Wearable Technology to Reduce Risk of DVT and Increase Patient Compliance

Study Protocol and Analysis Plan

Clinical Trials.gov NCT04995601

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SYNOPSIS

Title of Study	Wearable Technology to Reduce Risk of DVT and Increase Patient Compliance
Objectives	**Primary:** Conduct a randomized comparative study of DVT prophylaxis using either standard IPC (Group 1) or the RF MAC system (Group 2) in 300 patients after TJR surgery. Hypothesis 1: During the in-hospital portion of the study, participants who use the RF MAC will have at least a 25% higher adherence rate of wear time of a fully operational IPC device than those using standard IPC devices (control group). Hypothesis 2: Patients wearing the RF MAC in the first 24 hours following surgery will take at least 25% more steps as measured by an activity tracker than those patients using standard of care IPC devices. Hypothesis 3: Patients who use the RF MAC will have a mean gait speed at 14 postoperative days that is at least 20% higher than patients receiving standard of care as measured by the 4-meter walk test. Hypothesis 4: The time required for preparing patients to ambulate will be 50% less using the RF MAC than standard IPC devices. **Secondary:** 1) Measure patient reported outcomes (PRO) of comfort, device acceptance and ease-of-use. 2) Collect feedback from nurses and physical therapists.
Planned Number of Subjects and Duration of Involvement	The total duration of the study is expected to be 18 months (recruitment, enrollment, participation, case closeout, analysis, completion of final report). This study will include two groups. Group 1 will serve as the control group and will receive standard care. Group 2 is the intervention group and will receive the RF MAC system pre-and post-operative care and standard mobility targets. Group 1 will consist of 75 patients at each of two sites (total of 150 patients). Group 2 will consist of 75 patients at each of two sites (total of 150 patients). Patients will be assigned to a group by a site Research Coordinator using a random numbers generator at their final pre-operative appointment.
Patient Population	This study will be conducted on Adult patients (age 40-85) who are scheduled for a first elective total hip replacement (THR) or first or second (opposite knee) elective total knee replacement (TKA). Patients will have an anticipated hospital length of stay of 48 hours or less and will be discharged to home from the hospital. Enrolled participants must be able to perform self-care, have a BMI of between 18 and 39 and a calf circumference between 11 and 24.5 inches

Investigational Products	RF Movement and Compressions (MAC) System including a charging hub, MAC controllers for each limb, and disposable MAC straps for each limb.
Methodology Overview	Once IRB approval has been obtained, the sponsor team, Dr. Karen Giuliano (University of Massachusetts) and Dr. M. Terry Loghmani will begin training Research Coordinators at two study sites: Tufts Medical Center and Eskenazi Hospital. Research Coordinators will establish data collection methods (Case Report Forms) in REDCap (an online database for research data and surveys) at each site, RF MAC Systems will be shipped to the sites, charged and prepared for assignment to patients as they are enrolled in the study at their final pre-operative appointment. Each site will enroll 150 patients (300 patients total) and patients will be randomized in to one of two groups: Control (Group 1) or Intervention (Group 2). Participants will receive an identification number and all data collected will be password-protected. The study consists of two parts: in-patient and at-home. All participants will participate in both parts of the study. **In-Patient:** 1. In the pre-operative appointment, the Research Coordinator will enroll participants and they will be randomly assigned to a study Group (control or intervention) and baseline information will be collected on the CRF. 2. A 4-meter walk test will be performed and the Research Coordinator will enter results in the patients CRF. 3. On the day of surgery, the patient will receive standard of care for each site for patients undergoing a THR or TKA. Patients in the control group (Group 1) will receive the site's standard of care IPC for DVT prophylaxis. Group 2 (intervention) will receive the RF MAC System for DVT prophylaxis. In addition, patients in both groups will receive an activity tracker. 4. In the first 24 hours post-operative, the Research Coordinator will visit the patient's room for observation a total of two times. During these visits, the Research Coordinator will visually observe the status of the DVT prevention device (control or intervention) to determine if it is properly applied to the patient's lower extremities and fully operational. This information will be recorded in REDCap. For Group 1 (control), this information will be collected by via observation by the Research Coordinator and patient interview. For the MAC System Group 2, this information will be collected automatically by the device and recorded by the Research Coordinator during the periodic visits.

