Subject Name:_____
Last 4 digits SSN:_____
Date of Birth:_____

Department of Veterans Affairs

VA RESEARCH CONSENT FORM

Subject Name: _____ **Date:**_____

Title of Study: Effects of Evoked Resistance Training and Testosterone after Spinal Cord Injury

Principal Investigator: Ashraf S. Gorgey, PT, PhD **VAMC:** Richmond, VA

This Consent Form Includes Required Elements Of Informed Consent.

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Sponsor:
Protocol No:
Investigator name and address:

VA FORM **10-1086** IF MORE THAN ONE PAGE IS USED EACH PAGE MUST BE CONSECUTIVELY NUMBERED

ICF Template version 4/5/2011

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10/15/13

Subject Name:_____
Last 4 digits SSN:_____
Date of Birth:_____

Title of Research: Effects of Evoked Resistance Training and Testosterone after Spinal Cord Injury
Sponsor: VA RR&D
Protocol No:
Investigator Name and Address: Ashraf Gorgey, PT, PhD
1201 Broad Rock Blvd.
Richmond, Virginia 23249

1. What is this research study about? (Introduction)
You are being asked to volunteer for this research study because you are a person with a spinal cord injury (SCI). This study involves research with SCI to determine the effectiveness of surface neuromuscular electrical stimulation (NMES) accompanied with ankle weights and/or Testosterone patches (Tp) on body composition and metabolism. NMES is electrical shock exercise for your paralyzed legs. The Tp is approved by the Federal Drug Administration (FDA) and has been applied to people with SCI; however, we would like to test its effects on body composition and metabolism in people with SCI. The use of Tp is considered experimental.

For this purpose, after 4 weeks of no intervention, you will be randomly assigned (like a flip of a coin) to receive Resistance Training (RT) and Testosterone patches (Tp) or just testosterone patches (Tp) for 16 weeks. There will be 12 subjects in each group. The study visits for the RT+Tp group will be twice weekly to exercise the knee muscle groups in the sitting position for 16 weeks. The Testosterone replacement therapy will be a skin patch that will be alternated on both shoulders over the course of the study. We will also study the effects of detraining (received training or no training) on body composition and metabolic profiles.

The expected duration of your participation is 20 weeks (4 weeks no intervention+16 weeks training), twice weekly. If you choose to continue, you can be followed for additional 16 weeks.

You will be one of 24 subjects enrolled in this study.

2. What is expected of me? (Procedures)
If you agree to participate and sign this consent form the following study procedures will be done

A. <u>Measurements</u>
Day 1-McGuire VA Hospital

- You will be asked to undergo a complete physical examination, including a neurological assessment, and ASIA examination (One time- 30 to 45 minutes). Your blood pressure, heart rate and an electrocardiogram (EKG, heart tracing) will be done. Depending on the results of these tests the study doctor will discuss with you if you are eligible to continue in this study.

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- If you are eligible to continue, your weight, height, waist and abdominal measurements will be taken. Your body fat, lean and bone mass will be measured by dual x-ray absorptiometry (DXA) machine. While lying on a table, we will measure different components of your body. The measurements will be performed 3 times or 4 times (if you choose to continue for 16 week detraining period). The measurement will be done 4 weeks before starting the study, immediately before and then after the 16 week intervention. One more DXA will be done if you choose to continue for additional 16 weeks. The time commitment is 30 minutes per visit.

- Magnetic Resonance Imaging (MRI) scans will be obtained to measure abdominal fat, lower leg muscles size and bone strength in your legs. This procedure involves lying still on a table during the scan period. The measurements will be performed 3 times or 4 times (if you choose to continue for 16 week detraining period). The order of the measurements will be before and then after the 16 week intervention. Extra measurement will be done if you choose to continue for additional 16 weeks. The time commitment is 60 minutes/visit.

- You will then be escorted to the VCU Clinical Research Service (CRS) for dinner, and will remain overnight. The CRS is located on the 8th floor in the North Hospital at VCU. It is a section reserved only for subjects enrolled in research studies. You will need to sign a separate consent form for the procedures and test done at the VCUCRS.

