolotkova3@vt.edu, 678-435-3316)

VT:
- Dr. Andre Muelenaer (MD, andrem1@vt.edu)
- Dr. Christopher Arena (PhD, topher3@vt.edu)
- Seth Jarvis (BS, sethjarvis@vt.edu)
- Selah Wangler (Undergraduate student, wanglers@vt.edu)
- Leah Thomas (BS, MS student, leahrebecca@vt.edu)
- Jennifer Rechani (Undergraduate student, jennifer0605@vt.edu)

9.3 Is Carilion acting as one site of a multicenter study?

( ) Yes (•) No

9.7 Are any members of the research team listed on this IRB application under the jurisdiction of another institution's IRB?

(•) Yes ( ) No

Please state specifically which external personnel are under the jurisdiction of another IRB, their role on this research study and the type of interaction they will have with the subjects, the name of the institution's IRB(s), and an explanation as to why they are listed on this IRB application.

VTCSOM:
- Evgeniya Molotkova (BS, emolotkova3@vt.edu, 678-435-3316) Research duties are those listed in this IRB application. This individual is listed on this IRB application because this research project is being done as part of the research requirement for graduation from VTCSOM.

VT:
- Dr. Andre Muelenaer (MD, andrem1@vt.edu) Research duties are those listed in this IRB application. Dr. Muelenaer was an instrumental part in the development of the medical device to be tested and played an important role in advocating for its translation to the clinical realm.
- Dr. Christopher Arena (PhD, topher3@vt.edu) Research duties are as follows: provide the device, prepare the device,
ensure proper training of the study personnel, and post-processing of de-identified data, including none of the 18 HIPAA identifiers.
- Seth Jarvis (BS, sethjarvis@vt.edu) Research duties are as follows: provide the device, prepare the device,
ensure proper training of the study personnel, and post-processing of de-identified data, including none of the 18 HIPAA identifiers. Seth built the device from the ground up, with help from both Dr. Muelenaer and Dr. Arena.
- Leah Thomas (BS, **leahrebecca@vt.edu**) Research duties are as follows: provide the device, prepare the device,

ensure proper training of the study personnel, and post-processing of de-identified data, including none of the 18 HIPAA identifiers. Leah built the device from the ground up, with help from both Dr. Muelenaer and Dr. Arena.
- Selah Wangler (Undergraduate student, **wanglers@vt.edu**) Research duties are as follows: conduct of study procedures that result in research data, prepare or dispense study drug/device, adverse event documenting and reporting, data entry, data analysis (identified and de-identified)
- Jennifer Rechani (Undergraduate student, **jennifer0605@vt.edu**) Research duties are as follows: conduct of study procedures that result in research data, prepare or dispense study drug /device, adverse event documenting and reporting, data entry, data analysis (identified and de-identified)

Dr. Muelenaer, Tara Newberry (listed on this application), and Leah Thomas (VT collaborator) will train the entire research team, including Selah Wangler and Jennifer Rechani, on how to interact with patients and conduct study procedures that result in research data as well as document and report adverse events. This training will be logged and signed by one of the aforementioned trainers.

9.8 Are you requesting that Carilion Clinic serve as the IRB of record for the other participating institutions or organizations?

For more information on IRB reliance requests, please visit the Carilion Clinic IRB website or contact the IRB Office.

○ Yes ◉ No

9.11 Describe any plans for initial and ongoing training of the other sites on important aspects of the protocol.

The research team will complete training requirements set forth by Carilion Clinic standards. The principal investigator will work with members of the research team to accomplish this and provide continuing education and protocol training through lab meetings or via secure and encrypted Carilion Clinic email.

Dr. Muelenaer, Tara Newberry (listed on this application), and Leah Thomas (VT collaborator) will train the entire research team, including Selah Wangler and Jennifer Rechani, on how to interact with patients and conduct study procedures that result in research data as well as document and report adverse events. This training will be logged and signed by one of the aforementioned trainers.

9.12 Describe the plan to manage communication of information at the other sites that is relevant to the conduct of the research and the protection of human subjects, such as reporting of unexpected problems, protocol modifications, and interim results for all sites to the Carilion Clinic IRB.

For FDA-regulated clinical trials, the plan must include the plan for reporting serious adverse events or serious adverse device effects, significant new risk information, and any other reports mandated by regulation or policy.

The principal investigator will be involved in all aspects of this study and will be responsible for reporting any adverse events or protocol modifications to the Carilion Clinic IRB. This information will be shared with the rest of the research team during research meetings or using secure, encrypted Carilion Clinic email in the interim.

9.13 Describe the Carilion Clinic investigator's plan for oversight of research activities at other sites including verification of Institutional approvals, data safety monitoring, and ensuring data quality and integrity.

For FDA-regulated clinical trials, the plan must include the use of trained and qualified monitors to oversee the progress of the research.

All research activities will be conducted in a Carilion Clinic facility.

9.14 Will identifiable data or specimens be transferred, transmitted, or shared outside of Carilion?

For example, transfer of data or specimens from Carilion Clinic to an external collaborator (including VT, VTCRI, UVA, etc.).

(●) Yes ( ) No

9.15 Provide information about the types of specimens and/or data, including specific datapoints, that will be shared and the methods of storage of the data at the collaborating site. Include a description of the process for shipping the specimens and/or transmitting the data to the collaborator, including the method of encryption if sharing data electronically.

Data sharing will only occur with those delegated in section 9.2. Data will be stored and shared within RedCap. Carilion Clinic's REDCap software will be used as the central location for data collection. REDCap provides a secure, web-based application designed to support data management and collection for research/QA/QI studies. Carilion's REDCap servers are securely housed on site in a limited access data center, and all data are stored on Carilion's firewall protected network.

10.0 Human Subjects Research Description

10.1 In the opinion of the Principal Investigator, does this research impart minimal risk or greater than minimal risk to subjects?

As defined by regulation, minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Please note that the IRB makes the final determination of risk level and may ask you to change this based on their decision.

If this is a Conversion of a Paper Application, select the risk level that has been determined already by the IRB at most recent review per the most recent approval letter (expedited review = minimal risk, full board review = greater than minimal risk).

( ) Minimal Risk
(●) Greater than minimal

10.2 Does the research offer the prospect of direct benefits to the individual subjects?

( ) Yes (●) No

10.3 Select ALL the types of research activities that will be involved in your human subject research subject, or select None.

- [ ] Drugs, biologics or other FDA-regulated products (other than devices)
- [x] Medical devices
- [x] Review of data/records (i.e. prospective clinical data collection from medical records, reviewing previously collected data)
- [ ] Biospecimen collection (i.e. blood, tissue, urine, saliva)
- [ ] Analysis of existing specimens from patients and/or bank or repository
- [ ] Human genetic analysis or Recombinant DNA, or Gene Therapy
- [ ] Invasive medical procedures (i.e. lumbar puncture, biopsy, endoscopy, surgery, etc.)
- [x] Non-invasive medical procedures routinely employed in medical practice (i.e., physical measurements, EKG, EEG, moderate exercise, etc.)
- [ ] Imaging (i.e., x-ray, CT, DEXA, MRI, ultrasound, etc.), Use of Therapeutic or Diagnostic Radiation, Radioactive Drugs
- [ ] Task-based activities or games, or Psychometric Testing
- [x] Surveys, questionnaires, focus groups, or interviews
- [ ] Examination of educational practices, instructional techniques, curricula or classroom management
- [ ] Observations of public behavior
- [ ] Interventions or procedures involving deception
- [ ] Use of Internet

- ☐ Audio or Video recording
- ☐ International Research
- ☐ NONE OF THE ABOVE

10.4 Briefly describe the proposed research in language that can be understood by a non-scientist.

This description should summarize the objectives of the research and the procedures to be used, with an emphasis on what will happen to the subjects. If this is an application for the establishment of a research repository, summarize the objectives of the repository and how data/specimens will be used in the future.

Lymphedema is a painful and disfiguring condition related to the buildup of protein-rich fluid in the body's tissues. The goal of this research study is to determine the safety and efficacy of a novel, proprietary device in the treatment of upper extremity lymphedema. This device has been previously studied on healthy people that do not have a diagnosis of lymphedema. It was found that using the device on them does not cause significant changes to their vital signs or level of pain. Side effects are reported sometimes; however, these are to be expected and are also frequently reported when people receive the standard of care for their lymphedema.

Patients who have diagnosed lymphedema will be approached to participate in this study as part of their care. Patients will wear this device for approximately 40 minutes and then have certain measurements taken before and after doing so. These measurements include the size of their arm, how much pain/discomfort they are currently in, and if they experienced any side effects. After getting treatment with the device, they will receive the standard of care treatment for their lymphedema from their provider. After the standard of care has concluded, the previously mentioned measurements will be repeated. This data will be put together and analyzed to look for differences in arm size before and after treatment with the device as well as to look for the prevalence of side effects.

10.5 Provide background information about the research question(s.) Explain why the research is needed and include the relevance of this research to the contribution of this field of study.

Please include the current state of knowledge about your project topic by summarizing and synthesizing the available research (including published data) to provide justification for the study. Include a reference list of literature cited to support the protocol statement, either in your response below or as a supplemental document as part of the application packet.

Lymphedema is a chronic condition characterized by the buildup of protein-rich fluid in the body's tissues, leading to bothersome swelling. There are several causes of lymphedema, but it typically arises due to damage or dysfunction of the lymphatic system, which is composed of lymph drainage vessels and lymphatic fluid itself. Lymphatic drainage includes lymphatic capillaries, lymphatic trunks, and lymph nodes, creating one large lymphatic drainage network that is tightly controlled and highly associated with the circulatory system. Hydrostatic and oncotic forces push lymph out from the body's veins and arteries and into the body's tissues, where it is absorbed by lymphatic vessels and eventually recycled back into systemic circulation. Lymphatic fluid itself is very similar in composition to blood plasma, and it typically contains high levels of triglycerides, white blood cells, and bacterial debris. (Sleigh and Manna, 2022).

Lymphedema can be subdivided into primary and secondary causes. Primary lymphedema is due to underlying genetic mutations, often leading to the malformation and malfunctioning of the lymphatic system. Secondary lymphedema is caused by some sort of external damage or injury to the lymphatic system. Most cases of lymphedema are secondary lymphedema, most widely seen in the oncologic population, where invasive surgery to remove tumors or diseased lymph nodes disrupts lymphatic flow. In fact, it is estimated that approximately 1 in 5 women who survive breast cancer will go on to develop lymphedema. While the underlying etiology of lymphedema may vary, all lymphedema is staged in the same fashion, falling anywhere from Stage 0 to Stage 3. Stage 0 represents an "at-risk" state, where an individual has risk factors associated with the development of lymphedema, and Stage 3 represents a stage of lymphostatic elephantiasis (Sleigh and Manna, 2022).