	5. Steps in the first 24 hours will be measured using an activity tracker. The Research Coordinator will record mobility data from the tracker to the CRF. Patients in Group 2 will also have steps measured automatically by the RF MAC System. The Research Coordinator will also record mobility reported by the RF MAC system in the patient's CRF. 6. At least once during the first 24 hours of the in-patient period, the Research Coordinator will measure through observation and using a stopwatch, the amount of time required by a nurse to prepare the patient to ambulate (removing tubes, cords, etc.). 7. Prior to discharge, the Research Coordinator will conduct a second 4-meter walk test. Results will be recorded in the patient's CRF. 8. As the patient is preparing for discharge, the Research Coordinator will ask the care team to complete a brief survey regarding their experience with both the standard DVT prophylaxis device and the RF MAC System during their hospital stay. **At Home:** Once discharged, patients will continue involvement in the study at home. Patients in Group 2 will be sent home with their RF MAC System and a "patient packet" that includes a user manual, charging station, controllers, additional straps, a list of study contacts, a patient self-report journal, instructions for wear time and prescriptive mobility, and instructions for returning their devices and activity tracker at the end of the study. Patients in Group 1 will be sent home with instructions for the standard of care, and instructions on how to return their activity tracker. Patients in both groups will receive orders for standard of care from their healthcare team. This may or may not include IPC DVT prophylaxis for Group 1. Group 2 will receive orders for mobility and use of the RF MAC System. In addition, patients in both Groups 1 and 2 will receive daily at-home mobility goals from their healthcare team. 9. The Research Coordinator will record the prescribed at-home standard of care provided prior to discharge. 10. Patients in both groups will receive orders for at-home physical therapy for a minimum of 14 days, which is standard of care for TJR patients discharged to home. 11. Group 1 will receive standard of care DVT prophylaxis (which may be compression stockings, standard IPC or no orders) and a daily goal for steps (mobility). Compliance related to DVT prophylaxis will be self-reported by the patient in a journal in terms of total minutes per day. Compliance with mobility goals will be tracked using an activity tracker in addition to being self-reported.

	12. Group 2 will receive instructions on how many hours per day to use the RF MAC System and a targeted number of steps to achieve per day (from healthcare team). Primary compliance data with DVT prophylaxis will be self-reported in a patient journal. Data related to mobility goals will be collected by the RF MAC System and recorded each day by the patient. 13. A final 4-meter walk test will be administered by the Research Coordinator at the 2-week in-office visit and results will be entered into REDCap. 14. At the end of the study, patients will complete a brief survey regarding their experience with both the standard DVT prophylaxis device and the RF MAC System during their in-home recovery. All participants will receive $100 as remuneration for their study participation and be asked to sign a compensation receipt form. Participants at Tufts Medical Center will also receive $21 for parking reimbursement. 15. The home physical therapist will also be asked to complete a brief survey.

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1 INTRODUCTION

1.1 Overview: Deep Vein Thrombosis, Intermittent Pneumatic Compression and Circulation

Deep Vein Thrombosis (DVT) is a blood clot in a deep vein which occurs when venous blood flow is decreased. Lower extremity DVT requires immediate medical intervention, as it can cause a serious or fatal pulmonary embolus (PE). In the US, DVTs are a leading cause of preventable hospital death, affecting 350,000-900,000 patients and an estimated 60,000-100,000 annual deaths.[1,2] DVTs are the fifth most common reason for hospital readmission, the third most frequent complication of total joint replacement (TJR), and is associated with an estimated annual cost of $10 billion.[3]

The risk of DVT is increased in hospitalized patients for a variety of reasons including, chemotherapy, surgery, and any condition that causes a general decrease in mobility. Immobility is one of the easiest modifiable risk factors for prevention of DVT. In fact, one recent study showed patients spend as much as 95% of waking hours in bed while they recover.[4] In fact, DVT is the most feared complication of TJR, with more than 300,000 total hip and 700,000 total knee replacements performed annually in the U.S.[4] Current recommendations for postoperative DVT prevention after TJR include anti-coagulant medications and/or external compression of the lower limb for a minimum of 10-14 days.[5,6] Since the use of anticoagulants increases the risk of bleeding, if the same level of DVT prevention can be achieved with the use of external intermittent pneumatic compression devices (IPC), patients outcomes could be improved. The degree of enhanced blood flow, particularly in the femoral vein, is particularly important for effective DVT prevention, therefore, it is important to understand the blood flow enhancement efficacy of the available IPC products.

1.2 Impact of IPC on General Circulation

Some data support that the use of IPC can enhance blood flow throughout the body. Use of a laser Doppler flowmetry device has demonstrated that the use of an IPC that covered both the limbs and abdomen enhanced blood circulation to the forearms.[7] In another study, participants who received IPC therapy for 30 minutes twice a day for two consecutive days achieved an average increase in mean arterial pressure of 5mmHg, a decrease in HR of 4bpm, a significant increase in peripheral vascular resistance index (from 545 [440-1066] to 613 [369-1280] dynes s cm(-5) m(-2) [P = 0.013]) and reduction in cardiac index (from 3.4 [2.7- 4.5] to 3.2 [2.5-4.0] L/min per m2 [P = 0.034]).[8]

A study using an IPC on the thigh was shown to increase levels of oxygenated hemoglobin in ischemic limbs of patients with severe peripheral artery disease.[9] Traditional foot-calf IPC did not exhibit any associated increases in oxygenated hemoglobin. A similar study followed patients with critical limb ischemia that were considered amputation-bound. After use of IPC for 12 weeks, mean toe pressures increased from 38.2 to 67 mm Hg, popliteal artery flow velocity increased from 45 to

47.9 cm and cumulative survival at 12 months was 81.2% for IPC therapy users, compared with 69.2% in the control group.[10] This study was repeated in 2011 and 2013 with similar results.[11,12]

