Safety and Efficacy of Concentrated Autologous Concentrated Bone Marrow Aspirate (BMAC) in Preventing Wound Complications in Amputations (The MarrowCHAMP Study)

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RICHARD L. ROUDEBUSH VETERANS AFFAIRS MEDICAL CENTER
INFORMED CONSENT STATEMENT FOR RESEARCH

Safety and Efficacy of Concentrated Autologous Concentrated Bone Marrow Aspirate (BMAC) in Preventing Wound Complications in Amputations (The MarrowCHAMP Study)

Device Sponsor: Zimmer Biomet Biologics, Inc.

What We are Researching: This research project is hoping to find out if taking a special kind of cells from your own bone marrow and injecting them into your own leg before your planned lower leg amputation will decrease inflammation and prevent the chance of wound complications or a higher level amputation than planned.

Why You: You have a planned lower leg amputation recommended by your doctor.

Do You Have to Participate: No, participation is voluntary. You may choose to take part in this research or even leave the study at any time after you choose to take part. Your choice will not change the benefits to which you are entitled and will not affect your relationship with Roudebush VAMC or IU Health.

If you choose to participate in this research project, this is what we will ask you to do and what that means for you:

PROCEDURES

Physical exams and medical history collection

Blood draws to test your blood

Electrocardiogram (ECG) to check your heart function

Doppler tests to check the blood pressure in your legs

Bone Marrow Aspiration and Cell Injection Procedure before your amputation

RISKS

Accessing your medical records has the risk of a potential loss of confidentiality.

Blood Draws have the risk of discomfort, bruising, infection, excess bleeding, clotting, and fainting.

ECG has the risk of slight discomfort from the adhesive patches.

There are no known risks to doppler tests.

Bone Marrow Aspiration and Cell Injection Procedure has the risk of low red blood cells, (anemia), body pain, bruising, swelling, infection, and fever.

WHERE & HOW LONG

Procedures for veterans will take place at Roudebush VAMC.

Your overall participation will last 2 years.

There is no payment for your participation, nor cost to you for the research tests.

If you have questions, please contact Kristen Wanczyk, RN at (317)988-9548.

BENEFITS OF PARTICIPATING IN THIS RESEARCH: A possible benefit of your participation in this study is avoiding wound infection or more surgery to revise to your amputation; however, you may not benefit at all.

Please review the Informed Consent Statement for details about these topics and additional things you should know before making a decision about whether to participate in this study.

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

WHY IS THIS STUDY BEING DONE?

Study Purpose:

The purpose of this study is to determine the safety and explore the effectiveness of autologous (your own cells) BMAC injections in preventing wound complications after amputation. The study will research how tissue responds to the injected stem cells, BMACs ability to improve blood flow to a diseased area, and survival rate of these cells within the portion of your leg that will be amputated. The study doctor is researching this method to see if the special cells will prevent wound infection. The study doctor is also researching to see if this procedure can help increase blood flow to your leg after amputation and prevent the need for a second operation, called an amputation revision.

You are invited to participate in a research study to determine the safety and explore the effectiveness of autologous (your own cells) concentrated bone marrow aspirate (BMAC) in preventing wound complications after amputation. Mesenchymal stem cells are special cells in the body that may limit tissue destruction, repair injured tissue, and may possibly create new blood vessels (a process called angiogenesis). You were selected as a possible subject because you were told by your vascular doctor that you need an amputation soon – probably within 30 days, because of constant pain, death of tissue, or an open sore because of low blood flow. Amputation means the intentional surgical removal of a portion of the leg due to disease progression or infection.

The study is being conducted by Michael P. Murphy, MD, Indiana University, Department of Surgery. The purpose of this study is to collect information that will be used to determine if BMAC can be used to prevent wound problems after lower leg amputation that require more operations. We will also be collecting tissue samples from part of the leg that will be amputated (removed) so that we can understand what BMAC does. Dr. Murphy has no financial relationship with the design, conduct or outcome of this study. Dr. Murphy is acting as the Principal Investigator for this study and will not receive salary support for his time commitment to the study. Zimmer Biomet Biologics is providing the BioCue™ Concentration kits for this study. The BioCue™ Concentration device is an investigational device, which means it is not approved by the Food and Drug Administration.