Lymphedema in and of itself can be uncomfortable, if not downright painful. However, it also predisposes patients to developing secondary vascular, inflammatory, and infectious conditions as it progresses and becomes increasingly severe. Additionally, it may undermine patients' body image and self-esteem and affect their daily lives and personal relationships. Currently, once lymphedema develops, there is no definitive cure, only symptom management. The standard of care entails using a combination of outpatient decongestive lymphedema therapy

and manual lymph drainage alongside stringent home care characterized by the use of compression garments and therapist-taught manual lymph drainage techniques. However, oftentimes home care is not enough to control lymphedema between therapist appointments.

In recent years, medical devices have been developed to improve home care and lymphedema outcomes. There are many different types of lymphedema pumps currently available on the market. Unfortunately, across the board, they can be bulky, noisy, expensive, and require long periods of immobility while treatment takes place. There is a definitive need for new lymphedema technology that can improve patients' symptoms while being easier and more enjoyable to use than previous products. This study aims to evaluate a new, proprietary device designed at Virginia Tech through Carilion Innovations to address the problem of upper extremity lymphedema. A previously conducted safety study has demonstrated that this device does not cause significant changes in vital signs or pain. Additionally, the overwhelming majority of side effects associated with the use of this device are those expected with the standard of care. Being able to assess the efficacy and safety of this device in patients with lymphedema over the course of this study would provide a promising alternative to current lymphedema home care modalities that can improve lymphedema patient outcomes.

References:

1. Sleigh BC, Manna B. Lymphedema. [Updated 2022 Sep 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

10.6 State the research hypothesis or the question that the research will answer.

List the research objectives and expected outcomes. A primary outcome or objective must be identified. After the statement of the primary objective, secondary objectives may be listed. Objectives should be simple and specific.

Research Question: How can we utilize new technology in the treatment of lymphedema?

Hypothesis: Use of a recently developed, proprietary device will reduce lymphedema in the outpatient clinic setting.

Objectives:

1. Implement a new, proprietary device in the treatment of lymphedema.
2. Assess the safety and tolerability of the aforementioned device.
3. Assess pre- and post-treatment pain metrics and change in upper extremity circumference and induration for treatment with the proprietary device and the standard of care.

10.7 State how qualitative and/or quantitative data will be analyzed in order to answer the research questions.

Include an analysis from a statistician (or someone familiar with statistical methods) that either indicates the power calculation for the sample size necessary to meet the primary study outcome or objective OR a statement from the statistician indicating reasons why a power calculation is waived or not necessary for this study. Also include the statistical test(s) that will be used to analyze your primary study objective (t-test, chi-square, etc.). Secondary outcomes may be listed as descriptive.

If this is a proof of concept or feasibility study that includes limited efficacy testing, please provide a description on how your design will determine if an intervention should be recommended for broader efficacy testing. If a study is meant to be solely descriptive, then the primary outcome or objective must be limited in scope. As such, the study results apply only to the sample being studied, and conclusions cannot be drawn about the larger population.

This is required for ALL studies, as this section helps the IRB confirm the data being collected are relevant to the study aims and planned analysis.

Power Calculation

1. The most conservative approach of sample size calculation without counting for replication.
The sample size calculation for this study was based on paired samples t-test for testing the pre- and post-treatment outcomes. With an estimated effect size of 0.3, it will require a total sample of 90 patients with 0.8 power at 5% significance level using two-tailed test. The power calculation was performed using R4.2 (https://cran.r-project.org/).

2. Assuming a correlation of 0.5 (strong correlation between replicated measures)
The sample size calculation for this study was based on paired samples t-test for testing the pre- and post-treatment outcomes with 4 replicated measures. With an estimated effect size of 0.3 and a correlation of 0.5 between replicated measures, it will require a total sample of 57 patients at 5% significance level using two tailed test. The power calculation was performed using R4.2(https://cran.r-project.org/).

3. Assuming a correlation of 0.25 (moderate correlation between replicated measures)
The sample size calculation for this study was based on paired samples t-test for testing the pre- and post-treatment outcomes with 4 replicated measures. With an estimated effect size of 0.3 and a correlation of 0.25 between replicated measures, it will require a total sample of 40 patients at 5% significance level using two tailed test. The power calculation was performed using R4.2(https://cran.r-project.org/).

Plan for Statistical Analysis
All data obtained in this research study will be analyzed using a paired t-test.

Feasibility Study
Since this is the first time that the proprietary device will be used on patients and not on healthy volunteers, we are primarily aiming to establish safety, first and foremost, and efficacy, to ensure that the device works like it is supposed to do so. Because of these two factors, we plan on enrolling only 15 patients in this feasibility/pilot study, which is less than what was indicated to us through the power analysis.

10.8 Statistical Review

Name of statistician or person who prepared the statistical plan:	Department/Institution:	Date statistical review was conducted:
Ahmed N. Al-qaffas	HART	12/19/2022

Note: The statistician or individual that prepared the statistical plan must also be included on the study team if they meet the definition of key research personnel (ex: significantly involved in the study design, conduct, or reporting of the research).

If a statistical review has not been submitted, explain why:

11.0 Subject Population

11.1 Please select the population(s) being targeted, or likely to be included in this research study. (select all that apply)

- [ ] Medical Chart Review of patients only (no in-person contact)
- [ ] Normal Adults/Healthy Volunteers
- [ ] In-Patient Population
- [x] Out-Patient Population
- [ ] Patients in emergency situations
- [ ] Terminally ill patients
- [ ] Employees/Staff
- [ ] Students

- [ ] Children/Minors (anyone younger than 18 years of age in the state of Virginia. For research conducted outside of the state of Virginia, age of majority is dependent on state/local law)
- [ ] Prisoners
- [ ] Pregnant Women
- [ ] Fetuses
- [ ] Neonates of uncertain viability and/or nonviable neonates
- [ ] Adults with Impaired Decision-Making Capacity
- [ ] Persons with Limited-English proficiency (LEP) or Non-English Speakers
- [ ] Individuals of Childbearing Potential

11.2 Please indicate the total number of subjects anticipated to be enrolled at this site/by this investigator.

For the purposes of the IRB, a subject is enrolled once they have provided consent to participate, or for studies approved with a waiver of consent, once data has been collected on the subject.

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11.3 If the research involves multiple subject groups or cohorts at this site, provide the anticipated number of subjects in each of group or cohort (e.g., control/experimental, adults/children, etc.).

This research does not involve multiple subject groups or cohorts.

11.4 Provide the age range for the proposed subject population (e.g., 0-5 years old):

18 and older

11.5 Specify the inclusion criteria for each of the subject groups to be included in the research.

If there are multiple different groups being recruited with different eligibility criteria, instead add an Eligibility Criteria checklist for each group as a supplemental document after you complete this application. Please make note of this in the Inclusion Criteria below.

Order Number	Criteria
1	Patients 18 year of age or older
2	Clinical diagnosis of lymphedema
3	Receiving current, once weekly, lymphedema treatment by PT/OT
4	Participants must have the ability to provide consent for themselves

11.6 Specify the exclusion criteria for each of the subject groups to be included in the research.

If there are multiple different groups being recruited with different eligibility criteria, instead add an Eligibility Criteria checklist for each group as a supplemental document after you complete this application. Please make note of this in the Exclusion Criteria below.

Order Number	Criteria
1	Active infection
2	Active cancer (not in remission)
3	Diagnosis of/past medical history of deep venous thrombosis or pulmonary embolism
4	Active phlebitis
5	Diagnosis of congestive heart failure
6	Previous severe trauma (i.e. requiring extensive corrective surgery)

7	History of vascular surgery
8	Lesions of the skin or weeping skin in the treatment area

11.7 Is information being obtained about individuals other than the "target subjects" (such as a family member or colleague of the subject), making the other individuals "secondary subjects"?

○ Yes ◉ No

12.0 Informed Consent for Adult Subjects

12.1 How do you plan to obtain consent from ADULT subjects or their Legally Authorized Representative?

Check all that apply:

- ☑ Written consent document with signature (ie: obtaining signature from subject or Legally Authorized Representative)
- ☐ Waiver of written documentation of consent (ie: consent will be obtained through verbal confirmation from the subject or Legally Authorized Representative rather than through a signed document)
- ☐ Waiver of informed consent for minimal risk research (ie: typically appropriate only when the study does not involve any interaction or intervention with subjects)
- ☐ Waiver or alteration of the elements of informed consent (ie: research involving deception)
- ☐ Waiver of the informed consent document and process for PLANNED EMERGENCY RESEARCH. Contact the IRB before submission.
- ☐ No adults are being enrolled; this study is only enrolling children. (You will answer questions about the assent and parental permission process later.)

You must attach all consent forms, consent scripts, and information sheets in the Initial Submission Packet.

12.2 Is it expected that surrogate consent will need to be obtained from Legally Authorized Representatives (LARs) for some or all adult subjects?

○ Yes ◉ No

12.3 If the research includes more than one subject group or you have selected multiple responses above due to the inclusion of multiple subject groups, please specify the requested consent method for each group, or state N/A.

N/A

12.4 How will written consent be documented?

Click the Help bubble to the right for more information about requirements for eConsent before selecting this option.

- ☑ Traditional signed written consent form on paper document
- ☑ eConsent: signed via an REDCap or other electronic or web-based form
- ☐ Short Form Method (for non-English speaking subjects only)
- ☐ Other

12.5 Describe the process of obtaining consent and documenting the process, including the following:

- **Circumstances under which consent will be obtained, including how the potential participant will first be approached;**
- **Where the consent process will take place (ex: in person in a private clinic room, over the phone, through WebEx, etc.);**
- **When the consent process will take place and how long participants will be given to decide;**

- **If eConsent is being utilized, describe how you will first contact the potential participants and provide the consent form to them to review;**
- **Steps that will be taken to ensure voluntary participant and to minimize the possibility of coercion or undue influence;**
- **Any cultural considerations (ex: tribal or group permission requirements, age of majority, technological implications, etc.);**
- **If any participants do not speak English, whether a translator with witness will be used, whether translated materials will be used, whether the consent process changes based on the language;**
- **If multiple participant groups or consent procedures are to be included, these need to be clearly delineated;**
- **how participants will be provided with a copy of their signed consent;**
- **Describe the method you will use to document the consent PROCESS within each participants' research record /medical record (state which). This should include a process note or checklist that will document all the components listed above, the start and end time of the discussion, and is in addition to the signed and dated consent form (if applicable).**

For example, describe it consent will take place in the research office, in a private conference room, in the doctor's office, in a group setting, over the phone, etc.