1.3 Impact of IPC on Femoral Vein Circulation

Available data on femoral vein circulation support that circulation can be improved with IPC use. One study used both plantar-calf and calf IPC in healthy volunteers and found a significant increase in the maximum velocity of the femoral vein after just five minutes of use.[13] Another study on healthy subjects using the most common type of IPC demonstrated an over 300% increase in average peak velocity in the common femoral vein of each limb after each compression cycle.[14] In a group of inpatients getting prophylactic IPC status post total knee arthroplasty, ultrasonography found that blood volume and velocity was increased in both superficial and deep venous systems in the thighs.[15]

1.4 References

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2 DESCRIPTION OF THE INVESTIGATIONAL PRODUCTS

2.1 RF Movement and Compressions (MAC) System

The RF MAC System is a novel device that is applied to the lower legs of patients that provides intermittent active compressions to the calf muscles which results in increased blood flow in the veins, moving blood towards the direction of the heart and reducing the risk of clot formation.

The Movement and Compressions System is intended to be a portable and wearable system, prescribed by healthcare professionals, to treat the following conditions by stimulating blood flow in the legs:

- Aid in the prevention of DVT (deep vein thrombosis) by enhancing blood circulation; and,
- As a prophylaxis for DVT by persons expecting to be stationary for long periods of time.

During use, the system also monitors patient orientation and movement. It allows healthcare providers and users to implement individualized patient management plans for DVT prophylaxis and patient mobility protocols by utilizing data accumulated by the patient on the previous day as a benchmark. The data displayed on the device allows providers to monitor the patient's orientation, and activity, which can be used to identify risk factors for hospital-acquired events linked to immobility such as: deep vein thrombosis, pressure ulcers, pneumonia, atrophic muscles, and delirium.

The device can be used in the home or clinical setting. The device is intended for use in an adult patient population.

STUDY PURPOSE AND AIMS
The primary purpose of this study is to conduct a multi-site clinical trial of the RF MAC System. The study involves two study sites: Tufts Medical Center (Boston, Massachusetts) and Eskenazi Hospital (Indianapolis, Indiana). This study is funded by a Phase II SBIR awarded to Recovery Force from the National Institutes of Health, National Heart, Lung and Blood Institute (R44-HL132624-02).

2.2 Primary

Conduct a randomized comparative study of DVT prophylaxis using either standard IPC (Group 1) or the RF MAC system (Group 2) in 300 patients after TJR surgery.

Hypothesis 1: Study participants who use the RF MAC will have rates of adherence to wear time of a fully operational device that are at least 25% higher than those using standard IPC devices.

Hypothesis 2: Patients wearing the RF MAC in the first 24 hours following surgery will take at least 25% more steps as measured by an activity tracker than those patients using standard of care IPC devices.

Hypothesis 3: Patients who use the RF MAC will have a mean gait speed at 14 postoperative days that is at least 20% higher than patients receiving standard of care as measured by the 4-meter walk test.

Hypothesis 4: The time required for preparing patients to ambulate will be 50% less using the RF MAC than standard IPC devices.

2.3 Secondary

Measure patient reported outcomes (PRO) of comfort, device acceptance and ease of use and measure nurse perceptions of device acceptance and ease of use and collect feedback from nurses and physical therapists.

4. STUDY OVERVIEW

2.4 Study Approach

Once IRB approval has been obtained, the RF study team will begin working with site Research Coordinators to implement the study. The initial phase will focus on planning and training, followed by enrollment of initial patients.

Once patient enrollment begins, each site will recruit at total of 150 patients (75 in control group and 75 in intervention group). Inclusion criteria includes adult patients (age 40-85) who are having their first elective total hip replacement (THR) or first or second (opposite knee) elective total knee replacement (TKA), speak English and are expected a hospital stay of two days or less with plans to discharge to home from hospital (not a rehabilitation facility). In addition, participants must be able to perform self-care, have a BMI between 18 and 39 and a calf circumference between 11 and 24.5 inches.

Exclusion criteria includes patients scheduled for a partial joint replacement, TJR revisions, emergency surgeries, those with calf deformities that would not allow proper fit for external compression devices, or patients who are non-ambulatory, clinically malnourished or frail/deconditioned. Finally, vulnerable patients (pregnant women, prisoners, homeless and cognitively impaired) and those that do not speak English are excluded from this study. Product labeling and materials are currently only available in English.

Table 1: Clinical Study Plan				
Site	Eskenazi Hospital		Tufts Medical Center	
Principal Investigator	J. Watters, MD		M. Salzler, MD & M. Gordon, MD	
Group (1 is Control; 2 is Intervention)	1	2	1	2
Targeted Enrollment	75	75	75	75
Total Targeted Enrollment per Site	150		150	
Total Projected Study Enrollment	**300**			

Each site will record the total number of patients screened, the number of patients excluded and the reason for the exclusion. These screening statistics will be reported to the Sponsor at the conclusion of the study.

Study Preparation:
Training for implementation of the research protocol and all study procedures/documentation forms will be provided by Karen Giuliano, PhD, RN. Training for delivering the 4-meter walk test will be provided collaboratively by Drs. Karen Giuliano and M. Terry Loghmani.

Product training for the RF MAC device for use in both the hospital and home will be provided to the Research Coordinators at each site by the RF clinical training team.

