Department of Veterans Affairs

VA RESEARCH CONSENT FORM

Subject Name: _____ **Date:**_____

ICF Template version: 3/8/2016

Title of Research Study: Testosterone and Long Pulse Width Stimulation for Denervated Muscles after Spinal Cord injury
Sponsor: VA Merit Review
Protocol No: N/A
Investigator Name and Address: Ashraf S. Gorgey, MPT, PhD
1201 Broad Rock Blvd
Richmond, VA 23249

1. 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	**(804) 675-5424**	**(804) 659-0281**
Dr. Lance Goetz	**(804) 675-5455**	**(804) 351-3423**
Dr. Teodoro Castillo	**(804) 675-5000 ext. 4582**	**(804) 659-0186**
Dr. Timothy Lavis	**(804) 675-5455**	**(804) 351-0753**
Dr. Jeannie Rivers	**(804) 675-5112**	**(804) 338-1791**
Dr. Ranjodh Gill	**(804) 675-5424**	**(804) 539-7420**

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.

2. 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 to determine the effectiveness of testosterone replacement therapy (TRT) and long pulse width stimulation (LPWS) neuromuscular electrical stimulation (NMES) vs. testosterone replacement therapy (TRT) and standard NMES on your muscles and metabolism. LPWS and NMES use electrical shocks to exercise your paralyzed muscles. The difference is that the LPWS is electrical pulses penetrate deeper into the muscles.

If you participate, you will be randomly assigned (like a flip of a coin) to receive TRT+LPWS or TRT+NMES for a one year period. There will be 12 subjects in each group. During study visits, both groups will exercise the knee muscles in the sitting position. A series of tests/procedures described below will be done at the beginning of your participation, after 6 months and the end of 1 year.

The expected duration of your participation is ONE YEAR (3 weeks of testing + 49 weeks of training, twice weekly).

3. What is expected of me? (Procedures)

If you agree to participate and sign this consent form the following study procedures will be done.

A. Measurements

Day 1

- You will be asked to undergo a complete physical examination including rectal exam, (One time- 30 to 45 minutes). Your blood pressure, heart rate, an electrocardiogram (EKG, heart tracing) and electromyogram (EMG) will be done. The EMG measures muscle response to nerve stimulation of the muscle. A needle will be inserted into the knee muscle group to record muscle activity. Depending on the results of these tests the study doctor will discuss with you if you are eligible to continue in this study.

- If you are eligible to continue, your weight, height, waist and abdominal measurements will be taken. Your body fat, muscle and bone mass will be measured using x-rays (DXA) while lying on a table. The measurements will be performed 3 times. Each scan takes 20 minutes.

-Magnetic Resonance Imaging (MRI) scans will be obtained to measure abdominal fat and lower leg muscles size. MRI uses strong magnets to make detailed pictures of your body. This procedure involves lying still on a table during the scanning period. The measurements will be performed 3 times. Each MRI scan takes 45 minutes.

- You will lodge in room 1V-130 at the Spinal Cord Injury and Disorders Department (SCI &D) for dinner, and will remain overnight.

Day 2

- At 6 am, you will be awakened to measure your 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 be 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 45 minutes. Resting blood pressure will be obtained.

- Two IV lines (small plastic tubes) will then be placed in your arms, 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. Glucose and insulin will be injected into one IV-line Blood samples will be drawn from the other IV line. Three blood samples will be obtained. Glucose will be injected in to your vein over 20 seconds at the start of the test. Blood samples 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 12 tablespoons.

- During the 3 hour-IVGTT, a dietician will meet with you to ensure that you will follow a standard diet during the study. You will be asked to maintain a 3 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 two times during the course of the study (baseline and week 12) to make sure you follow the diet throughout the study.

- Immediately after the IVGTT three small muscle biopsy samples will be taken from the knee muscle group to determine the effects of exercise. A numbing medication will be injected at the biopsy sites and a 1/4 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 (3-4 pieces) will be collected, after which the site will be closed and a pressure dressing applied for at least 10 minutes.

-All of these tests, including muscle biopsy, will be done three times, before the study, 6 months and after 1 year of completing the study.

-You will be asked to complete a questionnaire about the level of your physical activity at the beginning, middle, and the end of the study. This will take approximately 5-10 minutes.

Randomization:

You will be assigned by chance (like the flip of a coin) to one of two groups **Group 1 TRT + LPWS** or **Group 2 the TRT + NMES.**

B. <u>Interventions for one year (TRT+LPWS vs TRT+NMES)</u>

- If you have been assigned to the TRT+LPWS group or the TRT+NMES (control group), you will receive one year of electrical leg shock with ankle weights that will be done while sitting in your wheelchair. These sessions will be done twice a week at the study site for a full year. Two adhesive patches will be placed on the skin over the knee muscle group. For the TRT+LPWS, we will explore the best stimulation parameters necessary to evoke twitches of the knee muscle.

- For the TRT+NMES 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 randomized in the TRT+NMES group (control group), you have the option to exercise at home using 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. 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 apply the ankle weights by the principal investigator. At the end of the one year 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).

- Both groups (TRT+LPWS or TRT+NMES) will be asked to place a testosterone (4mg/day-8 mg/day) 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 one year. 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 packages so we can determine if you are using the patches as instructed.

4. 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.

5. 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.

6. What are my risks? (Risks, Inconveniences, Discomforts)
Participation in this study may involve risks that are unknown at this time. Your condition may stay the same, may improve or may worsen from study participation.

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.