GENERAL

1. The occupational therapist (OT) listed at the beginning of this application will identify potential participants (based on established inclusion and exclusion criteria) from their patient pool. All consenting procedures will be completed by the Carilion Affiliated or VTCSOM IRB approved team members.

2. The occupational therapist will verbally bring up this research study during a patient's regularly scheduled treatment visit, which is typically about an hour long. Lymphedema is treated with a combination of massage and compression, giving the OT leeway to talk to a patient while they are delivering hands-on treatment. They will give a brief explanation of what will happen to the patient and how it will/will not impact their care. Only the occupational therapist will initially approach potential subjects.

3. If a patient expresses interest in participating in the study, the OT will give them an unsigned copy of the consent document to take home and read over. The OT will confirm their contact information and the best time to reach out to them. Then, the OT will reach out to a designated IRB approved research team member.

4. This encounter will be documented as a research note in Epic by a designated IRB approved research team member.

5. Two to three days after the initial contact has been made, a designated IRB approved research team member will attempt to contact the patient via phone call, limiting the number of attempts to three. There will be no voicemail left. If the designated IRB approved research team member cannot reach the patient during this time, they will not be included in the research study.

6. If the designated IRB approved research team member is able to successfully make contact with the patient, they will first confirm the patient's identity by asking them to state their name and date of birth. This will create a passcode based on known information (first two letters of legal first name followed by first two letters of legal last name followed by last 2 digits of birth year). Each section of the consent form will be reviewed in detail before consent is obtained. The designated IRB approved research team member will ask the patient if they have any questions about the study.

7. After the patient has expressed interest in the study and agreed to participate, they will be allowed to choose whether they would like to undergo consent in person, at their next regularly scheduled office visit or remotely, via eConsent.

IN PERSON

1. Upon arriving to their next regularly scheduled office visit, the patient will be brought back to a private treatment room by a designated IRB approved research team member.
2. An IRB Research team member will review the each section of the consent in detail with the participantThe patient will be asked if they have any further questions about the research study.
3. A number of teach-back and open-ended questions will be used to assess patient understanding regarding the research study and what is/is not expected of them. Once all applicable questions have been answered/addressed, the patient will physically sign a two paper copies of the consent form (one for the research team and one for themselves)

4. The participant will immediately receive their signed copy of the consent form.

5. A summary of the conversation, any pertinent questions that were addressed during the encounter, and the signed consent form will be recorded in a research note in Epic. Specifically, the following points will be recorded in the research note:

    - The method that was used to discuss the study with the potential subject (discussion happened in person)
    - The questions that the potential subject asked
    - The time the potential subject was given to make their decision
    - How long the conversation lasted

6. Research tasks will only be completed after the informed consent document is signed.

eCONSENT

1. The eConsent process will take place over the phone. The patient will be asked whether they would prefer to get the link to the eConsent form emailed or texted to them.

2. Once communication modalities have been confirmed, the designated IRB approved research team member will have to state the following: "Carilion Clinic cannot control the security of email or text messages once we send them, therefore we need your permission to text or email you the link to the eConsent form for the study we discussed. Please be aware that while the email title will not include your lymphedema, the body of the email will contain the link to the study. Someone else accessing your email/text messages could click on the link and read the consent, and therefore learn about your lymphedema, which you may consider to be of a private or sensitive nature. Do you still wish to receive the link to the eConsent via email/text?"

3. The patient will receive the link via their preferred modality and review it.

4. An IRB Research team member will review the each section of the consent in detail with the participant. The patient will be asked if they have any further questions about the research study.

5. A number of teach-back and openended questions will be used to assess patient understanding regarding the research study and what is/is not expected of them.
6. The subject will type their name and date and use their finger, cursor, or stylus (if it is available to them) to sign in the signature field.

7. The participant will receive a copy of their signed consent form via email or in person at their next regularly scheduled visit.

8. If the patient elects to receive a copy of their consent form via email, the designated IRB approved research team member will verbally state, "Carilion Clinic cannot control the security of email messages once we send them, therefore we need your permission to email you the copy of your signed consent. Please be aware that while the email title will not include your lymphedema the attachment to the email will contain study consent. Someone else accessing your email messages could click on the attachment and read the consent, and therefore learn about your lymphedema, which you may consider to be of a private or sensitive nature. By providing your email address, you are authorizing Carilion Clinic to email you a copy of your signed form." If a signed copy of the consent will be emailed to the subject using REDCap, the subjects must provide their e-mail address on the completion page, and the following statement will be included in the field where the email address is "Enter your email to receive confirmation message? A confirmation email is supposed to be sent to all respondents that have completed the survey, but because your email address is not on file, the confirmation email cannot be sent automatically. If you wish to receive it, enter your email address below."

9. A summary of the conversation, any pertinent questions that were addressed during the call, and the signed consent form will be recorded in a research note in Epic. Specifically, the following points will be recorded in the research note:

    - The method that was used to discuss the study with the potential subject (discussion happened over the phone)

    - The questions that the potential subject asked

- The time the potential subject was given to make their decision
- How long the conversation lasted
- The process of verifying the individual's identity over the phone and then with the eConsent signature, as described above

10. Research tasks will only be completed after the informed consent document is signed.

12.6 How will you ensure that subjects or LARs have sufficient opportunity to consider whether or not to participate?

Check all that apply:

- [x] Subjects will be provided the consent form to take home for consideration prior to signing.
- [x] Subjects will be allowed a waiting period to consider their decision.
- [ ] Other

Please specify waiting period:

2 to 3 days

12.7 How will the subjects' or LARs understanding of the consent information presented be assessed?

Check all that apply:

- [x] Subjects will be asked to "Teach-Back" the study to the researchers
- [x] Subjects will be asked open-ended questions about the research (purpose, procedures, risks, alternatives, voluntary nature)
- [ ] A tool or post-consent assessment will be used
- [ ] Other

Specify the "teach back" questions or open-ended questions that the subject will be asked to describe in their own words in order to assess their understanding.

Open-ended Questions:

- Can you please describe the study in your own words?
- What would you have to do if you decide to participate in the study?
- Is there anything that you can or can not do while participating in this study?
- How long will your participation in the study be?

Multiple Choice Questions:

- What will you do as part of the study?
  - Wear an investigational device as part of my therapy
  - Receive no therapy at all
  - Only complete surveys
  - None of the above

- I am able to withdraw from the study at any point in time.
  - True
  - False

- I will be asked to attend my appointments more frequently as a result of my participation in this study.
  - True
  - False

12.8 Utilizing eConsent has additional requirements. Please describe the following:

- **The method to verify the identity of the individual providing consent;**
- **How participants will sign the eConsent (ex: type their name, use stylus or finger to sign);**
- **If potential participants will sign the consent while having a virtual conversation or if they will have additional time to consider their participation;**
- **If use of LAR is being requested, how you will ensure this individual is an appropropriate LAR per Virginia requirements and verify their identity.**

1. The occupational therapist (OT) listed at the beginning of this application will identify potential participants (based on established inclusion and exclusion criteria) from their patient pool. All consenting procedures will be completed by the Carilion Affiliated or VTCSOM IRB approved team members.
2. The occupational therapist will verbally bring up this research study during a patient's regularly scheduled treatment visit, which is typically about an hour long. Lymphedema is treated with a combination of massage and compression, giving the OT leeway to talk to a patient while they are delivering hands-on treatment. They will give a brief explanation of what will happen to the patient and how it will/will not impact their care. Only the occupational therapist will initially approach potential subjects.
3. If a patient expresses interest in participating in the study, the OT will give them an unsigned copy of the consent document to take home and read over. The OT will confirm their contact information and the best time to reach out to them. Then, the OT will reach out to a designated IRB approved research team member.
4. This encounter will be documented as a research note in Epic by a designated IRB approved research team member.
5. Two to three days after the initial contact has been made, a designated IRB approved research team member will attempt to contact the patient via phone call, limiting the number of attempts to three. There will be no voicemail left. If the designated IRB approved research team member cannot reach the patient during this time, they will not be included in the research study.
6. If the designated IRB approved research team member is able to successfully make contact with the patient, they will first confirm the patient's identity by asking them to state their name and date of birth. This will create a passcode based on known information (first two letters of legal first name followed by first two letters of legal last name followed by last 2 digits of birth year). Each section of the consent form will be reviewed in detail before consent is obtained. The designated IRB approved research team member will ask the patient if they have any questions about the study.
7. After the patient has expressed interest in the study and agreed to participate, they will be allowed to choose whether they would like to undergo consent in person, at their next regularly scheduled office visit or remotely, via eConsent.

eCONSENT

1. The eConsent process will take place over the phone. The patient will be asked whether they would prefer to get the link to the eConsent form emailed or texted to them.
2. Once communication modalities have been confirmed, the designated IRB approved research team member will have to state the following: "Carilion Clinic cannot control the security of email or text messages once we send them, therefore we need your permission to text or email you the link to the eConsent form for the study we discussed. Please be aware that while the email title will not include your lymphedema, the body of the email will contain the link to the study. Someone else accessing your email/text messages could click on the link and read the consent, and therefore learn about your lymphedema, which you may consider to be of a private or sensitive nature. Do you still wish to receive the link to the eConsent via email/text?"
3. The patient will receive the link via their preferred modality and review it.
4. An IRB Research team member will review the each section of the consent in detail with the participant. The patient will be asked if they have any further questions about the research study.

5. A number of teach-back and open-ended questions will be used to assess patient understanding regarding the research study and what is/is not expected of them

6. The subject will type their name and date and use their finger, cursor, or stylus (if it is available to them) to sign in the signature field.
7. The participant will receive a copy of their signed consent form via email or in person at their next regularly scheduled visit.

8. If the patient elects to receive a copy of their consent form via email, the designated IRB approved research team member will verbally state, "Carilion Clinic cannot control the security of email messages once we send them, therefore we need your permission to email you the copy of your signed consent. Please be aware that while the email title will not include your lymphedema the attachment to the email will contain study consent. Someone else accessing your email messages could click on the attachment and read the consent, and therefore learn about your lymphedema, which you may consider to be of a private or sensitive nature. By providing your email address, you are authorizing Carilion Clinic to email you a copy of your signed form." If a signed copy of the consent will be emailed to the subject using REDCap, the subjects must provide their e-mail address on the completion page, and the following statement will be included in the field where the email address is "Enter your email to receive confirmation message? A confirmation email is supposed to be sent to all respondents that have completed the survey, but because your email address is not on file, the confirmation email cannot be sent automatically. If you wish to receive it, enter your email address below."
9. A summary of the conversation, any pertinent questions that were addressed during the call, and the signed consent form will be recorded in a research note in Epic. Specifically, the following points will be recorded in the research note:
    - The method that was used to discuss the study with the potential subject (discussion happened over the phone)
    - The questions that the potential subject asked
    - The time the potential subject was given to make their decision
    - How long the conversation lasted
    - The process of verifying the individual's identity over the phone and then with the eConsent signature, as described above
10. Research tasks will only be completed after the informed consent document is signed.