Study materials, including enrollment forms and surveys will be transferred to REDCap at each site. Each site will receive the following supplies:

- RF MAC Systems to meet patient enrollment goals
- Pedometers
- Waterproof bag for pedometers (worn around the neck)
- Stopwatch timers
- Digital height/weight and BMI scale
- Automated timing gates

- Electrical tape
- Gait belts
- Cones
- Measuring tape
- Measuring wheel
- Postage-paid packaging for returning devices

RF will be responsible for the shipping and installation of the RF MAC hardware. The additional single patient use leg straps will be shipped to each site by RF throughout the study to meet each site's enrollment cadence. The product must be stored in a cool, dry and locked location until they are distributed to participants. Each product package will include a User Manual and the MAC Solution brochure. Patients will also receive a paper journal for recording steps and use of the RF MAC System during the at-home study period.

In-Patient:
In the pre-operative appointment, the Research Coordinator will enroll participants and they will be randomly assigned to a study group (control or intervention). Patients will be assigned a participant number and that number will be recorded on their Informed Consent and the CRF. Only the Research Coordinators at each site and the PI will have access to the key that connects participant numbers to patient names.

A baseline 4-meter walk test will be performed and the Research Coordinator will enter results in the patients CRF. The protocol for the 4-meter walk test is described in the site protocols found in Appendix A (Tufts Medical Center) and Appendix B (Eskenazi Hospital).

On the day of surgery, the patient will receive standard of care for each site for patients undergoing a THR or TKA. Patients in the control group (Group 1) will receive the site's standard of care IPC for DVT prophylaxis. Group 2 (intervention) will receive the RF MAC System for DVT prophylaxis. In addition, patients in both groups will receive an activity tracker and corresponding waterproof pouch to hold the activity tracker. The display screen of the activity tracker will be covered with tape during the study period. Tape will be removed by Research Coordinators and data will be collected from the device at the end of the study period.

Research Coordinators will be responsible for providing device training to participants prior to discharge. This will be conducted using verbal explanation, demonstration and return demonstration. It is expected to require 10-15 minutes to complete training on the RF MAC System and review all required study materials, the use of the activity tracker and follow-up requirements.

In the first 24 hours post-operative, the Research Coordinator will record the total number of minutes that the DVT prevention device (control or intervention) was properly applied to the patient's lower extremities and fully operational. For Group 1, this information will be collected via patient interview and Research Coordinator observation. The Research Coordinator will visit the patient at least two (2) times in the first 24 post-operative hours and visually observe if the DVT devices are on the patient as directed by the standard of care, are fully operational and are correctly positioned. The Research Coordinator will note visual observations for each visit in the CRF. In addition, the Research Coordinator will ask the patient if they have kept their DVT devices on as directed by the healthcare team. The patient's response will be recorded on the CRF.

For Group 2, the MAC System will automatically capture time in use and display results on the device. Following the same protocol, the Research Coordinator will visit Group 2 patients at least two (2) times during the 24 post-operative period to observe if the RF MAC is in use, properly positioned (the device will not operate unless it is properly positioned) and will record the time displayed for DVT prophylaxis on the patient's CRF. In addition, the Research Coordinator will ask the patient if they have kept the DVT devices on as directed by the healthcare team. this information and results will be captured from the device display by the Research Coordinator and recorded in REDCap.

For both groups, steps in the first 24 hours will be measured using an activity tracker and the Research Coordinator will record this information in REDCap. For patients in Group 2, steps will also be measured automatically by the RF MAC System. The Research Coordinator will read the display screen on the MAC and record steps taken during the first 24 post-operative hours.

For both groups, at least once each day during the in-patient period, the Research Coordinator will measure through observation and using a stopwatch, the amount of time required by a nurse or other healthcare worker to prepare the patient to ambulate (removing DVT prophylaxis tubes, cords, etc.). The purpose of ambulation, time required to prepare the patient and time required to return the DVT prophylaxis will be recorded on the CRF.

Prior to discharge, the Research Coordinator will conduct a 4-meter walk test and record the results in REDCap and include a note of any assistive walking device used during the test. The Research Coordinator will also record the information on the display of the RF MAC at time of discharge (Group 2 only) and the number of steps on the activity tracker.

As patients in Group 2 are preparing for discharge, the Research Coordinator will coordinate survey completion for the patient and members of the care team (nurses, physical therapists, etc.).

Patients will receive at home orders for DVT prophylaxis, physical therapy and mobility goals. These orders will be recorded in the patient's CRF by the Research Coordinator. Group 1 will receive standard of care DVT prophylaxis (to be noted in the CRF) and Group 2 will take the RF MAC home to continue DVT prevention using the device.

At Home:
Once discharged, patients will continue involvement in the study at home.

Patients in both groups will receive orders for standard of care from their healthcare team. This may or may not include IPC DVT prophylaxis for Group 1. Group 2 will receive orders for use of the RF MAC System. Patients in Group 2 will be sent home with their RF MAC System and a "patient packet" that includes a user manual, charging hub, controllers, additional straps, a list of study contacts, and instructions for returning their devices at the end of the study. Patients in Group 1 will be sent home with the standard of care (as noted in their CRF)

In addition, patients in both Groups 1 and 2 will receive daily at-home mobility goals from their healthcare team (which were noted in the CRF at discharge).

