VA Department of Veterans Affairs	VA RESEARCH CONSENT FORM
Version Date [Date of submission]: February 2018	**Page: 1 of 12**
Subject Name:	**Informed Consent Date:**
Principal Investigator: Ann M. Spungen, EdD	**VAMC: James J Peters**

Protocol: SPU-14-031

Title of Study: A Randomized, Crossover Clinical Trial of Exoskeletal-assisted Walking to Improve Mobility, Bowel Function and Cardio-Metabolic Profiles in Persons with SCI

1. Purpose of study and how long it will last:

You are being asked to participate in a research study. You qualify for participation because you have paraplegia and you are not able to stand or walk. The purpose of this study is to evaluate an exoskeleton device and mobility skills in the device. The exoskeleton device has been registered and approved with the Food and Drug Administration (FDA) for use in a hospital setting for the purposes of standing, walking and stair climbing. This study is being sponsored by the Department of Defense and the National Center of Excellence for the Medical Consequences of SCI at the James J. Peters VAMC. If you qualify for participation in this study, this device will be strapped onto your legs, hips and trunk, and will allow you to stand, walk and climb stairs. This study is broken up into 5 periods. The first is the pre-testing period (2 visits). For the second period (12 weeks), you will be randomly selected for either exoskeletal-assisted walking (WALK) or usual activities (UA). The third period (2 visits) will be a repeat of the first pre-testing period. Period 4 (12 weeks) will be either WALK or UA, whichever you did not participate in during period 2. Period 5 will be post testing (2 visits), which is the same as periods 1 and 3.The total time required to participate in this study is 26 weeks. We plan to enroll 132 participants for this study at 3 research sites: James J. Peters VAMC, Kessler Institute of Rehabilitation and University of Maryland Rehabilitation and Orthopaedic Institute.

Inclusion criteria:

1. Males and females, 18-70 years old;
2. Traumatic or non-traumatic paraplegia >6 months in duration;
3. Motor level SCI of T3 & below (All sites) and T2 & above (JJPVAMC and KIR/KFRC), where the site investigator &/or study physician will decide which device is safest for use on a case-by-case basis in higher cord lesions (T4 and above);
4. Unable to ambulate faster than 0.17m/s on level ground with or without an assistive device and are wheelchair-dependent for community mobility;
5. Height 160 to 190 cm (63-75 in or 5'3" to 6'3" ft);
6. Weight <100kg (220lb);
7. Able to hold crutches &/or walker; and
8. Able to sign informed consent.

Exclusion criteria:

1. Diagnosis of neurological injury other than SCI including:
    a. Multiple sclerosis, stroke, cerebral palsy, amyotrophic lateral sclerosis, traumatic brain injury, Spina bifida, Parkinson's disease, or

b. Other neurological condition that the study physician considers in his/her clinical judgment to be exclusionary;
2. Severe concurrent medical disease, illness or condition;
3. Recent lower extremity fracture within the past 2 years;
4. DXA results indicating a t-score below -3.5 at the femoral neck or the total proximal femur bone and knee BMD <0.60 gm/cm^2;
5. Diagnosis of heterotropic ossification of the lower extremities which affect range of motion or proper measurement of BMD measurements;
6. Significant contractures defined as flexion contracture limited to 25° at the hip, 20° at the knee, and ankle flexion corrected with an orthotic;
7. Untreated hypertension (SBP>140, DBP>90 mmHg);
8. Symptomatic orthostatic hypotension with standing that does not resolve after attempts at upright posture that were made over several days, and standing by the participant is deemed to pose a health risk, as determined by a physician, because of symptomatic orthostatic hypotension;
9. Systemic or peripheral infection;
10. Atherosclerosis, congestive heart failure, or history of myocardial infarction;
11. Trunk and/or lower extremity pressure ulcers;
12. Severe spasticity (defined by an Ashworth score of >4.0 or clinical impression of the study physician or physical therapist);
13. Psychopathology documentation in the medical record or history of that may conflict with study objectives;
14. Pregnancy and/or lactating females.
15. Brain injury with score on mini-mental status examination less than 26
16. Diagnosis of coronary artery disease that precludes moderate to intense exercise;
17. Deep vein thromboses in lower extremities of less than 6 months duration; and
18. Other illness, that the study physician considers in his/her clinical judgment to be exclusionary