12.9 If the enrollment of subjects who cannot read the consent form, due to visual impairment, literacy, or other issues, is anticipated, how will consent be obtained and documented?

Refer to 45 CFR 46.117(b)(2) or 21 CFR 50.27(b)(2) for information regarding when the use of a short form is appropriate. A witness to the consent process is needed.

- [x] N/A
- [ ] Short form
- [ ] Other mechanism
- [ ] Consent form read to participant with witness present

12.10 How will you ensure research participants remain informed about the study and continue to agree to participate in the research study after their initial informed consent has been obtained?

- [ ] N/A

If new information arises that may affect the participants willingness to participate, this information will be presented to the participant so that they may decide if they would like to continue. This information would be passed down from the Data Safety Monitoring Committee.

13.0 Privacy and Confidentiality

13.1 Does the research include interaction with or observation of subjects?

- (•) Yes
- ( ) No

13.3 Select the data points that will be reviewed, collected, recorded, or created for research purposes, including screening or recruitment.

Check all that apply:

- [x] name

- [ ] all geographic subdivisions smaller than a 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 the Census:
- [x] an element of a date, except year, for dates related to an individual, including birth date, admission date, discharge date and date of death; and all ages over 89 and all elements of such ages may be aggregated into a category of age 90 or older
- [x] telephone numbers
- [ ] fax numbers
- [x] electronic mail address
- [ ] social security number
- [x] medical record number/ master patient index (MPI)
- [ ] health plan beneficiary numbers
- [ ] account numbers
- [x] hospital account receivable (HAR)/contact serial number (CSN)
- [ ] certificate/license numbers
- [ ] vehicle identifiers, including license plate number
- [ ] device identifiers and serial numbers
- [ ] Web Universal Resource Locators (URLs)
- [ ] Internet Protocol (IP) address numbers
- [ ] biometric identifiers, including finger and voice prints
- [ ] full face photographic images and any comparable image
- [ ] any other unique identifying number, characteristic, code
- [ ] None of the above

13.4 Will any of the above data points be reviewed, collected, recorded, or created from the medical record (or other healthcare records)?

(•) Yes ( ) No

Since you plan to access or use PHI from the Medical Record, you must contact the HART Team at Carilion Clinic immediately to ensure the data you will need is accessible and to discuss data management and storage. Do not proceed with the submission of this application until you have done so.

13.5 Is the private information being requested the minimum necessary to meet the research goals?

(•) Yes ( ) No

13.6 Under the HIPAA Privacy Rule, when accessing or using PHI, a HIPAA Authorization of the subject must be obtained, or the IRB must grant a waiver.

Indicate which of the following apply (more than one may be selected):

- [x] The HIPAA Authorization is embedded in the research consent document.
- [x] A partial waiver of the requirement for HIPAA Authorization is requested (e.g., for screening or for some subjects, such as a retrospective cohort)
- [ ] A full waiver of the requirement for HIPAA Authorization is requested
- [ ] The HIPAA Authorization will be sought but one or more required elements will be eliminated or altered
- [ ] The PHI accessed or used for this research is a Limited Data Set (LDS) and a Data Use Agreement (DUA) is or will be in place prior to accessing or obtaining the LDS.
- [ ] HIPAA Authorization will be obtained as a separate document (only permitted if required by sponsor)
- [ ] Other

13.7 Will educational records protected under the Family Educational Rights and Privacy Act (FERPA) be accessed or used for the research?

○ Yes ◉ No

13.8 Does the research involve the administration or use of surveys, interviews, or other evaluations or examinations protected under the Protection of Pupil Rights Amendment (PPRA)?

○ Yes ◉ No

13.9 Will the research records (other than the consent form) and/or specimens contain data that is identifiable, coded, or de-identified?

- ☑ Identifiable (includes direct identifiers or information such that subject identities could be ascertained)
- ☐ Coded or linked (identifying information that would enable the investigator or collaborator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, etc., and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens)
- ☐ De-identified or unlinked (specimens/data cannot be linked to specific individuals by anyone, including the Carilion investigator, either directly or indirectly through coding systems)

13.10 Where will research data be stored during the period the research is active? Describe the security controls in place, including physical safeguards for paper records and technical safeguards for electronic records

Storage options other than those listed below are NOT currently permitted, including the use of Carilion provided or personal laptops, flash drives or other portable devices, non-Carilion cloud or other hosted environment. Any exceptions to the list above must be approved by the Carilion Privacy and Information Security Officer and documentation provided to the IRB.

- ☐ Hardcopy data in a locked office in a locked cabinet
- ☑ Electronic data on a password protected, secure drive on a Carilion server (contact mmtenzer@carilionclinic.org to set up a shared drive)
- ☑ REDCap (contact mmtenzer@carilionclinic.org to discuss use of REDCap)
- ☐ Sponsor's electronic data capture system
- ☑ SPARC Carilion Secure Research Environment (contact mmtenzer@carilionclinic.org to discuss)

13.11 Provide any additional information pertaining to the storage and management of the research data.

Best research pratice is to have data management plan which will help you manage and protect your data, meet funder requirements, and help others use and protect your data, if shared. A well structured project can help protect the confidentiality of patient and participant data. Carefully planned data management also allows for a better use of your time and resources. For guidance on data management pratices, please review the Harvard Catalyst document and upload your data management plan into the Supplemental documents.

Carilion Clinic's REDCap software will be used as the central location for data collection. REDCap (research electronic data capture) provides a secure, web-based application designed to support data management and collection for research/QA/QI studies. Carilion's REDCap servers are securely housed on site in a limited access data center, and all data are stored on Carilion's firewall protected network. The Health Analytics Research Team supports the proper development of projects and surveys in REDCap, observing appropriate change control and enforcing appropriate security controls. Data collection projects are built with a study-specific data dictionary, enforcing intuitive, accurate, consistent and complete data entry. REDCap also provides a survey tool for building and managing online surveys. Health Analytics Research team restricts user access to the IRB-approved project research team utilizing the approved processes and standards of TSG. REDCap is HIPAA compliant and provides audit trails. Data can be easily exported in several formats to a secure network directory for combination with extracted data, if appropriate, and analysis with common statistical packages.

Carilion Clinic's SPARC secure research environment will be used to store and analyze the datasets for analysis. SPARC (Storage and Programs Accelerating Research Collaborations)is Carilion's web-based, secure research

environment, that provides accessible storage of research project files in addition to advanced analytics programs to apply to those files for analysis. Current product offerings are SAS Viya and Statistics, R and R-studio, Python, and NVIVO, in addition to Microsoft Excel, Powerpoint and Word.AWS offerings may be possible to implement, depending on the needs of the project.Once access is authorized through an IRB approved protocol and a signed end user agreement, the clients utilize their institution's credentials to sign in.Data are prevented from download from the environment, without appropriate permissions and managed by the Health Analytics Research Team (HART). Folders are set up specifically for each approved project, with access limited to the research team, as specified on the protocol. This mitigates most of the risk of privacy breach.

13.12 How long will research records, data, and specimens be retained following completion of the study? Where will study records will be retained when the study has been closed (long-term storage)?

Describe when and how the identifiers, if applicable, will be destroyed. If specimens will be retained, describe where.

Please note that any data involving PHI must be maintained for a minimum of 6 years, and data that does not contain PHI must be maintained for a minimum of 3 years. In many cases, identifiers will need to be retained after the research is completed (e.g., for publication or data verification purposes or because of contractual requirements or grant terms).

Please click the Help bubble to the right for more information on minimum storage requirements.

Research data will be maintained on REDCap for at least 6 years after the conclusion of the study per Carilion Clinic SOP.

13.14 Please state the specific identifiers that will be recorded/documented within the research records, including on specimens, and why they are needed.

Patient name, DOB, telephone number, and electronic mail address will be recorded/documented within the research records. Patient name and DOB is necessary to link longitudinal data points with the correct individual. Telephone number and electronic email address is necessary for the consent process.

13.15 Who will have access to identifiers?

Research team members who have been approved by the IRB will have access to identifiers.

13.16 How will access to the identifiers be protected?

All data will either be stored on Carilion Clinc's REDCap, SPARC research environment, or within a secured and encrypted shared drive provided by Carilion Clinic. Shared drive may only be accessed through apps. carilionclinic.org. Outside collaborators cannot access the shared drive.

13.17 Describe whether data will be aggregated/summarized in publications or presentation, or whether individual participant results will be published/presented.

Data will be aggregated and summarized in publications and presentations. No identifiers will be listed.

13.18 Will research records include information that subjects or others might consider to be sensitive in nature?

E.g.,communicable disease status, substance abuse, mental health information, illegal behaviors, etc.

○ Yes ◉ No

14.0 Request for Partial Waiver, Full Waiver, or Alteration of HIPAA Authorization

14.6 Describe how you will utilize PHI for purposes of recruitment and describe how the use of PHI in this study poses no greater than minimal risk to participants' privacy.

A partial waiver of authorization will be requested to access PHI for the purpose of pre-screening patients and assessing eligibility criteria. Pre-screening by chart review poses no greater than minimal risk to participants' privacy because all chart review activities are conducted through EPIC, a secure, password-protected environment. Access to PHI will be limited to research team members involved in patient pre-screening, as indicated in sections 3 and 4, in order to further protect patient privacy. Additionally, data collected will be protected using REDCap.

14.7 Describe why the research could not practicably be carried out without the use of PHI for recruitment.

In this study, access to PHI is necessary for determining study eligibility. Designated study team members will need access to clinic schedules and patient charts in order to verify if participant meets eligibility criteria and is a candidate for a study introduction conversation.

14.8 Describe why the research could not be practicably carried out without the partial waiver for recruitment.

Pre-screening by chart review would not be possible without a partial waiver of HIPAA authorization. This study has several important inclusion/exclusion criteria that must be met prior to enrollment. The study team members do not want to potentially introduce this project to patients who are ineligible. Additionally, it is not feasible to obtain consent/HIPAA Authorization from every patient in order to verify eligibility.