Patients in both groups will receive orders for at-home physical therapy for a minimum of 14 days, which is standard of care for TJR patients discharged to home. The Research Coordinator will record prescribed physical therapy in the patient's CRF.

Group 1 will receive standard of care DVT prophylaxis (which may be compression stockings, standard IPC or no orders) and a daily mobility goals. Daily mobility goes are expected to prepare patients to complete 2,000 steps a day by the end of the 2-week study period. Compliance will be measured using the activity tracker provided at study enrollment. Patients will be asked to wear the tracker at all times, except during sleep. At the conclusion of the study, the Research Coordinator will record the total activity per day. In addition, the Research Coordinator at each site will call study participants two times during each week of study participation to ensure participants are wearing the activity trackers.

Group 2 will receive instructions on how many hours per day to use the RF MAC System and a targeted number of steps to achieve per day (from healthcare team). Primary compliance data will be self-reported and collected by the Research Coordinator. Data related to mobility goals will also be collected with the activity tracker. A secondary method of data collection will be the RF MAC System itself. At the end of each day, patients in Group 2 will record the data on the display of the RF MAC System screen, filling in the data for each category in a paper diary provided by the Research Coordinator (provided to Coordinators by Recovery Force). The paper diary will include an image of the screen and users will write the data they see on the screen at the end of each day.

The Research Coordinator will call each participate (in both groups) two times a week during the two-week study. Telephone calls will focus on 1) reminding patients to comply with orders; 2) reminding patients to wear their activity tracker; and 3) reminding patients to comply with DVT prevention orders. The Research Coordinator will answer any questions and confirm the participants are complying with study requirements. The Research Coordinator will also review with the patient the return procedures for the RF MAC, which will involve bringing the device with them to their two-week post-operative office visit.

The patients in both groups will be reminded the day before their 2-week appointment via a telephone call to bring their activity tracker with them to their appointment. The patients in Group 2 will be reminded to also bring back the RF MAC System in its entirety with them to their appointment.

At the 2-week follow up appointment, the Research Coordinator will conduct a final 4-meter walk test. Results will be recorded on the patient's CRF in REDCap.

Once the walk test is complete, the Research Coordinator will direct the patient to complete a final survey. Next, the patients will return all study equipment (activity tracker and the RF MAC System) to the Research Coordinator. Patients who return all equipment will receive their $100 remuneration for study participation. Renumeration will be reduced by 50% to $50.00 for any patients who do not return their equipment. Patients who did not return the devices will receive a postage-paid package for returning both the activity tracker and RF MAC device to Recovery Force. Once the equipment has been received by Recovery Force, the additional $50 remuneration will be mailed to the participant. In addition, participants at Tufts Medical Center will receive $21 stipend as reimbursement for parking costs.

Research Coordinators will also send at-home physical therapists of individuals in Group 2 a link to a brief survey about the RF MAC.

2.5 Study Duration

The total duration of the study is expected to be 18 months (site training, recruitment, enrollment, participation, case closeout, analysis, completion of final report). This study will include two groups. Group 1 will serve as the control group and will receive standard care. Group 2 is the intervention group and will receive standard care and the proposed intervention, the RF MAC System. Group 1 will consist of 75 patients at each of two sites (total of 150 patients). Group 2 will consist of 75 patients at each of two sites (total of 150 patients). Patients will be assigned to a group by a site Research Coordinator using a random numbers generator at their final pre-operative appointment.

3 STUDY POPULATION

3.1 Sample Size and Target Study Population

The following vulnerable patients will be excluded from the study: pregnant women, prisoners, homeless and cognitively impaired. Data will be collected at two locations, one site for each cohort.

Each of the two study sites are responsible for recruiting participants in the study (150 total participants, with 75 in each of two study groups).

3.2 Recruitment Methods

Study recruitment at each site will be coordinated with the pre-op team. The initial recruitment will occur during the pre-op visit. Surgeons will recruit patients using direct referral from within the PI/Co-investigator's own clinic and inform them of the study, and ask if they are interested in participating. If the patient is interested, the Research Coordinator will complete the Informed Consent process with the subject and explain the study and answer all questions. This will include reviewing and signing consent.

Patients will be provided a consent form describing the study and containing sufficient information to make an informed decision about participation. Patients who decide to participate will sign the IRB approved consent form and the subject in order to process the payment at the end of the study. Tufts Medical Center uses the CliniCard system, which is a pre-loaded debit card that subjects will be given a copy for their records, at the end of their post-operative appointments when all interventions and surveys have been completed and the device has been returned. Study participants will receive a review of study participation requirements at the anesthesia appointment.

3.3 Patient Selection

The eligibility criteria for prospective enrollment of subjects are shown in **Table 1**.

Table 2: Inclusion/Exclusion Criteria for Enrollment of Subjects	
Inclusion	This study will be conducted on adult volunteers, aged 40-85 years who speak English.
Exclusion	The following vulnerable patients will be excluded from the study: pregnant women, prisoners, homeless and cognitively impaired. Individuals who do not speak English will be excluded from this study.