HOW MANY PEOPLE WILL TAKE PART?

If you agree to participate, you will be one of up to twelve (12) subjects who will be participating in this research.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you must sign this consent form prior to undergoing any study related procedures. If you agree to participate in the study, the following things will happen:

If you currently have malignant cancer of any kind or if you have had malignant cancer within the last 5 years, with the exception of adequately treated non-melanoma cutaneous carcinoma (basal cell carcinoma of the skin), you cannot take part in this study.

You will be scheduled to receive BMAC injections into your leg at approximately 7 days before amputation. It is possible that your day of amputation might be moved to an earlier date if the study doctor feels it is necessary based on your health.

The following evaluations will be carried out or retrieved from your medical record at the baseline screening period (before the cell injection procedure) to determine if you are eligible for the study:

Baseline screening includes:

- Complete medical history and physical exam. Your medical history includes: your current medications (including start dates) and medications you have taken in the past 30 days; all medical problems that you have now or used to have; all surgeries and procedures that you have had; all information about you such as age, gender, race, height/weight
- Vital signs such as blood pressure, heart rate, respiratory rate, and temperature
- Pregnancy test for women of childbearing age
- Blood tests: infectious disease labs, complete blood count, serum chemistry, liver panel, lipid panel, and hs-CRP (measures the level of inflammation in your blood). These tests will be obtained to make sure you do not have current infection, and to make sure your kidneys and other organs are functioning normally. If you are on certain blood thinner medications, a pre-operative blood test to check your blood clotting ability may be performed. This will require approximately one teaspoon of blood drawn from a vein in your arm.
- Electrocardiogram (ECG) to check your heart function
- TcPO2 (skin oxygen measurement in your lower leg)

If you have not recently been to a vascular clinic visit at VA, a screening exam will be performed at Dr. Murphy's clinic location on the first floor, C-Wing, PV clinic at the VA Medical Center (VAMC) in Indianapolis, Indiana. If you are in-patient in the VAMC, Dr. Murphy will visit you at your room. During the screening assessment period, a total of up to 26 mL (less than 2 tablespoons) of blood may be collected for blood tests and lab analysis. If you have recently had these blood tests or lab analyses done within the last 30 days, we will use these recent values to determine your eligibility. We will not repeat these tests after you consent to participate in the study. The screening portion of the study is expected to last approximately 1-2 hours. If you require a serum pregnancy test, an additional 6 mL of blood will be collected.

DEVICE DESCRIPTION:

CAUTION—Investigational Device. Limited by Federal (United States) Law to Investigation Use.

The BioCue™ Kit is the device used to separate and collect your bone marrow used in the procedure. It contains six disposable BioCue™ Separator tubes. Bone marrow is drawn from the hip bones and is then placed into BioCue™ Separator tubes. The separator tubes are placed into a machine that spins

the tubes (a centrifuge), allowing the bone marrow to concentrate into different layers. One of these layers contains stem cells and it is this layer that is used in the investigational treatment.

Bone Marrow Aspiration and BMAC Injection Procedure:

During this visit prior to the surgical procedure, a small amount of blood (up to 26mL or less than 2 tablespoons) will be drawn from a peripheral vein for lab analysis. Blood will be drawn before your cell injection procedure, the day of your amputation, and at follow-up visits at week 2 (+/- 2 days), week 6 (+/- 4 days), week 12 (+/- 7 days), week 18 (+/- 2 weeks), and week 24 (+/- 2 weeks). Blood will be drawn a total of up to seven times during the study. The total amount of blood drawn for the entire study is about 182 milliliters or about 3/4 cup.

All subjects will receive conscious sedation, or general anesthesia, as determined by the study doctor, to control pain. General anesthesia may be used due to the large volume of bone marrow being collected. Once the anesthesia has been administered, bone marrow will be removed from your pelvic bone from two sites in your lower back with a large needle. The needle will remove bone marrow located inside your pelvic bone. Inside the bone marrow are the special cells, called mononuclear cells, or stem cells, that may develop new blood vessels. A total of about 1¼ cups (303 milliliters) of bone marrow will be withdrawn.