14.9 Do you assure that any data identifying subjects used in this study will not be disclosed to anyone other than the research team, sponsor, and oversight groups?

(●) Yes ( ) No

14.10 Do you assure that you will not re use or disclose this data for any other research unless you receive IRB approval?

(●) Yes ( ) No

15.0 Sharing of Research Data/Specimens

15.1 Describe the data or specimens to be transferred, transmitted, or shared and the purpose of sharing.

All data obtained as a result of this study (see attached data collection tool) will be stored in the secure, Carilion Clinic research environment, which includes REDCap, Shared Drives, and SPARC. Data will only be shared with research team members without a conflict of interest, and they will have password-protected access to the aforementioned secure tools. Only research team members who been approved by the IRB will have access. This access will be established and maintained by the Carilion Clinic HART team. Furthermore, these collaborators will have access to patient identifiers only as necessary to interact with patients, conduct study tasks, and communicate with the rest of the research team.

15.2 Describe procedures for verifying that proposed use is consistent with the informed consent under which materials were collected.

Any data collected as part of this research study will only be shared, transferred, or transmitted to the collaborators of this IRB application who have completed necessary CITI trainings as verified by the VT and Carilion IRB. Only research team members who have been approved by the IRB to have access will have access to this data. No identifiable data will be transferred or transmitted outside of Carilion REDCap or Sparc.

15.3 Categorize the identifiability of the data/specimens that will be shared.

(●) Identifiable (data/specimens includes direct identifiers such as name, identifying elements of PHI, or that the type or nature of the information is such that the identify of individual subjects may readily be ascertained)

( ) Linked/coded (a link exists from the specimen to the identifiable information)

De-Identified (The specimens/data CANNOT be linked back to the identifiable information or medical record by anyone)

15.4 Describe the information to be shared in detail, including which of the 18 HIPAA identifiers or other sensitive information will be shared, and justify the need to share identifiable data.

Describe who will maintain the link, if applicable.

As part of this research project, we will collect patient name, date of birth, email address, and telephone number. All consenting procedures will be completed by the Carilion Affiliated or VTCSOM IRB approved team members. This information is necessary to share with outside collaborators from VTCSOM and VT in order to properly pre-screen patients and obtain informed consent. This sharing will be limited to members of the research team who have been approved by the IRB to have access. This information will be stored on the secure, password-protected Carilion Clinic research environment as set up and maintained by the Carilion Clinic HART team. Additionally, measurements and survey data as detailed in section 18.3 will be collected during the study. This is detailed on the data collection tool provided in the supplemental documents, which will be used as the REDCap template.

15.5 Who will data or specimens be sent to or shared with, including their name, title, and role on research?

This sharing will be limited to certain members of the study team who have been approved by the IRB to have access. These team members have completed the necessary CITI training as dictated by Carilion Clinic, which has been verified by the VT IRB.

15.6 Describe how the data or specimens will be transferred, transmitted, or shared and how it will be protected in the new location.

Once data is obtained, it will not be transferred to locations outside of Carilion Clinic. All data obtained as a result of this study (see attached data collection tool) will be stored in the secure, Carilion Clinic research environment, which includes REDCap, Shared Drives, and SPARC. Data will only be shared with the VTCSOM and VT collaborators listed on this IRB protocol, and they will have password-protected access to the aforementioned secure tools. This access will be established and maintained by the Carilion Clinic HART team. Furthermore, these collaborators will have access to patient identifiers only as necessary to interact with patients, conduct study tasks, and communicate with the rest of the research team.

15.7 Who will be responsible for supervision of non- Carilion Clinic personnel to ensure the appropriate storage and security of the data/specimens, and that future proposed research has undergone IRB review?

The Carilion Clinic PI listed on this IRB application will be responsible for the supervision of non-Carilion Clinic personnel to ensure appropriate PHI storage and security. All data that is generated as part of this study will remain protected within Carilion Clinic. Currently, there is no plan to use this data for outside research purposes. If this data were to be transferred outside of Carilion Clinic for the purpose of further research, it will be the PI's responsibility to collaborate with external investigators to ensure that the proposed research has undergone IRB review.

15.8 Who will own the specimens/data once they are shared?

Please submit any signed agreements in the Initial Submission Packet.

Carilion Clinic will own all data created over the course of this research project.

15.9 If the specimens being shared will be retained in a repository for possible future research, provide the protocol for the repository and the external investigator's IRB approval letter for the repository in the Initial Submission Packet.

N/A

16.0 Research Settings/Performance Sites

16.1 Indicate the sites where research activities will occur, or from which subject data or specimens will be obtained, and a brief

summary of the activities that will occur at each.

☐ N/A (Select this option if this research is a Medical/Chart Review ONLY)

	Site	Summary
☐	CRMH	
☐	CRCH	
☐	CNRVMC	
☐	CFMH	
☐	JCHS	
☐	CRMH Rehab	
☐	Riverside	
☐	Crystal Spring Medical Office Building	
☐	Other Carilion Clinic Physician's Office	
☐	Blue Ridge Cancer Care (BRCC) / US Oncology	
☐	Fralin Biomedical Research Institute at VTC	
☐	VT Blacksburg Campus	
☐	Assisted Living Facility or Nursing home	
☑	Other Locations (specify): Carilion Clinic Outpatient Therapy	213 Gilbert Street, Blacksburg VA 24060 2900 Lamb Circle, Entrance 8, Christiansburg VA 24073

17.0 Applicable Regulations for ClinicalTrials.gov Registration

17.1 Is this study FDA-regulated?

(•) Yes ( ) No

17.2 Is this research funded wholly or in part by NIH?

( ) Yes (•) No

17.3 Is this study a Clinical Trial, as defined by FDA or NIH, and therefore needing registration on ClinicalTrials.gov? Click the help button to the right to learn more about the definition of a clinical trial.

(•) Yes ( ) No

17.5 Is the clinical trial already registered in ClinicalTrials.gov?

(•) Not yet, but clinical trial will be registered prior to enrolling any subjects
( ) Yes
( ) No, this clinical trial will not be registered

ClinicalTrials.gov #:

TBD

Note: The following statement must be included verbatim in the consent form for trials that are/will be registered on ClinicalTrials.gov:

"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."

17.6 Who is responsible for registering this trial in ClinicalTrials.gov and ensuring information is updated, as necessary? Please provide a name if the person is at Carilion or listed on the research team, or state the sponsor or lead site if the sponsor or lead site will register the trial.

The responsible party for an applicable clinical trial (ACT) must register the trial and submit results information. The responsible party is defined as:

- ***The sponsor of the clinical trial, as defined in 21 CFR 50.3; or***
- ***The principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for the submission of clinical trial information***

The responsible party for an ACT must submit the required clinical trial information **no later than 21 days** after enrollment of the first participant, but registration is highly recommended before enrollment begins due to some journal requirements.

Dr. Andy Muelenaer

18.0 Study Procedures

18.1 Provide a step-by-step description of the research procedures and/or and interactions with human subjects.

Provide a study schedule and list all activities or procedures that will be performed and describe the frequency and duration of research procedures, diagnostic and research

tests, questionnaires or surveys, specimen collection, and experiments, including screening, intervention, follow-up etc in step-by-step chronological order. State the length of time subjects will be in the study and the expected amount of time required for each study visit or activity. Describe how, when and where research activities will be administered and analyzed. If the research includes blinding, indicate whether researchers or subjects will be "unblinded" to study assignment and describe when and how this will be done.

1. For each study visit, participants will be asked to arrive 45 minutes before the beginning of their regularly scheduled follow-up visit. Research activities will take 45 minutes.
2. Upon early arrival to their regularly scheduled appointment, participants will be fitted for their very own, "athletic sleeve" by a member of the research team. This athletic sleeve will be used throughout the duration of the study. Patients will be asked to come wearing a tank top or short-sleeved t-shirt. If they do not come dressed as such, they will have the opportunity to change in a private space.
3. Before donning the athletic sleeve, a member of the research team will measure the patient's upper limb circumference and induration and administer a baseline survey using the first section of the Lymphedema Life Impact Scale (LLIS - document attached). Upper extremity circumference will be measured in centimeters at several points, which are: palmar crease, the wrist below the styloid process, wrist + 10 cm, wrist + 20 cm, wrist + 30 cm, and wrist + 40 cm. Upper extremity induration will be measured at the same points as circumference. These measurements are being taken solely for research purposes and should take approximately 3 minutes.
4. The athletic sleeve will be donned by the patient and the novel therapeutic device will be placed over it. A standardized sequence of vibratory therapy will be applied. The standardized sequence of vibratory therapy is as follows
    - This code goes through a series of 5 total phases for a 36 minute total treatment. The details of
      each phase, and the total time spent in that phase are detailed below.
        - Proximal Prep Phase (Total Time: 7 minutes) All proximal motors, 5-8, are on for the entire phase.
        - Distal Prep Phase (Total Time: 7 minutes) All distal motors, 1-4, are on for the entire phase.
        - Decongestion Phase (Total Time: 4 minutes) Moving proximal to distal, motor 8 to 1, the motors are turned on for 30 seconds then turned off before moving to the next motor pair.
        - Clearing Phase (Total Time: 4 minutes) Moving distal to proximal, motor 1 to 8, the motors are turned on for 30 seconds then
          turned off before moving to the next motor pair.
        - Reabsorption Phase (Total Time: 14 minutes) Moving distal to proximal, motors are turned on at different intensities mimicking a wave pattern.
    - The pattern moves up the arm for 16 cycles. Use of this device will not impact standard of care in any way. The participant may ask to stop the research session at any time
5. The participant may ask to stop the research session at any timeThe athletic sleeve will then be removed, and a member of the research team will measure the patient's upper limb circumference and induration and administer a survey using the first section of the Lymphedema Life Impact Scale. These measurements are being taken solely for research purposes and should take approximately 3 minutes. Patients will be asked if they experienced any side effects or adverse effects.
6. Standardized decongestive therapy will be performed by qualified personnel. This step takes approximately 1 hour and would happen regardless or whether or not patients are enrolled in this study. The exact sequence and modality of therapy varies significantly from patient to patient, but a "typical" treatment session is as follows.