4 STUDY MATERIALS

4.1 Investigational Products and Accessories

4.1.1 RF Movement and Compressions (MAC) Device

The RF MAC Device is a novel device that is applied to the lower legs of patients that provides intermittent active compressions to the calf muscles which results in increased blood flow in the veins, moving blood towards the direction of the heart and reducing the risk of clot formation.

The Movement and Compressions System is intended to be a portable and wearable system, prescribed by healthcare professionals, to treat the following conditions by stimulating blood flow in the legs:

- Aid in the prevention of DVT (deep vein thrombosis);
- Enhance blood circulation;
- As a prophylaxis for DVT by persons expecting to be stationary for long periods of time.

During use, the system also monitors patient orientation and movement. It allows healthcare providers and users to implement individualized patient management plans for DVT prophylaxis and patient mobility protocols by utilizing data accumulated by the patient on the previous day as a benchmark. The data displayed on the device allows providers to monitor the patient's orientation and activity, which can be used to identify risk factors for hospital-acquired events linked to immobility such as: deep vein thrombosis, pressure ulcers, pneumonia, atrophic muscles, and delirium.

The device can be used in the home or clinical setting. The device is intended for use in an adult patient population.

4.1.2 RF Movement and Compressions (MAC) Device Safety and Handling Issues

The Recovery Force MAC System consists of three components: the strap, designed for single patient use; and the controller, designed for multi-use, and the charging hub. If you are, or may be, pregnant, do not use. Recharge battery using an outlet readily accessible for quick disconnect. Do not use where aerosol (spray) products are being used or oxygen is being administered. Electromedical devices have the potential for explosion in these situations. Never use pins or other metallic fasteners with this product as these could damage the wiring of the device. Care must be taken when operating this equipment around other equipment to avoid reciprocal interference. Potential electromagnetic or other interference could occur to this or to the other equipment. Try to minimize this interference by not using other equipment in conjunction with this device. Keep and store when not in use out of reach of children, pets, pests, and away from water. No modification of this equipment is allowed. No user serviceable parts inside. If you experience pain, swelling, sensation changes, discomfort or any unusual reactions (including allergic reactions to the materials in this device) while using the device, stop using the device and consult your physician immediately. If pulsing or throbbing occur, the device may be wrapped too tightly. Loosen immediately. This device should not be used adjacent to or stacked upon other devices.

4.2 Other Study Materials

Study notebooks to maintain study documents, including signed Informed Consents and all applicable information, and additional forms to be collected and retained by the study institution during the course of the study and maintained for three (3) years following the study completion date.

5 STUDY PROCEDURES

5.1 Study Data

Eligible subjects will be invited to participate in the study using a convenience sampling strategy. Potential subjects must provide informed consent to participate. To be eligible for participation, subjects must speak English and be between the ages of 40-85.

5.2 Procedures for Study Closure

5.2.1 Routine study close-out

The study will end when Recovery Force has obtained all data necessary to complete its studies of the test products. Study close-out will follow Recovery Force standard procedures and may include, but is not limited to, review of regulatory documents, collection of completed case report forms, reconciliation of study records, removal or destruction of ancillary study supplies, record retention and final report submission to the IRB.

5.2.2 Suspension or premature termination of the study

This study may prematurely terminate at any time because of a regulatory authority decision, a change in opinion of the IRB, or at the discretion of Recovery Force. If the study is temporarily suspended, Recovery Force will provide guidance on timing and procedures for resuming the study. If the study is prematurely discontinued, all study materials must be collected, and all study forms completed to the extent possible.

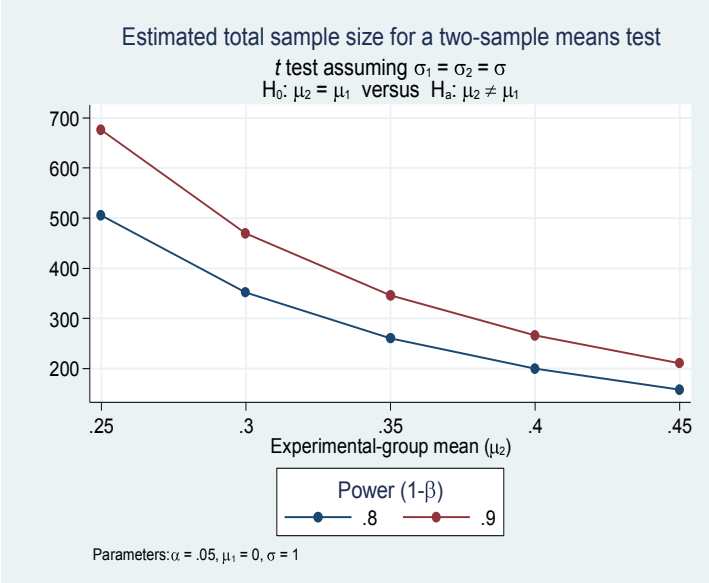
6 DATA QUALITY ASSURANCE

Study monitoring is planned at 6 months. The Principal Investigator will be responsible for the accuracy of all study data.