2. Description of the Study Including Procedures to be Used:

If you consent to participate in this research study, you will be asked to visit Room 7A-13 at the James J. Peters VAMC and the following procedures will occur:

WALK Period: You will be asked to participate in exoskeletal-assisted walk sessions 3 times/week for 12 weeks. During these sessions, your WALK skills will be evaluated at least 1 time per week. WALK skills include: Exoskeletal-assisted walking tests for the 10 meter walk time (WT), 6min WT, and TUG. It was observed during the Phase II trial that weekly assessment of the walking tests provided structured feedback to the participants regarding their progress in mastering the use of the powered exoskeleton and was useful in motivating the participants. Additional mobility skills (turning, wall rest, stopping, and navigating doors) will be assessed throughout the WALK arm; but not to be considered as part of the primary outcomes. At all times during exoskeleton walking, participants must use both crutches.

UA Period: You will participate in your usual activities for 12 weeks, while keeping a provided log. During this period you will be asked to complete 6 bowel function surveys (every 2 weeks) to be compared to your bowel function during WALK period.

Body Composition: A dual energy x-ray absorptiometry (DXA) scan for regional and total body fat, lean and bone tissue masses will be performed three times: at baseline, at crossover, and after the second arm of the study for both the WALK and UA arm interventions. You will be asked to lie on a padded tabletop. A machine will use a very low dose radiation which will tell us the amount of muscle, fat and bone you have in your body. The maximum radiation you will be exposed to for each scan is as follows:

Scan Type	Entrance Dose	Effective Dose	Scan Time
Total Body	6 μGy	8.62 μSv	739 sec

We estimate all of these DXA measurements combined will sum up to less than 35 μSv of absorbed radiation. This measurement is minimal even when compared to a routine chest x-ray which has an approximate dose of 60 μSv. In addition the average person in New York City receives approximately 3000 μSv/year. Therefore you would have to have all these tests done 100 times to receive an equivalent dose. You will be asked to do this procedure once during the screening evaluation. This procedure will be done again during the post training evaluations.

ISNCSCI: A neurological evaluation for sensory and motor function, level of injury and lower extremity motor scores will be performed according to the ISNSCI standards. This exam will be performed three times: at baseline, at crossover, and after the second leg of the study for both the WALK and UA arm interventions.

Bowel function surveys: The 10Q BFS and the BSS will be administered before both interventions and then bi-weekly (2x/month) for a total of 16 times during the two arms of the study. This information will be used to determine key components to a participant's weekly bowel regime. The Bowel Management item bank short form from the SCI-QOL will be performed three times: at baseline, at crossover, and after the second arm for both the WALK and UA arm interventions.

SCI-QOL: The Spinal Cord Injury Quality of Life measurement tool will be performed three times: at baseline, at crossover, and after the second arm for both the WALK and UA arm interventions.

Blood draw: Over the whole study, a total of three phlebotomy samples (10 ml/time) will be drawn after an overnight fast. The draws will consist of the following: fasting plasma insulin (FPI, 2 ml, green top tube), fasting plasma glucose (FPG, 1 ml, grey top tube), total testosterone (TotT,1 ml, red top tube), and estradiol (E2/E3, 1 ml, red top tube). To measure your lipid profile (cholesterol) and immune system factors, 4_ml of blood will be drawn, of which 3 ml will be sent to Quest Diagnostics and 1_ml sent to Dr. Ona Bloom, at The Feinstein Institute for Medical Research, Manhasset, NY. The Quest and immune system transfer tubes will labeled only with your participant ID number and study time point, These amount will be collected 3 times over the course of the whole study before intervention, at crossover WALK or UA) and after intervention (WALK or UA).