- Treatment today included:
- Manual Therapy provided for 30 minutes:
    - Large Vibration tool (**https://www.rehab-store.com/p-magic-wand-massager.html**) was applied at moderate pressure/compression on low setting x 3 minutes on each quadrant of the upper extremity covering anterior and posterior side of proximal arm and forearm to decrease pain, inflammation, and protein rich edema.
    - Large Vibration tool was then used to assist in lymphatic flow by using sweeping motion from distal to proximal on the upper extremity.
    - Small vibration tool (**https://www.rehab-store.com/p-rolyan-mini-massager.html**) was applied to posterior side of the upper extremity in horizontal position and secured with a Coban wrap (**https://fsastore.com/nexcare-no-hurt-self-adherent-wrap-3-in-x-80-in-tan/23594.html?gad_source=1&gclid=Cj0KCQiAnrOtBhDIARIsAFsSe51So6bK8D3doGZZBzIxJLCcWTedkUUnBubn2Jr6nw7FyfTDwd9nGKcaAnMpEALw_wcB**) at minimum pressure x 6 min to decrease protein rich edema and lymphatic stagnation in distal forearm.
    - After removal of Coban and small vibration tool, patient's forearm induration changed from moderate to mild.
    - Patient tolerated massage techniques of effleurage, petrissage, and cross friction to help alleviate pain, discomfort, muscle adhesions, and immobility to upper extremity and shoulder girdle area.
    - Myofascial release completed to pec, bicep, and deltoid to decrease fascial adhesions, decrease chronic inflammation, decrease pain, and increase range of motion.
    - Manual lymphatic drainage performed to abdomen, trunk, and upper extremity to increase lymphatic flow and decrease stagnation in tissues.
    - Manual Lymph Drainage performed to stimulate lymph nodes and lymphatic vessels to increase their activity and promote lymph flow using techniques of 3 seconds on/3 seconds off skin stretch and feathering toward inguinal lymph node group.
    - Patient tolerated active moving cupping techniques this date to lateral trunk to decrease fibrosis and edema.
    - NDT treatment techniques provided during manual treatment of placement and hold, loading and joint compression provided for postural alignment to increase upright posture to decrease pain while engaging in ADLs and IADLs.
- Therapeutic Activity provided for 30 minutes:
    - Therapist applied US to insertion of pec major to decrease adhesions and edema. US was applied at non thermal setting at 3 megahertz, 20% duty cycle and 1.5 output while patient was placed in active stretch x 7 minutes.
    - Patient instructed on stretching exercises of shoulder flexion and abduction.
    - Patient completed stretches with minimal assistance to maximize range of motion.
    - Patient instructed on each type of massage and pressure and sequence for each.
    - Patient educated on at home whole body exercises including light intensity cardio to increase strength and endurance.
    - Patient instructed on pain relief techniques of using massage and vibration tools to decrease pain. Patient's caregiver instructed on all types of massage and sequence and pressure for each to decrease pain.

7. At the conclusion of the standardized decongestive therapy, the measurements and surveys conducted in step 3 will be repeated. Patients will also be asked if they experienced any side effects with the standard of care treatment.

8. This series of steps will be repeated at the patients' weekly follow-up visits for four weeks. Standardized decongestive therapy for lymphedema is most often performed on a weekly basis (and is one of the inclusion criteria for this study). Therefore, choosing this visit frequency would not greatly alter a patient's schedule or ability to perform other daily tasks. At the end of the four weeks, the patients will receive a $20 Kroger gift card as compensation for their participation.

9. If a patient chooses to withdraw from the study early or needs to be removed from the study for their own safety, notes will be added to research documentation and the patient' s Epic chart indicating their departure from the study. Going forward, they would receive standard decongestive therapy as before their participation in the study. They will receive a prorated compensation fee for their participation.

10. Study subject limb circumference, induration data, and survey data will be analyzed using a paired t-test.

You must attach surveys, instruments, interview questions, focus group questions, etc. in the Initial Submission Packet and label them clearly.

18.2 Specify which procedures, tests, visits, etc. described above are part of usual standard of care at Carilion Clinic and which are being performed solely for research purposes. If procedures, tests, visits are routinely performed for clinical care, but are providing data for this research study, state this as well.

Measurements of upper extremity circumference and induration along with assessment of pain level and presence /absence of side effects/adverse effects will be collected solely for research purposes. Use of the novel therapeutic device will also be done solely for research purposes. Standardized decongestive therapy is performed as part of the usual standard of care for lymphedema at Carilion Clinic. Patients would receive this if they were not part of this study. While decongestive therapy is routinely performed as part of clinical care, it is also producing data for this study, as we will be measuring upper extremity circumference and induration along with assessing the participant's pain level and experience of side effects after administration of this therapy.

18.3 Describe the data collection methods and how data be compiled and collected for assessment. State whether the data/specimens to be utilized in the repository are already in existence (retrospective) or if the data will be generated in the future (prospective).

- **"Retrospective data" is data that is already in existence at the time of application receipt by the IRB. Retrospective is in reference to the date the data was GENERATED, not the date the data is COLLECTED. If all data is retrospective, please provide the start date from which data will be collected and the end date, and note that ALL data must be in existence at time of submission of this application.**
  - **Example: This IRB application is being submitted on 12/1/21 and is collecting data on a standard of care surgery and looking at patient outcomes. All surgeries for this retrospective studies will be completed between 11/31/2018 and 11/31/2021 (the day before the study is submitted to the IRB). This study will likely qualify for a waiver of consent.**
- **"Prospective data" includes any data (including data from the medical record) that are not currently in existence at the time of receipt of the application by the IRB, even if the data is being collected solely for Standard of Care. Prospective data collection typically requires informed consent from the participant to be able to use their clinical data or specimens for research purposes. If all data is prospective, please state date range from which data will be generated.**
  - **Example: This IRB application is being submitted on 12/1/21 and the study is collecting data on a standard of care surgery and looking at patient outcomes. All surgeries for this prospective studies will be completed between 1/1/2022 and 1/1/2025. This study will require informed consent UNLESS a waiver of consent is requested and justified.**

Attach a copy of your data collection tool or spreadsheet listing exactly what data is to be gathered during this research study.

This research project will collect prospective data. The research team will collect the following specific measurements:

- Upper extremity circumference (measured in centimeters)
- Upper extremity induration

- Lymphedema Life Impact Scale (LLIS - first section only)
- Any side effects or adverse effects experienced

All measurements will be taken by designated study team members.

Upper extremity circumference will be measured in centimeters at several points, which are: palmar crease, the wrist below the styloid process, wrist + 10 cm, wrist + 20 cm, wrist + 30 cm, and wrist + 40 cm. Upper extremity induration will be measured at the same points as circumference.

Induration will be measured using a durometer (Rex Gauge Co. Model 1600 Dial Durometer Type OO) placed on the aforementioned points on the ventral surface of the proximal forearm.

Lymphedema-related physical complaints will be measured using the first section of the Lymphedema Life Impact Scale, a validated survey already widely used in the clinical care of lymphedema.

Side effects and adverse effects are thoroughly detailed in section 23.1. Side effects include, but are not limited to, a skin tingling sensation, pain/soreness/swelling, dizziness, headache, nausea, and shortness of breath.

These side effects will be recorded in the Data Collection Tool template inside the secure Carilion Clinic research environment.

18.4 Describe how long individual participants will be actively in the study. If there will be a period of time after the active component of the study where participants will still be in the study (ex: participants outcomes are being extracted from the medical record at 1 year, but the last research study visit was at 3 months), state this as well.

Patients will be actively participating in the study once a week, for four weeks.

18.5 Describe how long the entire study is expected to last, including data analysis.

Patient recruitment for this study would take anywhere from 6 to 8 months. Each study participant will have 4 weeks of treatment, but each participant may not start at the exact same time, so study activities will take anywhere from 2 to 3 months. We will spend one month compiling and analyzing data. Altogether, this research project will take anywhere from 9 to 12 months.

18.6 Describe the qualifications of study personnel conducting the research procedures. This could include medical training specific to conducting the interventional procedures in this research, phlebotomy training for those drawing blood, study protocol specific training to be provided by the sponsor, or any other training to demonstrate that the research personnel are appropriately quailified to conduct the study.

The specific interventional procedures involved in this research study include donning and doffing of the proprietary device, implementation of the proprietary device, measurement of limb circumference, and induration, and administration of the LLIS. The PI will ensure that all study team members have completed CITI training and are well-versed in the above procedures.

Research team members will be trained on the use of the device by one of the inventors. Training will include the following benchmarks

- Putting the device on a study subject's arm and adjusting it so that it fits snugly
- Connecting the device to the external power bank and turning it on. Turning the device on is simple, and involves flicking a switch
- Carefully removing the device from a study subject's arm
- Safely storing the device in its designated space

Research team members without a demonstrated conflict of interest are able to obtain measurements that result in the creation of data. Dr. Muelenaer, Tara Newberry (listed on this application), and Leah Thomas (VT collaborator) will train the entire research team on how to interact with patients and conduct study procedures that result in research data as well as document and report adverse events. This training will be logged and signed by one of the aforementioned trainers.

18.7 Please describe appropriate alternatives to the study procedures or course of treatment.

(For example: not to participate, standard of care treatment, other research study, same treatment offered off study)

At any point in time, patients may choose to opt out or not participate in the study. This will be made abundantly clear before any data is collected. If patients choose not to participate, they will only receive the standard of care for lymphedema, which is decongestive lymphatic drainage massage, and they will not receive treatment with the experimental device

19.0 Research Involving Device(s)

19.1 Device Name:

View Details	Device Name	Is the Device FDA Approved
⊟	LymphaVibe	No

Manufacturer/Supplier of Device	VT BEAM
Will Devices be supplied at no Cost	Yes
Is the Device FDA Approved	No
Is an IDE necessary	No

19.2 Describe any credentialing procedures and training in the use of the device that will occur prior to use.

Since the device (LymphaVibe) to be used in this research study is novel and proprietary, there is no official credentialing procedure.

Dr. Muelenaer, Dr. Arena, Leah and Seth all played an important part in the development of this device from the ground up and know its operation inside and out. These individuals will formally train everyone else listed on this IRB in proper donning and doffing, operation, storage, maintenance, and troubleshooting of this device. Those that are trained on the use of this device will be maintained on a log in the Research Binder.

The below research team members may be trained on the device. This largely depends on individual research member schedules and how well individuals are able to cover research visits (i.e. less research team members may be trained if the need is not as great)

- Dr. Ralph Brown (PI)
- Annette Fielder (OT)
- Evgeniya Molotkova (medical student)
- Cara Spivey (research coordinator)
- Selah Wangler (undergraduate student)
- Jennifer Rechani (undergraduate student)

19.3 Who will assume primary responsibility for the storage of the device used in this study?

Name:

Seth Jarvis and Leah Thomas

19.4 Describe storage and control of the device, including precautions being taken to minimize the chances of device use by health care providers not listed on this application.

(Ex: special ordering requirements, labeling, separate stocking, etc.).