7 STATISTICAL METHODS

7.1 Determination of Sample Size and Planned Analyses

Dr. Karen Giuliano (University of Massachusetts) is responsible for statistical design and power on this study. First, the team will test the group differences on demographic profiles and between RF1400 (Group 2) and standard-of-care (Group 1). If unbalances on any of these characteristics exist, the Horvitz-Thompson weights or propensity scores will also be adjusted to adjust for bias (d'Agostino, 1998). Dr. Giuliano will also compare the characteristics of the individuals who will drop out of the study with those who complete the study and create weights to adjust for any potential bias. For study, Recovery Force hypothesizes that the in-hospital outcomes measures (minutes of use in the first 24 postoperative hours, number of steps in the first 24 postoperative hours and the amount of



time required by acute care nursing staff to get the patient ready to ambulate) for the patients in RF1400 group (Group 2) will significantly outperform those in standard IPC prophylaxis group (Group 1). Similarly for the Aim 2 at-home outcome measures, (minutes of use per day in the first 14 days of at home use and gait speed at 14 days using the 4-meter walk test, Recovery Force hypothesizes that patients in RF1400 group (Group 2) will significantly outperform those in standard of care group (Group 1). All outcomes are continuously measured. To test Aim 2, let E1 be the indicator variable of group 1 (E=1) vs. group 2 (E1=0), and Y stands for the outcome variable, Z refers to other relevant background and/or clinical variables (age, gender, comorbidities, etc.), the analysis of covariance (ANCOVA) model will be used to assess the difference between groups, i.e., and the team will have $Y = \beta_0 + \beta_1 E1 + \beta_2 Z + \varepsilon$, estimated to give corresponding b parameters for β by ordinary regression. The significance of coefficient of β_1 will be tested to show the group differences. The interaction term of treatment indicator and center indicators will also be tested to examine the homogenous treatment effect across the two study sites. The study was powered assuming 80% of power and 0.05 significance level; the study will require 130 patients per group to detect a medium effect size (EF) of 0.35 difference between groups for a continuously measured outcome. Assuming up to a 15% dropout, each site will enroll 150 patients in each group. The graph below shows the different sample size requirements to detect a certain EF at power of 0.8 or 0.9.

7.2 Bias Minimization

All subjects meeting the specified eligibility criteria will be enrolled using a convenience sampling strategy.

8 ADVERSE EVENT REPORTING

8.1 Non-Device-Associated Adverse Events

Adverse events occurring during the enrollment period should be documented by the Investigator in progress notes but will not be collected or analyzed by Recovery Force unless considered serious.

Serious adverse events (SAEs) encountered during study enrollment will be documented by the Investigator and reported to Recovery Force immediately upon discovery. SAEs are defined under current Good Clinical Practice (cGCP) guidelines as events that result in one or more of the following:

- life-threatening illness or injury;
- permanent impairment of a body structure or a body function;
- medically necessary in-patient hospitalization;
- medical or surgical intervention necessary to prevent permanent impairment to body structure or function; or
- fetal distress, fetal death, or congenital abnormality.

SAEs will be reported using an Unanticipated Adverse Device Effects (UADE) form which serves the dual role of capturing pertinent SAE information per industry guidelines and capturing device

information pertinent to medical device standards. Other serious events that affect the rights, safety, or welfare of subjects must also be documented on the UADE form and must be reported immediately to Recovery Force and to the Investigator's IRB according to that IRB's policies.

8.2 Device-Associated Adverse Events

8.2.1 Definition of an unanticipated adverse device effect (UADE) event

A UADE event, as defined by cGCP guidelines, is any SAE, life-threatening problem, or death caused by or associated with a device (or with the process of evaluating a device) if that SAE, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated, serious, device-associated problem that relates to the rights, safety, or welfare of subjects or operators using the investigational product system or the comparator product system.

8.2.2 Reporting of device-associated adverse events

The Investigator will be responsible for reporting any UADEs to Recovery Force and to the Investigator's reviewing IRB. UADEs will be documented by the Sponsor on UADE forms.

8.3 Recovery Force Contact for Serious Adverse Event Reporting

Jason Bobay
jbobay@recoveryforceusa.com
317-719-5359

9 RISK ANALYSIS

9.1 Potential Risks of the Investigational Product and Clinical Investigation

All subjects will be entering the study voluntarily and the nature of this study should involve minimal risk for study subjects. The only anticipated risks include the possibility of discomfort with the use of the RF MAC Device and potential for feeling uncomfortable with legs exposed during the data collection process. . There is also potential for lack of patient satisfaction with the device.

9.2 Potential Benefits of the Investigational Product and Clinical Investigation

It cannot be promised that you will receive any medical benefits from being in this study.

9.3 Minimization of Risks

Patients who experience discomfort with the device can discontinue use immediately to avoid further discomfort.

10 INVESTIGATOR RESPONSIBILITIES

10.1 Site Qualification and Study Oversight

The PI is responsible for general administration of the study. Before the study, the PI must:

- Sign the Protocol Signature Page
- Provide financial disclosures to Recovery Force, per Title 21CFR 54 (see **Section 12.4** below).