Day 2- VCU Clinical Research Service

- At 6 am, you will be awakened for determination of basal metabolic rate (BMR). The BMR test is performed to determine how much oxygen your body uses at rest. This measurement requires that a large clear plastic dome is placed over your head and the air you breathe will be measured. The dome placed over your head will provide you with plenty of air. You will be instructed to remain awake, but quiet and still, during this testing procedure which will take approximately 30 minutes. Resting blood pressure and fasting labs will be obtained.
- An IV line will then be placed in your arm, and blood samples will be drawn at 6.30, 7.00 and 7.30 am.

- This will be followed by a 3-hour intravenous glucose tolerance test (IVGTT). An IVGTT examines your sugar tolerance and how your body uses insulin. An IV line (small plastic tubes) will be placed in an arm vein, for the injection of glucose and insulin. Another IV line will be placed in the opposite arm, and the arm will be warmed. This increases blood flow and makes it easier to obtain blood samples from the IV line. Three baseline blood samples for measurement of glucose and insulin will be obtained. Glucose will be injected in to your vein over 20 seconds at the start

of the test. Blood samples for measurement of glucose and insulin levels in your blood will be taken at multiple times between minutes 3 and 180 of the test. Twenty minutes into the test, a small dose of insulin will be injected into your arm vein. The total amount of blood drawn during the entire study is about 7 tablespoons.

- During the 3 hour-IVGTT, a dietitian will meet with you to ensure that you will follow a standard diet pattern during the 16 week-interventions (45% carbohydrate, 35% fat and 25% protein). You will be asked to maintain a 5 day food record during the course of the study. The forms will be evaluated weekly by the dietitian to provide monthly feedback. You will be asked to meet with the dietitian five times during the course of the first 20 weeks (baseline 1, baseline 2, 4, 8 and 12 weeks) to make sure you follow the diet throughout the study. No meetings will occur during the detraining period.

- **Day 2- VCU Clinical Research Service or McGuire VA Hospital**

- Immediately after, small muscle biopsy samples will be taken from the knee muscle group to determine the effects of exercise or patches. A numbing medication will be injected at the biopsy sites and a ¼ inch skin incision will be made with a small surgical scalpel. A special biopsy needle will be inserted through the skin incision and into the muscle and a small amount of muscle (3 pieces) will be collected, after which the site will be closed and a pressure dressing applied for at least 10 minutes. Muscle biopsy will be done twice, before and after the interventions. You are free to return home after this.

Day 5-McGuire VA Hospital

- Three days after completing the muscle biopsy, you will be asked to return to McGuire VA Medical Center to measure the force that can be generated from your knee muscle group as well as the tone in your muscle by using a biodex chair. The chair is located at the SCI Exercise Physiology laboratory. You will be transferred to the chair by using a ceiling lift. Then each knee muscle group will be stimulated with electrical stimulation current and the force will be recorded. These measurements will be done 3 or 4 times (if you choose to continue for 16 week detraining period). The measurements will be done 4 weeks before starting the intervention, immediately before and then after the 16 week intervention. Your time commitment is 30 minutes/ visit.

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Randomization:
You will be assigned by chance (like the flip of a coin) to one of two groups **Group 1** RT +Tp (Resistance Training (RT) and Testosterone patches (Tp) or the testosterone patches (Tp) group **(Group 2).** A diet recall form will be given to you to record everything you eat and drink for 5 days. You will be asked to give this form to the study staff.

B. **Interventions for 16 weeks (RT+Tp vs Tp) at the McGuire VA Hospital**

If you have been assigned to the RT+Tp **group**, you will receive 16 weeks of electrical leg shock with ankle weights that will be done while sitting in your wheelchair. Two adhesive patches will be placed on the skin over the knee muscle group. Electrical current from the stimulator will be slowly increased in 5-second intervals to cause full leg extension. Once full knee extension is achieved in a sitting position, an extra 2 lbs of weight will be added on a weekly basis. Each session will be consisted of 4 sets of 10 knee extensions and it will last for 30-40 minutes. Training will be alternated between right and left legs.