The BioCue™ Kit will then be used to remove a special layer of BMAC from your bone marrow right there in the operating room. The cell separation process takes approximately 40 minutes. This procedure will take place in a surgical suite at the VA Medical Center in Indianapolis, Indiana. A portion of up to 10 mL of bone marrow will be collected for laboratory analysis in Dr. Murphy's research labs located at VAMC, Room D-3007. Testing of up to 6 mL of bone marrow may be done at the local laboratory at your site or they may be sent to an outside laboratory. This sample will be analyzed to determine if your bone marrow is free from contaminants, and the number and types of cells contained within it. Any samples sent to an outside lab will not contain information that will identify you.

Approximately one week before your scheduled amputation, we will inject autologous BMAC, into the muscles of the leg that is to be amputated. BMAC includes stem cells that can become different types of cells during the process of growth and development. All subjects will receive approximately 25 injections into their leg above the amputation site and up to 5 injections spanning an area of approximately 3 x 10 x 3 cm (about the size of a candy bar) in the muscle into their lower leg, below the amputation site. This site will be marked with permanent ink and will later be removed at the amputation surgery. Prior to injections, the study doctor may remove a small amount of tissue from your lower leg with a small needle (needle biopsy) to compare it to tissue that is collected at your amputation procedure. This donor cell injection procedure is considered part of the research study and all costs will be billed to the research study grant account.

The study doctor or anesthesiologist may determine that it is safest for you to undergo general anesthesia for the bone marrow aspiration and BMAC injection procedure versus conscious sedation. If general anesthesia is used for this procedure, you may stay overnight at VAMC on the 7th or 8th floor. The study doctor will examine you the next morning and discharge you home. If you are in-patient, you will return to your wardroom.

Surgical Amputation Procedure:

Before your amputation surgery, which is considered routine and not part of the research study, up to 26 milliliters of blood, less than 2 tablespoons, will be drawn from a peripheral vein. During your surgery, a small amount of skeletal muscle from the BMAC injection site in your lower leg (the part of your leg that will be removed) will be collected for this study. The study doctor will remove approximately 3 x 10 x 3 cm (about the size of a candy bar) of tissue from this area.

Small portions of nerve segments, up to 20 cm total, may be collected from the amputated part of your leg. These samples, which will not identify you, will be sent to Indiana University for analysis.

After your amputation surgery, you will stay overnight at RLR VA Medical Center. Dr. Murphy will perform follow up visits as routine standard of care prior to your discharge from the hospital. You will be discharged home three to four days after your surgery. You may need to stay longer if you require additional monitoring for your health and safety, such as being placed into a rehabilitation unit or facility to help you adjust to moving around after your amputation. We will follow your health for 12 months to see if you have developed any problems with these injections and to see if we can determine if these injections have had any effect in keeping your leg healthy and free of infection.

It is important for you to follow the directions for treatment and the study. The study requires you to return to the study doctor for follow-up evaluations of your progress at post-op amputation day 3 (+ 5 days), week 2 (+/- 2 days), week 6 (+/- 4 days), week 12 (+/- 7 days), week 18 (+/- 2 weeks), and week 24 (+/- 2 weeks) post-amputation procedure. A week 52 phone call will be made to check on your health and see if you have remained free of infection or further revisions to your amputation site. After your 52-week phone call, you will have completed participation in the study.

Follow-up visits will take place at the VA Medical Center in Indianapolis, Indiana in the Peripheral Vascular clinic on the first floor C-wing, Specialty Clinic 3. At follow up visits, you will have an exam, TcPO2 to check the blood oxygen level near your amputation site, ECG to check your heart function, and a blood draw. Blood draws will be completed in the outpatient blood draw clinic on the first floor. Each visit is expected to last approximately 2 hours. The visits listed are considered standard of care, which means that they are visits that would normally be scheduled for follow-up of an amputation procedure, whether or not you consent to be in the study.

The study team will collect information about you from your medical records and use it for this study.

WILL I RECEIVE MY RESULTS?

If you participate in this study, we may learn things about you from the study procedures that could be important or interesting to you. Depending on the information, you might need to meet with professionals with expertise to help you decide what to do with the information. We do not have money or funds available to cover the costs of any follow-up consultations or actions. We will share the following information with you:

- Any information that might be immediately critical to your health will be shared with you or your health care provider.