Holter Monitor: A 24-hour Holter Monitor will be used to collect heart rate and blood pressure data for analysis of heart rate and blood pressure variability. The 24-hour Holter monitor provides accurate beat-to-beat measurement of heart rate and blood. The Holter monitor will be placed around the chest for heart rate assessment and a blood pressure cuff will be placed around the upper arm to monitor blood pressure which will self-inflate approximately every 20 minutes over the 24 hours of monitoring.

Postural orthostatic hypotension blood pressure tolerance test (OH BP): Participants will be in the supine position on a bed or elevated gym mat and beat-to-beat heart rate (HR) will be recorded for 60 seconds, followed by passive re-positioning to the seated position on a bed or elevated gym mat with the hip and knee at a 90° angle and the lower leg hanging off the side. Passive repositioning will be accomplished by one staff member lifting the participant's torso by the shoulders, while supporting the head and neck, and a second staff member shifting the subject perpendicular to the bed and allowing the participant's legs to hang off the side.

Participants will be instructed not to assist in the passive movement during this transition, and will be supported by staff.

3. Description of any Procedures that may Result in Discomfort or Inconvenience:

- When you first stand up you may experience some dizziness, become lightheaded or faint because you are not used to standing. Study team members will be by your side while you use the exoskeleton device.
- During the exoskeletal training, you may experience an increased rate of breathing (shortness of breath), dizziness, and chest pain or potentially an irregular heartbeat. If you experience any chest pain or irregular heartbeats during training, you will make the study physician aware and the test will be stopped immediately. During this portion of the study you may also experience muscle and joint aches, joint sprain, broken bones, blood pressure variations, skin abrasions, swelling or bruising due to rubbing while the harness supports your body weight. You may also bruise due to manual contact or due to braces worn on the lower limbs. While the risk of a broken bone is small, it is possible during this portion of this study.
- You are being asked to participate in a study that requires a strong commitment of your time. In order for us to effectively test the utility of the exoskeleton device the number and frequency of the sessions are needed. If you miss more than 80% of your training sessions we may consider removing you from the study.
- If you are a woman of child bearing age we must be sure that you are not pregnant to participate in this study. *Since this research may have unknown effects on an unborn child and should not be done during pregnancy. It is necessary for a pregnancy test to be done first. To your knowledge you are not pregnant at the present time. You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study.*
- The risks of a blood draw include the possibility of a bruise or infection at the site of skin puncture, temporary faintness and rarely, temporary loss of consciousness due to vasomotor instability (i.e. the blood vessels reflexively swell resulting in a fall in blood pressure which is commonly called "vasovagal episode").

4. Expected Risks of Study:

- The risks of blood draw include the possibility of a bruise or infection at the site of skin puncture, temporary faintness and rarely temporary loss of consciousness due to vasomotor instability (i.e., the blood vessels reflexively swell resulting in a fall in blood pressure which is commonly called "vasovagal episode").
- A DXA scan carries a small risk associated with low levels of radiation used in the scan. The total amount of radiation exposure from the DXA is approximately $1/5^{th}$ to $1/10^{th}$ of that received from a routine chest x-ray.
- During the exoskeletal training, you may experience an increased rate of breathing (shortness of breath), dizziness, and chest pain or potentially an irregular heartbeat. If you experience any chest pain or irregular heartbeats during this time, you will make the study staff aware and the test will be stopped immediately. During this portion of the study you may also experience muscle and joint aches, joint sprain, broken bones, blood pressure variations, skin abrasions, swelling or bruising due to rubbing while the harness supports your body weight. You may also bruise due to manual contact or due to braces worn on the lower limbs. The largest possible risk associated with testing the powered exoskeleton is falling. The potential of this occurring will be minimized by having study staff highly experienced in gait training be present during all exoskeletal training. While the risk of a broken bone is small, it is important to understand that it is possible during this portion of this study. Other possible risks include discomfort, triggered spasm, reflex bowel or bladder activity, skin pressure/friction or autonomic instability during use of the device. Last, the device itself could malfunction.