The device will be stored securely, outside of the Carilion Clinic facility where research activities will be taking place as to avoid confusion between it and any other routinely utilized equipment. It will be brought in as needed for each patient and returned to its storage area afterwards. While in the clinic for study procedures, the device will be stored in a clear plastic tub that is labeled with the PI name, IRB number, and research study title. In addition to this information, the verbiage "Do NOT use as part of routine care. This device is for research activities ONLY" will be clearly written on the container. Providers at the aforementioned facility are aware of this research taking place and know that this device is investigational and currently for research use only.

Attach the PMA or cleared (510k) by FDA if used in accordance with labeling, or for investigational devices, attach sponsor/FDA risk assessment documentation if available in the Initial Submission Packet. Attach sponsor device manual of operations if available.

20.0 Research Review of Data/Records

20.1 What types of records will be reviewed for this research study?

- [x] Medical record/medical chart
- [ ] Films/x-rays
- [ ] Data in a database
- [ ] Hospital administrative/billing records
- [ ] Quality improvement records
- [ ] Publically available database
- [ ] Other

Provide a detailed description about your selection above, including if the records are already in existence at the time of this submission or if you will be accessing future records, and special permissions that may be needed to access the data/records:

Carilion Affiliated or VTCSOM Research Team members who have been approved by the IRB to access identifiable information will be reviewing medical records to confirm patient eligibility for this research study. The records that will be used in this study are already in existence at the time of this submission.

20.2 What is the original purpose of the data being reviewed?

- [x] Clinical Care
- [ ] Collected as part of routine business activities
- [ ] Research Study
- [ ] Collected under Repository Protocol
- [ ] Other

20.3 If collected as part of a previous research study or repository protocol, enter the IRB number for the study.

N/A

20.4 Is the data identifiable private information or Protected Health Information (PHI)?

- (•) Yes
- ( ) No

21.0 Incidental Findings

21.1 Does this study involve any imaging procedures (x-rays, CT, MRI, PET, ultrasound, etc.) specifically for research purposes?

- ( ) Yes
- (•) No

21.2 Does the research include any of the following?

- [ ] Exams, blood tests, genetic tests or markers, or other tests or procedures that may generate incidental or secondary findings, including disease or conditions other than the one under study, or familial relationships including paternity and ancestry.
- [ ] Testing for communicable diseases
- [x] None

22.0 Identification/Recruitment of Subjects

22.1 How do you plan to identify potential subjects?

To "identify" a potential subject refers to procedures to determine which individuals may qualify to participate in the study in order to decide which individuals to contact about taking part.

Check all that apply:

☑	Existing Record Review, including Medical Chart Review, Clinic Schedule Review, or QA-QI Database Review.	Select all that apply: ☑ Patients' records reviewed will be those from research team's own patient population ☐ Patients' records will be those from other physicians or medical practices' patient population ** You must request Waiver of Informed Consent and, if any HIPAA identifiers are collected, a Waiver of HIPAA Authorization for recruitment purposes.*
☐	Researchers who ARE NOT treating clinicians of potential subjects will ask treating clinicians for referrals of eligible patients interested in the study.	Select all that apply: ☐ Treating clinicians will identify potentially eligible patients and obtain patient permission before providing researchers with patient contact information. ☐ Treating clinician will provide documentation of patient permission in a email/letter to researcher, and researcher must document permission in research record. **You must request a Waiver of Informed Consent/HIPAA Authorization for recruitment purposes.*
☐	Potential subjects will not be directly identified by the researchers from existing records. The potential subject will obtain IRB-approved information about the study from an advertisement, flyer, brochure, website, grand rounds presentation, department meeting, etc. In most cases, the potential	Comments:

	subject will contact the researcher if interested.	
☐	Review of Registry/Database in which individuals have previously signed a consent giving their permission to be contacted for future studies.	Comments:
☐	Student Records	Comments:
☐	Other	Please specify other:

22.2 Please describe the identification process.

List all information you plan to collect and record during the identification process PRIOR to contacting potential subjects. This includes the inclusion/exclusion criteria and demographics to determine if a person qualifies for a study before contacting that person to be a potential subject.

1. Prior to starting the day, the occupational therapist listed in this application will scan their clinic schedule and identify patients that meet study inclusion/exclusion criteria. This occupational therapist works at both of the locations listed above.
2. They will verbally bring up this research study to eligible patients during their regularly scheduled treatment visit, which is typically about an hour long. Lymphedema is treated with a combination of massage and compression, giving the occupational therapist (OT) leeway to talk to a patient while they deliver hands-on treatment. The OT will give a brief explanation of what will happen to the patient and how it will/will not impact their care.
3. If a patient expresses interest in participating in the study, the occupational therapist will give them an unsigned copy of the consent document to take home and read over. The OT will verbally confirm that the patient is interested in participating in this study. Additionally, the OT will confirm the patient's contact information (phone number and email address if applicable) and the best time to reach out to them. Then, the OT will reach out to a member of the research team and relay the patient's contact information.
4. After receiving the patient's demographics (name and DOB) from the OT, a designated member of the research team (who is Carilion Affiliated or a VTCSOM student and has been approved by the IRB) will access the patient's chart via Epic and confirm their eligibility according to the inclusion/exclusion criteria.

22.3 Through what methods will potential subjects be contacted or recruited?

Check all that apply. To "recruit" a potential subject refers to the initial contact method you plan to use to convey information to a potential subject to determine if he or she would be interested in taking part in your study.

- ☑ Direct in-person contact
- ☑ Telephone call
- ☐ Letter
- ☐ E-mail
- ☐ Brochure
- ☐ Radio/Television script
- ☐ Newspaper Ad
- ☐ Online advertisement (including Facebook, Twitter, Craigslist, other websites, etc.)

- [ ] Flyer/Poster
- [ ] Snowball sampling
- [ ] Clinical trial website posting
- [ ] Other
- [ ] None (there will be no interaction or intervention with potential participants in this study)

22.4 Please provide any additional details about how potential subjects will initially be contacted, who will contact them, or how they will be introduced to the research.

- ***If recruitment material is being mailed, emailed, or otherwise distributed, describe where/how the distribution list will be obtained.***
- ***If potential subjects will be recruited by telephone, describe how many times the research team will attempt to call / leave a voice message.***
- ***When subjects respond to recruitment material, describe the information that will be provided to them about the study and the information that will be collected from subjects (e.g. name, telephone number, etc.). Describe also, how many times you will attempt to respond to call the subject back / leave a voice message.***

1. The occupational therapist (provider) listed at the beginning of this application will identify potential participants (based on established inclusion and exclusion criteria) from their patient pool.
2. The provider will verbally bring up this research study during a patient's regularly scheduled treatment visit, which is typically about an hour long. Lymphedema is treated with a combination of massage and compression, giving the provider leeway to talk to a patient while they are delivering hands-on treatment. They will give a brief explanation of what will happen to the patient and how it will/will not impact their care.
3. If a patient expresses interest in participating in the study, their provider will give them an unsigned copy of the consent document to take home and read over. The provider will confirm that the patient is agreeable to being contacted by the research team and confirm their contact information and the best time to reach out to them. Then, the provider will reach out to a member of the research team and relay the patient's contact information.
4. Contact by telephone will only occur once the potential participant has been approached in person and verified interest in the study. Initial contact by phone will only occur by Carilion Affiliated or VTCSOM IRB approved team members unless the participant gives verbal permission to be contacted by a VT Team member, which will then be documented in the research record
5. This encounter will be documented as a research note in Epic by a member of the research team.
6. Two to three days after the initial contact has been made, a designated member of the research team will attempt to contact the patient via phone call, limiting the number of attempts to three. If the research team member cannot reach the patient during this time, they will not be included in the research study.
7. If the study team is able to make contact with the patient, they will have the option to either undergo e-consent or choose to sign the consent form at their next regularly scheduled office visit. All consenting procedures will be completed by the Carilion Affiliated or VTCSOM IRB approved team members.

22.5 After potential subjects are identified, describe the pre-screening process that will take place prior to obtaining informed consent.

This could include asking questions to a potential subject to determine whether he or she meets eligibility criteria, for example: patients will answer questions about their medical history, be expected to come to the first screening visit after fasting, stop taking medications, change diet, etc. To comply with HIPAA regulations, only the minimum necessary protected health information may be collected at this time. This means only questions relating to the inclusion and exclusion criteria may be asked.

- [ ] No prescreening will take place

During the pre-screening process, patients will be asked to confirm their legal name and date of birth (to verify identity). They will also be asked to verify their past medical history, as our inclusion criteria stipulates a current diagnosis of lymphedema. Additionally, patients will be asked about their current health, as our exclusion criteria excludes patients with certain chronic conditions from participating in the research study.

22.6 Indicate whether pre-screening information will be retained on persons who do not ultimately participate in the study and what specific information, including identifiers, will be retained.

Identifiers from patients that decide to not participate in the research study will be maintained on file. This is for the sole purpose of creating a running list so that patients who are not interested in participating are not contacted more than once.

Attach all recruitment materials, letters, phone scripts, flyers, etc. in the Supplemental Documents section after you complete the IRB application.

23.0 Risks and Risk Minimization and Benefits

23.1 List the possible risks, discomforts, or harms to subjects associated with the research.

If the risks differ based on group assignment, describe for each group. Estimate the (1) probability of occurrence, (2) the seriousness, and (3) the duration of each risk. If this information is captured in the protocol or investigators brochure (IB) or other materials, indicate the document and page numbers where the information can be located.

Possible risks, discomforts, or harms include:

Physical: The pressure of the device is less than that of an inflated blood pressure cuff. It is most comparable to a blood pressure cuff that has been well-fitted, but has not been inflated. The device utilizes a level of vibration that has been demonstrated to be similar to devices currently in use by lymphedema therapists. Please see this **link** for a commercially available vibrator that is similar to what is typically used.

- Skin tingling sensation
    - Skin tingling sensation is a common occurrence, but it is mild and will subside after treatment has ended.
- Pain, soreness, or swelling
    - Pain, soreness, or swelling is an uncommon occurrence, but it is mild and will subside after the device is removed and treatment has ended.
- Dizziness
    - Dizziness is an uncommon occurrence, but it is mild and will subside after treatment has ended.
- Headache
    - Headache is an uncommon occurrence, but it is mild and will subside after treatment has ended.
- Nausea
    - Nausea is an uncommon occurrence, but it is mild and will subside after treatment has ended.
- Shortness of Breath
    - Shortness of breath is an uncommon occurrence, but it is mild and will subside after treatment has ended.