- If you are assigned to the RT+Tp group, a small clear mask will be placed on your face and you will be asked to ride a Functional Electrical bicycle, which is a stationary bicycle at the start of the study and again at the end of 16 weeks to determine the amount of energy you use during exercise. This will measure how much energy you use. Your heart rate will be measured.

- Both groups (RT+Tp or Tp) will be asked to place a testosterone patch on clean dry skin of your shoulder to wear at all times. The patch will be changed once a day before bedtime on the right or the left shoulder over the course of the 16 weeks. The blood testosterone level will be measured every 4 weeks and the dose will be adjusted if necessary. You will also be asked to report to the SCI Exercise Physiology laboratory at the end of every 4 weeks and return the empty testosterone patch package so we can determine if you are using the patches as instructed.

C. Detraining (reduced intervention or no intervention) after 16 week intervention (optional).

If you are involved in the RT+Tp, you will have the option to be one of the six subjects that will continue training once weekly in addition to the Tp **or** will be one of the other six that will receive no intervention and come only for measurements at the end of 16 weeks of detraining. If you are involved in the Tp group, only six subjects in the Tp group will stop the Testosterone patches and come only for measurements at the end of 16 weeks of Both groups will be reexamined after 16 weeks. Both groups will be asked to turn in weekly food diaries.

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D. Home-based training (optional)

- 5 participants will be asked to exercise at home for 8 weeks. The exercise routine will include Neuromuscular Electrical Stimulation (NMES) accompanied with ankle weights and Telehealth communication (a service offered by the Department of Veterans Health Administration). Telehealth communication will be provided by video conference. Sixteen weeks after the end of the training, 5 participants in the RT+Tp group will be invited to participate in the home-based training on the basis of first-come, first-served.

- If you are not enrolled to participate in VA Telehealth activities then a form will be completed to register and provide permission before you may participate. Registration with SCI Home Telehealth is typically completed with the McGuire SCI Home Telehealth Coordinator, Melodie Anderson, MSN RN.

- You will be provided a portable neuromuscular unit as well as ankle weights. You will be trained on how to use the neuromuscular unit and applying the ankle weights by the principle investigator. At the end of the 8 weeks intervention, you will return the neuromuscular unit and the ankle weights.

- You will need to provide your own working computer with webcam, microphone, and speakers (headphones or earphones).

- You will receive 8 weeks, twice weekly, of electrical leg shock with ankle weights that will be done for one leg while sitting in your wheelchair. The opposite leg will not be trained. Two adhesive patches will be placed on the skin over the knee muscle group. Electrical current from the stimulator will be slowly increased in 5-second intervals to cause full leg extension. Once full knee extension is achieved in a sitting position, an extra 2 lbs of weight will be added on a weekly basis. Each session will consist of 3 sets of 10 knee extensions and it will last for 30-40 minutes.

- At the beginning and at the end of this optional 8 weeks, , both thighs muscle size will be measured by MRI as previously stated.

3. Will the research benefit me? (Benefits)

It is possible that you may receive no benefit from participating in this study. Information from this study may help others in the future.

4. What are my alternatives to being a research subject? (Alternative Therapy)

You do not have to participate in this study to receive treatment for your condition. Your alternative is to decline participation in the study.

5. What are my risks? (Risks, Inconveniences, Discomforts)

What may present a risk?	Possible Risk/Side Effect	How often has it occurred?
Venous catheter insertion and Blood draws	1. Localized swelling, soreness, bruising, and chance of infection, bleeding, pain, light-headedness or possible fainting. A total of 7 tablespoons will be collected.	It occasionally occurs
Muscle Biopsy	1. Localized swelling, soreness, bruising, chance of infection, bleeding, pain, lightheadedness or possible fainting	It is uncommon
Insulin Sensitivity Tests	1. Hypoglycemia (low blood sugar) with dizziness, sweating, and nausea 2. Seizures, coma, or death	1. It occasionally occurs. 2. Unlikely
IV line failure	Discomfort, swelling, redness over the IV line site causing failure to use the line. Another IV will need to be placed in another part of your arm.	Occasionally occurs
Pressure wound from skin irritation during exercise	Break in your skin creating a wound requiring daily wound care.	Occasionally occurs, but n more so than usual activitie
DXA	No significant risk This research study will involve exposure to radiation from 3 whole body DEXA scans (4 if you are participating in the detraining phase). This radiation exposure is not necessary for your medical care and is for research purposes only. All radiation increases the risk of developing cancer in the future. The total amount of radiation that you will receive in this study is equal to less than one day of exposure from natural background radiation. The McGuire VA Medical Center Radiation Safety Committee has reviewed the use of	Unlikely