To minimize the above risks the following precautions will be taken:

1. The study team members will be trained by representatives from the manufacturer and the study team of PTs, physicians and biomedical engineers from the USA hospital that performed the first study.
2. Your medical chart will be reviewed. You will also be examined by the study team physician (who is also a Staff SCI Physician and Physiatrist) before being cleared for participation.
3. To prevent tripping over any obstacles, the areas used for the sit-to-stand, stand-to-sit, walking, and stepping will be checked before and during each session to be free of any obstacles.
4. To prevent a potential fall, a trunk harness with hand straps or the pelvic belt of the exoskeleton device will be used by the study staff. This will provide stabilizing assistance during the sessions as

appropriate. You will be flanked by two study team members, one on each side during all WALK sessions. You will never be left unattended when using the exoskeleton device during a session.

5. HR and BP will be monitored throughout the sessions.
6. The power source of the system will be supplied with a fully charged battery and a back-up battery.
7. You will be examined on the system contact points for skin redness, irritation or breakdown before and after each session. If evidence of skin redness, irritation or breakdown exists, alternate placements for straps and/or padding will be used to protect the area. Participants who have continued breakdown will be temporarily discontinued.
8. You will be checked after each session for signs of swelling. If present, you will be instructed to elevate your feet, possibly use compression socks for the next session(s), and/or reduce the upright time or training frequency. If swelling persists, you will be referred to your primary care physician. Training sessions will be discontinued if need be.
9. A measurement of the bone mineral density will be obtained as part of the screening for participation in this study. If your bone mass is too low, you will be excluded from the study.
10. The quality of life survey will ask you questions about your mood/feelings. If during the review of your completed survey(s) the study team identifies that you have depression or that you are a risk to yourself or others, you will be taken to the emergency department for an evaluation, and your primary SCI physician notified.
11. Upon completion of the study, you will not have access to this device. If you develop feelings of sadness or become depressed after completion, tell a member of the study team and they will assist you in finding care.

There also may be risks and discomforts that cannot be foreseen.

5. Expected Benefits of the Study:

There may be no direct benefit to you from this study. But, any information we get from this study will help others. There are possible benefits by taking part in this study such as you may feel healthier and happier because of regaining an ability to be upright with the exoskeletal device. The health-related benefits of standing and walking are unknown at this time.

6. Other Treatments Available:

This study is being done for research purposes, no clinical care or rehabilitation therapy that you are scheduled for will be withheld from you. As such, there are no other treatments available in place of the exoskeleton system. Please note: The exoskeletal system is not a cure for paralysis; it is an external device that permits you to stand and walk.

7. Use of Research Results:

We (I) will let you and your physician know of any significant new findings s made during this study which may affect your willingness to participate in this study. All research material generated from the study will remain in the possession of Dr. Ann Spungen and her study team. Only study team members will have access to the research materials obtained from you for this study. Coded physical materials will be secured in a locked file cabinet behind locked doors at the James J. Peters VAMC. Electronic data without your name or other identifying information will be stored on secured VA networks, behind VA electronic security systems, in access-restricted folders. Your identifiable and personnel health information (PHI) will be protected by coding your identity. Only the study team members will have access to the code.

We may ask to video record you for the purposes of viewing yourself walk to help improve your abilities. If you do not wish to be video recorded we will not do so. In some instances, we may ask to use your video recordings at various presentations. A separate waiver will be presented to you at that time for you to give permission for use of any video recordings of you during your training sessions.

☐_____ By checking this box and initialing, you agree to be contacted by the Principal Investigator or her investigative team at a future date for additional studies being conducted in the Center of Excellence for the Medical Consequences of SCI.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. No information by which you can be identified will be released or published unless required by law. Research Investigator files will be destroyed six years after the end of the fiscal year when the research project has been completed per Records Schedule DAA-0015-2015-0004-0032, Section 7.6, Research Investigator Files.