Confidentiality:

- Potential loss of confidentiality and release of medical information

Potential of this risk is low since data is shared only with personnel listed in this IRB application and is stored securely in the Carilion Clinic research environment (REDCap, SPARC, and secure Shared Drive). This risk is of moderate seriousness and the duration of the risk is as long as this study is active plus 6 years, as Carilion Clinic SOP stipulates that study data be maintained for 6 years after the conclusion of research activities.

There may also be risks of stress, emotional distress, embarrassment, or inconvenience.

Citations:

1. Lerner, R. “Complete decongestive physiotherapy and the Lerner Lymphedema Services Academy of Lymphatic Studies (the Lerner School).” Cancer vol. 83,12 Suppl American (1998): 2861-3. doi:10.1002/(sici)1097-0142(19981215)83:12b+<2861::aid-cncr39>3.0.co;2-v

2. Szuba, A., Achalu, R. and Rockson, S.G. (2002), Decongestive lymphatic therapy for patients with breast carcinoma-associated lymphedema. Cancer, 95: 2260-2267. **https://doi.org/10.1002/cncr.10976**

23.2 Define adverse events (AEs), serious adverse events (SAEs), and unanticipated problems (UAPs) for the study. Describe the protocol-specific reporting procedures, including who will be responsible for each step (e.g., PI), timeframes for reporting, how reports will be distributed, and follow-up that will occur.

Ensure that the reporting procedures meet the reporting requirements of Carilion Clinic IRB, the FDA, NIH, OHRP, sponsor, study leadership and any other regulatory body that applies to the study, as applicable. Please note that all Carilion Privacy breaches must also be reported to the Privacy office by the PI. Noncompliance must be reported to the IRB as well as Office of Integrity and Compliance.

Adverse events (AEs):

- Pain, soreness, or swelling in the area being treated or adjacent areas that is NOT alleviated with removing the device
- Headache
- Dizziness
- Nausea
- Shortness of breath
- Skin irritation or rash

Serious adverse events (SAE):

- Infection at the site of treatment

Unanticipated problem (UAP):

- N/A

PI will be responsible for reporting any AEs, SAEs, or UAPs.

23.3 Describe the actions that will be taken to minimize the risks associated with participation in this research.

If this research includes risks that might require immediate or prompt medical management, describe access to/availability of emergency medical equipment and trained personnel at each setting where procedures that impart physical/health risks will take place. If this information is available in the study protocol indicate the page numbers where the information can be located.

Participants will be asked verbally whether the external non-clinical team members can be present to perform the research activities. A clinically trained Carilion team member (not an inventor) will be present to perform and oversee all research activities. Clinical research team members may also be present who could provide assistance in a medical emergency. Medical equipment will be present as needed. The participant will be monitored closely during data collection in the clinic. To protect confidentiality research records will be stored on secure and encrypted Carilion Clinic servers.

23.4 For studies involving drugs, devices, biologics, or imaging, describe the type of pregnancy testing that will occur and how frequently it will be conducted on women of reproductive potential.

Include:

- ***If pregnancy testing will not be conducted, provide the reason.***
- ***State the types of birth control methods women of reproductive potential will be instructed to use.***
- ***If women will not be instructed about acceptable methods of birth control, provide the reasoning.***
- ***Describe the birth control methods men of reproductive potential will be instructed to use. If men will not be instructed about acceptable methods of birth control, provide the reasoning.***

While this research study does involve a medical device, there is little evidence to suggest devices and treatment techniques that are similar pose any threat to a woman of reproductive potential. Therefore, this study does not require routine pregnancy testing.

23.5 Does the research include screening tools, questionnaires, or procedures that may indicate the presence of serious depression and/or suicidal ideation?

○ Yes ◉ No

23.6 Describe the Data Safety Monitoring Plan or Data Safety Monitoring Board, or indicate the page(s) of the protocol or name of the document where this information can be located. While a robust Data Safety Monitoring Plan is REQUIRED for greater than minimal risk studies, a plan should also be in place for studies that are minimal risk. Please click on the Help circle to the right for information on writing a DSM plan based in risk levels of the research.

Include:

- ***The data that will be reviewed, including safety data, untoward events, and efficacy data;***
- ***Who is responsible for reviewing the data;***
- ***How the safety information will be obtained and documented (e.g., case report forms, by telephone calls with participants, printouts of laboratory results, etc.);***
- ***The frequency or periodicity of review of cumulative data;***
- ***The statistical tests for analyzing the safety data to determine whether harm is occurring;***
- ***Any conditions that trigger an immediate suspension of the research or other action for the research.***

For this study, a Data Safety and Monitoring Committee (DSMC) will be established. The committee consists of a physician, lymphedema therapist, and biomedical engineer. They will be familiar with the project, but will have no direct involvement in it. The DSMC will review any reports of anticipated side effects, unanticipated side effects, serious adverse events and unanticipated problems. The study population consists of 15 subjects. Routinely, after each of the first 2 cohorts of 5 study subjects each, the DSMC will conduct a review. The DSMC will only have access to de-identified data. Until this review is completed, and the DMSC makes a recommendation to continue, no subjects will be enrolled and studied. The DMSC will make its determinations based upon review of data that includes the incidence of side effects (physical risks and harms outlined in section 23.1) and incidence of adverse events and serious adverse events (outlined in section 23.2) For occurrence of any unanticipated side effects or adverse events, the study will be immediately suspended, and these conditions will be reviewed by the DSMC, followed by reporting to the IRB. The study will only continue if recommended by the DMSC and permitted by the IRB. Data that will be provided to the IRB if the Stop/Pause is activated will be submitted in writing, and include full disclosure of all data collected, and any written annotations associated with the study in the patient chart. A recommendation of whether the study should continue without modification, continue with modification, or no longer continue from the DSMC will be provided to the IRB in writing after each meeting is held.

23.7 Describe the plans and rationale for conducting an interim analysis.

○ Yes ◉ No

23.8 Have stopping rules been established for the study, including for reasons of futility?

(●) Yes ( ) No

Describe the stopping rules:

If any of the following were to occur during the course of the research study, the study will be discontinued.

- Bleeding or bruising
- Interference with electronic devices such as, but not limited to, hearing aids and mobile phones
- Any evidence of increasing edema with use of the device

23.9 Are there defined criteria (ex: rates of adverse events) for when study interventions should be discontinued?

(●) Yes ( ) No

Describe the criteria:

If any of the following were to occur during the course of the research study, the study will be discontinued.

- Bleeding or bruising
- Interference with electronic devices such as, but not limited to, hearing aids and mobile phones
- Any evidence of increasing edema with use of the device

23.10 Are there exams or procedures that the subject will be asked to have done or follow to safely withdraw from the study?

( ) Yes (●) No

23.11 Will subjects who withdraw from the interventional component of the study be asked for their permission to continue to gather information about them through follow up visits, phone calls, records review, or other methods?

( ) Yes
(●) No
( ) N/A

23.12 Describe the potential benefits to science and/or society expected from this research.

In general, we do not expect patients to directly benefit from this research study. They will still be receiving the standard of care decongestive lymphatic massage from their occupational therapist, and use of the device will do little to change overall outcomes. If this study is able to demonstrate both safety and efficacy of the device, this opens up further opportunities for comparison against existing pneumatic pumps and other devices labeled for at-home use. Devices that are currently available on the market are bulky, expensive, and not very user friendly, and this device can provide a much needed solution for providing lymphedema maintenance care between appointments with a lymphedema-specialized occupational therapist.

23.13 Are individual subjects expected to directly benefit from participating in this research?

Note: Compensation is not considered a benefit.

( ) Yes (●) No

24.0 Costs and Compensation

24.1 Will the subject, or the subject's insurance, be responsible for any medical costs incurred as a result of participation in the research?

Take into account medical costs associated with study procedures, drugs, or devices.

○ Yes ◉ No

24.3 Will subjects be reimbursed for any expenses related to their research participation, including medical costs, travel, parking, or transportation?

○ Yes ◉ No

24.4 Will subjects receive any monetary compensation (cash, check, or giftcard) or non-monetary gifts, incentives, or tokens of appreciation for participating in this research?

Note: Reimbursement for costs is not considered compensation. Use of raffles or lotteries are discouraged at Carilion Clinic since the compensation is not being equitably dispersed to participants. Raffles and lotteries may be permitted on a case-by-case basis with appropriate justification.

◉ Yes ○ No

Please ensure the following language is in the consent document:

Include if payment for the study will be less than $100 in the next calendar year:
Payments made to you as compensation for your participation will be tracked by the research team. This information will be submitted to Carilion's financial department for central tracking. If you receive greater than $600 from Carilion in a calendar year, this is considered taxable compensation and will be reported to the Internal Revenue Service (IRS). You will be issued a 1099 tax form by Carilion if you meet this reporting threshold.

Include if payment for the study will be $100 or more in the next calendar year: In order to receive compensation for your participation, you will be asked to complete an Internal Revenue Service (IRS) W-9 form. Your social security number will be required to complete the IRS form. Compensation to study subjects greater than $600 in a calendar year is considered taxable compensation and is reportable to the Internal Revenue Service (IRS). Carilion will be required to provide your name, social security number, address, and amount of payment to the IRS. You will be issued a 1099 tax form by Carilion if you meet this reporting threshold. This information and your payment amount will be kept secure and confidential in our research financial records and Carilion's financial office. This information will not be associated with the study name or the research data you provide as a participant

24.5 Please describe the compensation.

Include the amount and method of payment, and the distribution plan for the payment (payment received at each visit, payment at end of study, completion bonus, etc.). If a non-monetary item will be provided, state the approximate retail value of the item, when subjects will receive the item, any conditions or requirements that must be fulfilled for subjects to receive the item(s), and a picture of or link to the item online, if possible.

All participants will receive a $20 Kroger gift card for their participation at the conclusion of their study visits. If the participant does not complete all study visits, their compensation will be prorated at $5 per study visit and will be provided to them after their last study visit.

24.6 If the research involves children or adults unable to consent to participation, explain who will receive the monetary compensation or non-monetary item(s).

☑ N/A

25.0 Application Questions Complete

25.1 You have now completed the IRB Application. Please click Save & Continue to proceed to the Initial Submission Packet.

Date Completing Form:

02/29/2024

The Initial Submission Packet is a short form filled out after the IRB application has been completed and is where you will attach protocol-related documents, such as consent forms and recruitment materials. You will also be able to conduct a final review of the IRB application.

The PI will be required to sign off on the final Initial Submission Packet. The study may then proceed to the Department Signoff, if necessary based on the application type selected, and may require COI review before proceeding to the IRB.

You can view the Submission History of the study at any time to determine the status.