- **Anthropometrics**
  - Bruising, discomfort. This occasionally occurs.

- **Venous catheter insertion and blood draws**
  - Localized swelling, soreness, bruising, and chance of infection, bleeding, pain, lightheadedness or possible fainting. A total of 12 tablespoons will be collected. This occasionally occurs.

- **IV line failure**
  - Discomfort, swelling, redness over the IV line site causing failure of the IV. Another IV will need to be placed in another part of the arm. This occasionally occurs.

- **Insulin Sensitivity Tests**
  - Hypoglycemia (low blood sugar) with occasional dizziness, sweating, and nausea. This occasionally occurs. Seizures, coma, or death, is unlikely to occur.

- **Basic Metabolic Rate**
  - Anxiety, apnea (difficulty breathing), and claustrophobia. This occasionally occurs.

- **Autonomic Dysreflexia**
  Symptoms of autonomic dysreflexia (AD) include sudden high blood pressure and possibly headache, sweats, blurred vision, stuffy nose, and nervousness. There is a small risk that blood pressure could become very high and cause a stroke. This is unlikely to occur, but can be a life threatening condition. If AD occurs, the study is stopped, and the bladder emptied, which usually causes the AD to resolve on its own. A medication called nitroglycerin paste is kept in the laboratory in case it is needed to apply to the chest for AD. This medication can cause low blood pressure, dizziness and headache, which is treated by removing the paste and leaning your head down.

- **DXA**
  Fall during transfer. This is unlikely to occur. This research study requires you to have 3 DEXA scans which involves exposure to radiation in the form of X-rays. 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 about 9 extra days of exposure from natural background radiation. The McGuire VA Medical Center Radiation Safety Committee has reviewed the use of 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.

- **MRI**
  - Anxiety, dizziness, and claustrophobia. This occasionally occurs.

- **Muscle biopsy**
  - Localized swelling, soreness, bruising, chance of infection, bleeding, pain, lightheadedness or possible fainting. The numbing medication can cause allergic reaction including local skin rash and rapid heart rate. This is uncommon.

- **Resistance training and LPWS electrical stimulation**
  - 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.
  - Fracture.
  - Autonomic dysreflexia (slow heart rate, high blood pressure, headache flushing & sweating) which may be life threatening.

- Pressure ulcers.
- Fainting, heart attacks or death.
- Chemical burns to the skin.
- These are unlikely to occur.

- **Testosterone Replacement Therapy**
  - Serious reactions:
    - Severe rash at site of the patches, worsening heart failure that may cause shortness of breath and, swelling of the body, enlarged prostate causing difficulty in urination, increase in red blood cells which may cause blood clots in the legs (cause swelling), chest pain, shortness of breath and rarely death and brain damage (causing a stroke), infertility, prostate cancer, difficulty in breathing during sleep, blood in urine.

  - Common reactions:
    - Skin irritation, back pain, enlarged prostate, headache, irritations of the skin, depression, enlarged breasts, increase cholesterol which may increase the risk of heart disease, chills, diarrhea, fatigue, frequent urination, pain during urination, reduced sex drive, inflammation of prostate, rash, acne, confusion.
  - This occasionally occurs.
  - In case of skin irritation, steroid cream may be used and will be provided. Side effects of steroid cream include thinning of skin, increase in number and size of small blood vessels under the skin, increase risk of skin infection, and change in skin coloration.

- **EMG**
  - Localized swelling, soreness, bruising, chance of infection, bleeding, pain.

7. Will I get paid? (Compensation)

You will receive $3,000 for your participation in this study ($500 every two months) until the end of the one year duration of the study. The compensation offsets for transportation costs and participation in the study. If you are in the TRT+NMES group and you have chosen to use Telehealth option, you will receive $1200 for your participation in the study ($200 every two months).

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

8. 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.

9. Does pregnancy prevent me from participating? (Pregnancy)
Women will not be eligible to participate because of the unknown risks that involve using Testosterone patches.

10. 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. A research injury is any injury or illness caused by your participation in the study. In the event of a research injury, necessary medical treatment will be provided to assist your recovery from the injury. For research related injury, the VA must provide necessary medical treatment regardless of whether you are a Veteran or a non-Veteran.

This agreement to provide medical treatment does not include treatment for injury/illness that is not a result of the study. To help avoid injury, it is very important to follow all study directions. You are not giving up any of your legal rights by signing this form.

11. 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, accrediting agencies, 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, or as required by law. All subjects will be identified by an assigned number and their initials. Subjects' research charts will be kept inside a locked file cabinet in a locked office. Only study staff will have access to your study records and medical information.

The ways your study doctor will use your study-related health information and the people who may receive it are identified in a separate form entitled, Authorization for Use & Release of Individual Identifiable Health Information for Veterans Health Administration Research. You will be asked to sign that form to show that you give permission for these uses and sharing of your information. You do not have to sign the authorization form. However, if you do not sign, you will not be able to participate in the study.

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.

12. 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. Ashraf S. Gorgey, MPT, PhD* 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.

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 take **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 Merit Review,** FDA, McGuire IRB may also end the study at any time.

13. Date of Consent Form Revision, 4/20/2018, 2/22/2019, 2/16/2022

Subject Name:_____ Date:_____

Research Study Title: **Testosterone and Long Pulse Width Stimulation for Denervated Muscles after Spinal Cord injury**

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

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. By signing below, I am agreeing to participate in this research study. I will receive a signed copy of this consent form.

_____ _____

Subject's Signature Date

_____ _____

Signature of Person Obtaining Informed Consent Date