All specimens obtained during this study will be stored in the Basic Science Laboratory at The Center of Excellence on the Medical Consequences of Spinal Cord Injury located at the James J. Peters Veterans Affairs Medical Center, Bronx, NY. Blood specimens will also be sent to Quest Diagnostics and to The Feinstein Institute for Medical Research for analysis. All specimens sent to Quest or Feinstein will be coded with your participant ID number. Only the research team will have access to the link between your participant ID number and your name. None of your personal health information will leave the VA.

In order to comply with federal regulations, research records identifying you may be reviewed by the following: Representatives of the sponsor or sponsors [Department of Defense, Authorized representatives of the Bronx VAMC (e.g. Institutional Review Board, Research Compliance Officer) and VA, including the Office of Research Oversight (ORO), Federal Agencies such as the Government Accounting Office (GAO), VA Office of Inspector General (OIG), Food and Drug Administration (FDA), and the Office for Human Research Protections (OHRP).

Because this research involves articles regulated by the FDA, the FDA may choose to inspect and copy medical or research records that identify individual research subjects. If this study was initiated on or after March 7, 2012, a description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include a summary of the results. You can search this web site at any time.

8. Special Circumstances:

A copy of your signed informed consent form and signed HIPAA authorization for participation in the study will be included in your medical health record.

9. Compensation and/or Treatment in the Event of Injury:

The VA must provide necessary medical treatment to a research subject injured by participation in a research project approved by a VA R&D Committee and conducted under the supervision of one or more VA employees. Further information about compensation and medical treatment may be obtained from the medical administration service at this VA medical center.

10. Voluntary Participation:

You are not required to take part in this study; your participation is entirely voluntary you can refuse to participate in this study or withdraw your participation in this study after you consent without penalty or loss of VA or other benefits to which you are entitled.

11. Termination of Participation:

You may decline to participate now or you can withdraw from the study at any time after signing consent. If you decline to participate or withdraw, your regular medical treatment will not be interrupted or withheld. If you decide to withdraw from the study at a later date, you will sign a form to revoke your previous authorization. If you decide to withdraw from this research study please notify us. This will not interfere with your regular medical treatment, if you are a patient. If you miss more than 80% of your sessions, your participation may be terminated by the investigator without regard to your consent.

12. Costs and Reimbursements:

As a veteran or non-veteran, you will not be charged for any treatments or procedures that are part of this study. For veterans who are required to pay co-payments for medical care and services provided by VA, these co-payments will continue to apply for medical care and services provided by VA that are not part of this study.

You will receive $20 per visit for 54 visits to help defray the costs of travel. The total payment over 54 visits is $1,080. Payments will be direct deposited into your bank account. It typically takes 6-8 weeks for payment to arrive.

13. Contact Person(s):

(a). To obtain answers to questions about the research, report or seek treatment for a research-related injury, or to voice concerns or complaints about the research contact the following (investigator/research team):

- During the Day: **Dr. Ann M. Spungen, 718-584-9000, x5814**
- After Hours: **Pierre Asselin, MS, 626-788-3437**

(b) To voice concerns or complaints about the research from someone outside of the research team, contact the following:

I understand that should I wish to discuss my participation in this study with any other doctor or layperson, I can contact Mary Sano, Ph.D. ACOS/R&D Program by requesting an appointment at (718) 741-4228 hospital extension 4228, first floor in the research building, room 1F-01 If I have questions, concerns and/or complaints or to offer input , I can ask one of the researchers listed above or contact Dr. Sano. Medical problems during the course of the study should be addressed to the investigator at the phone listed above.

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Subject Name:	Informed Consent Date:
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Protocol: SPU-14-031

Title of Study: **A Randomized, Crossover Clinical Trial of Exoskeletal-assisted Walking to Improve Mobility, Bowel Function and Cardio-Metabolic Profiles in Persons with SCI**

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Dr. Ann Spungen or her delegate has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law. This study has been explained to me. I have had a chance to ask questions. I voluntarily consent to participate in this study. I will receive a signed copy of this consent form.

Subject Signature	Date	Time

Person Obtaining Informed Consent (Print Name) (Investigator or Delegate as indicated on Assurance Page)	Signature of Person Obtaining Informed Consent	Date