	radiation in this research study and has approved this use as involving acceptable risk and necessary to obtain the research information desired. Please tell your doctor if you have taken part in other research studies or received any other medical care recently involving radiation.	
Electrical Stimulation Exercise	1. Light-headedness, shortness of breath and altered heart rate& blood pressure leading to autonomic dysreflexia. Muscle soreness at your neck, upper back, shoulders, arms & hands 2. Fracture 3. Autonomic dysreflexia (slow heart rate, high blood pressure, headache flushing &sweating) which may be life threatening 4. Pressure Ulcers 5. Fainting, heart attacks or death	Unlikely Unlikely Unlikely Unlikely Unlikely
Testosterone Patches	**Serious reactions** Severe rash at site where you place the patch, worsening heart failure that may cause difficulty for pumping blood, swelling of your body, enlarged prostate causing difficulty in urination, increase in red blood cells which may cause blood clots in your legs (cause swelling), lungs (result in chest pain, shortness of breath and rarely death) and brain (causing a stroke) , decreased ability to father children, prostate cancer, difficulty in breathing during sleep, blood in urine **Common reactions** Application site reactions, back pain, enlarged prostate, headache, irritations	

	of the skin, depression, enlarged breasts, increase cholesterol which may increase your risk of heart disease, chills, diarrhea, fatigue, frequent urination, pain during urination, reduced sex drive, inflammation of prostate, rash, acne, confusion	occasionally occurs

All drugs have the potential to cause allergic reactions including the drugs used in this study. Allergic reactions may be mild to severe, and include the following symptoms: chills, fever, skin rash, hives, itching, watery eyes, swelling, headache, difficulty breathing, difficulty swallowing, severely low blood pressure, organ failure, and death. Serious allergic reactions require immediate medical attention.

6. Will I get paid? (Compensation)

You will receive $1200 for your participation in this study according to the following schedule. After completion of the initial 4 weeks of testing, you will receive $200. After 50% completion of the exercise training or Tp intervention (8 weeks), you will get $400 and after completing the last 8 weeks and the final testing sessions, you will receive an additional $600. You will get an extra $400 if you decide to complete an extra 16 weeks of the study. If you are one of the 5 subjects continuing for the extra 8 weeks using the Telehealth communication you will get $200. Additionally, you will be provided $10 per visit to the laboratory to offset transportation costs.

If you receive payments from the Department of Veterans Affairs they will be reported to the IRS along with your social security number.

7. Will I have to pay? (Cost of Participation)

You will not have to pay for care received as a subject in a VA research project regardless of whether you are a veteran or a non-veteran. If you get a bill for research services contact your study doctor or research nurse. Some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by the VA that are not part of the study.

There is no guarantee that the medicines you will receive during this study will be continued after the study is completed. If you are a veteran and are eligible for care you may continue to receive the same medicine after the study only if the medicine is routinely available at McGuire VAMC and your physician decides that it is the most appropriate treatment.

8. Does pregnancy prevent me from participating? (Pregnancy)

Women will not be eligible to participate because of the unknown risks that involve using Testosterone patches.

9. What if I get injured? (Research Related Injury)
In the event of injury resulting from your participation in this research study, McGuire Veterans Affairs Medical Center may or may not provide compensation, depending on applicable federal regulations. For research related injury, the VA must provide necessary medical treatment regardless of whether you are a veteran or a non-veteran.