During the study, the PI must ensure that:

- The study is conducted ethically;
- Case report forms (CRFs), including Subject informed consents, are provided with each transfer of data requiring informed consent; and
- All other study forms are completed as outlined by this study protocol.

In the case of completion or termination of the study or an Investigator's role in the study, all study materials must be returned to Recovery Force.

10.2 Case Report Forms/Electronic Data Records

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method(s) used.

Original CRFs are the sole property of Recovery Force and should not be made available in any form to third parties, except for authorized representatives of Recovery Force or appropriate regulatory authorities, without written permission from Recovery Force.

It is the PI's responsibility to ensure completion, review, and approval of all CRFs. CRFs must be signed by the PI or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is true. At all times, the PI has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs.

10.3 Access to Source Documents

Recovery Force or its agents and appropriate regulatory authorities shall be granted direct access to all study-related documents to perform verification that the protocol and all applicable Good Clinical Practices (GCPs), and regulations are being followed and to confirm that study documents are complete and accurate. It is important that Investigator(s) and their relevant personnel be made available during monitoring visits and any audits or inspections, and that sufficient time is allotted for the process.

10.4 Financial Disclosure

Investigators must provide Recovery Force with sufficient, accurate financial information in accordance with local regulations to allow Recovery Force to submit complete and accurate financial certification or disclosure statements to the appropriate health authorities. Investigators are responsible for providing information to Recovery Force concerning their relevant financial interests during the course of the study and for one year after completion of the study. Conflicts of interest should be disclosed as required by law.

Recovery Force is the sponsor of this study. This study is funded by a Phase II SBIR awarded to Recovery Force from the National Institutes of Health, National Heart, Lung and Blood Institute (R44-HL132624-02).

10.5 Deviations from the Study Protocol

An Investigator may not deviate from the study protocol without prior approval by Recovery Force unless the deviations are necessary under emergency circumstances to protect the rights, safety, or well-being of human subjects or the scientific integrity of the clinical investigation. These deviations must be documented and promptly reported to Recovery Force and, if applicable, to the IRB providing oversight of the study. Protocol deviations may result in corrective and preventive actions and/or disqualification of the Investigator.

10.6 Record Retention

To enable evaluations and/or audits from regulatory authorities or Recovery Force, the PI and all sub-investigators agrees to retain all study records, including copies of all CRFs, UADE forms, and source documents, for three (3) years following completion of the project dependent upon the study data. The Investigator must obtain written permission from Recovery Force before disposing of any records, even if retention requirements have been met.

If an Investigator relocates, retires, or for any other reason withdraws from the trial, Recovery Force must be notified in advance, and study records must be transferred to a designee acceptable to Recovery Force. This designee might be another Investigator, another institution, or Recovery Force itself.

10.7 Publication Policy

The results of this study may be submitted for publication to a medical journal. The PI agrees that any publication of data from this study will comply with Recovery Force publication policy, the instructions to authors outlined by the editor of the journal or conference proceedings where the data is to be published, and the spirit of recommendations made in the good publication practice guidelines (GPP3) of the International Society of Medical Publication Professionals. Recovery Force has the right to review any manuscripts, presentations, or abstracts that originate from this study or that utilize these data before they are submitted for publication or other means of communication.

11 ETHICS AND COMPLIANCE

11.1 Investigational Device Exemption

Although exempt from IDE regulations as noted in Title 21 CFR 812.2(c), the conduct and performance of this study will be in accordance with applicable Recovery Force and Investigator responsibilities as described in Title 21 CFR 809 and Title 21 CFR 812.

11.2 Informed Consent and De-Identification

11.2.1 Prospectively collected data

All subjects will be given a copy of the IRB-approved informed consent form (ICF) to review before their study participation begins. The Research Coordinator will explain all aspects of the study in lay language and answer all of the potential participant's questions regarding the study. If the participant decides to participate in the study, s/he will be asked to sign and date the ICF. Subjects who refuse to participate or who withdraw from the study will be treated without prejudice.

11.3 IRB Review

The PI is required to obtain IRB oversight of the research study. The IRB must be provided with the Recovery Force-approved study protocol. Performance of the study may not begin until written evidence of IRB approval has been provided to Recovery Force.

The conduct and performance of this study will be in accordance with applicable Recovery Force and Investigator responsibilities as described in Title 21 CFR 812 and other Good Clinical Practice guidance.

IRB/Ethics Committee oversight will be required as human subjects or data from humans are being used. This protocol and the associated informed consent document(s) (if applicable) must be submitted to the IRB for review and approval. Performance of the study at a given site may not begin until written evidence of IRB oversight has been provided to Recovery Force study manager. IRB Review and approval must comply with Title 21 CFR 812 Subpart D.

11.4 Confidentiality of Data and Patient Records

All patients who are enrolled will be assigned an identification number. A list of participant names and their corresponding medical record numbers and participant identification numbers will be kept in a password protected file. Only the research team members and Principal Investigator will have access to this information.

11.4.1 Provisions to Protect the Privacy Interests of Participants

The PI and/or study institution shall provide sufficient information to allow the IRB to evaluate the researcher's provisions to maintain the confidentiality of data.

Privacy data will be maintained in accordance with HIPAA and other applicable policies and local law.