10. Who Will See My Information? (Confidentiality)
The confidentiality of your research records will be maintained according to professional standards of confidentiality and VA regulations. Records identifying you may be reviewed by the members of the research team, , the Research and Development Committee and its sub-committees, Association for the Accreditation of Human Research Protection Programs, officials from the Veterans Health Administration, the Office of Research Oversight, the VA Office of the Inspector General, Richmond VAMC, and other federal oversight agencies such as the Food and Drug Administration, Office for Human Research Protections, and VCU or as required by law.

The records and data pertaining to the research participant will protected by keeping them in locked file cabinets, on computer protected with passwords, and in locked. Only the PI, Ashraf S. Gorgey, will have access to the data.

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 information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time

Information published or presented about the results of this study will not identify you. If you are a non-Veteran receiving care as part of this study, you will have an electronic VAMC medical record created for you. You will also be given a VA Notice of Privacy Practices.

11. Do I have to participate in this study or can I withdraw from the study? (Voluntary Participation and Withdrawal)
Participation in this study is voluntary and you may refuse to participate without penalty or loss of benefits to which you are otherwise entitled. The study staff will answer any questions you may have about the study. You are free to withdraw your consent and stop participation at any time. If you decide to withdraw from this study, you should contact Dr. Gorgey to discuss termination of your participation. It is important that you do this so that Dr. Gorgey can withdraw you safely. Stopping will in no way change the quality of care you receive now or in the future at this institution or your right to participate in other studies.

Withdrawal from a research study may have serious effects on your health or welfare. The following withdrawal procedures are necessary for your safety and for orderly termination of your participation in this research study. You will be told how to stop using the Testosterone Patches and a follow up visit with your regular provider will be confirmed.

Any significant new findings that develop during the research study that may affect your decision to continue participating will be provided to you as soon as possible.

Your participation in this research study may be ended without your consent for the following reasons

- If the study doctor believes, for any reason, that it is within your best interest.
- If you develop side effects that are considered dangerous.
- If you refuse to use Testosterone Patches or fail to return for follow-up as recommended by your study doctor or fail to follow the study doctor's instructions.
- If you refuse to have tests that are needed to determine whether Testosterone Patches are safe and effective.
- If you require treatment with drugs that are not allowed in this study.
- If other causes prevent continuation of the clinical research study.
- VA RR&D, FDA, McGuire IRB may also end the study at any time.

12. Whom should I contact for questions? (Contacts)

If you have any questions, concerns or complaints regarding this study, unexpected reactions, or you are injured and become ill as a result of participation in this study please call AM or PM:

	Office	Off Hours
Dr. Ashraf S. Gorgey	(804) 675-5000 ext. 3386	804-750-4814
Dr. Robert A Adler	(804675-5424	804-659-0281
Dr. Teodoro Castillo	(804) 675-5000 ext. 4582	804-659-0186
Dr. Jeannie Savas	(804) 675-5112	804-338-1791
Dr. Ranjodh Gill	(804675-524	804-539-7420
Dr. Timothy Lavis	(804) 675-5000 ext. 3391	804-659-0248

If you are unable to reach any of the study staff listed and need immediate medical assistance, please call the VAMC hospital operator at 800-784-8381 and ask for the Emergency Room physician to obtain advice, or call the Emergency Room directly at (804)-675-5527. If you have any questions, concerns or complaints about your rights as a research subject you may contact the McGuire Institutional Review Board (IRB) at (804) 675-5676. The IRB is responsible for reviewing research in humans and making sure that their safety and rights are protected.

13. Date of Consent Form Revision: 04/06/2012, 07/10/12, 9/21/2012, 2/1/2013, 6/28/2013, 8/30/2013, 10/10/2013

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Department of Veterans Affairs

Subject Name: _____ Date:_____

Title of Study: : Effects of Evoked Resistance Training and Testosterone after Spinal Cord Injury

Principal Investigator: Ashraf Gorgey VAMC: Richmond, VA

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above.

Dr. Gorgey (or an associate) 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. I will receive a signed copy of this consent form.

_____ _____
oject's Signature Date

_____ _____
Signature of Person Obtaining Informed Consent Print Name/Date

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