- Test results from blood draws and ECG tracings during your study participation. This information may be helpful for your health in the future.

If you decide that you want this information, results can be mailed to you or information can be given to you over the telephone. Please **initial** one of the following options:

_____ Yes, I want to be provided with this information.

_____ No, I do NOT want to be provided with this information.

The results of this study may be published, but your records or identity will not be revealed unless required by law. You will be told about new information that may affect your health, welfare, or willingness to stay in the study. Your participation may be terminated by the investigator without regard to your consent if he feels that it is in your best interest to do so. In addition, Indiana University or the FDA could discontinue further enrollment of people into this study. Should your participation in the study be stopped, a full explanation and possible alternatives will be discussed with you.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While on the study, the risks are:

Blood Draws

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and fainting are also possible, although unlikely. In order to minimize these risks, blood will be drawn by experienced technicians. We will also try to collect blood for the study when you are already getting a blood draw for your regular medical care.

Changes in Blood Cell Counts

Because of blood draw and bone marrow harvest volume, anemia (low level of red blood cells) is an expected and likely risk. Dizziness, fatigue, and shortness of breath are common symptoms of anemia. Rare complications include rapid heartbeat, chest pain, or need for a blood transfusion. Other possible changes in blood cell counts include decreased platelets and changes in white blood cell counts. With decreased platelets you may be more prone to bleeding or take longer to stop bleeding. Prior to discharging you after your procedure, a blood draw will be obtained to check that your blood cell counts are within appropriate range for your safety.

Anesthesia (Local and General)

Local anesthesia is the use of medications to eliminate pain in a specific area of your body. The medication makes you numb to pain but you may still feel pressure. In addition to the local pain control, your doctor will administer a medication (sedative) to relax you during the procedure.

Risks of local anesthesia include allergic reaction to the medication. However, most local anesthesia adverse effects are dose-dependent. That is, the risk of side effects increase with the amount of anesthetic that you are given. These dose-dependent side effects can include convulsions or seizures, coma, respiratory arrest (stoppage of breathing), low blood pressure, changes or defects in heart rhythm and death.

General anesthesia is the use of medications to provide a deep sleep with total unawareness of pain and is used during procedures that can be anxiety producing, uncomfortable, painful, or pose an increased risk for injury with movement. The study doctor or anesthesiologist may determine that it is safest for you to undergo general anesthesia for the bone marrow aspiration and stem cell injection procedure versus conscious sedation due to the larger volume of bone marrow that will be aspirated

The risks for general anesthesia may depend on your overall health condition. In addition to severe peripheral arterial disease, other diseases you may have, such as cardiac disease and/or diabetes, can increase the risk of complications from general anesthesia. These risks include nausea, vomiting, aspiration, blood vessel injury, nerve injury, lung injury, heart attack, stroke, kidney failure, infection of the lung, infection of the urine system (bladder or tubes that carry urine), allergy to drugs, brain damage, and death. The breathing tube may cause some discomfort similar to a sore throat for a few days after the procedure. Rarely, a tooth may be injured when the breathing tube is placed. An anesthesiologist from VAMC will be present to administer the anesthesia to minimize these risks.

Conscious Sedation

This type of sedation is safe and effective for patients who need minor surgery. An anesthesiologist will administer the conscious sedation. You may receive medicine through an intravenous line (IV, in a vein) or a shot into a muscle. You will begin to feel drowsy and relaxed very quickly. You may fall asleep, but you will wake up easily to respond to people in the room. Your breathing will slow down, and your blood pressure may decrease.

Possible risks of conscious sedation include problems with your breathing (if you are given too much medicine). An anesthesiologist will be watching you during the whole procedure. Health care providers have special equipment to help you with your breathing, if needed. You will be monitored frequently during your procedure to make sure you are okay. An anesthesiologist will be present at all times during the procedure to monitor and minimize risks from occurring.

Bone Marrow Collection from the Hip Bones

Your lower back is expected to be sore for about one week where the bone marrow was collected and you may have some bruising over the two puncture areas. Minor complications, including low blood pressure, fainting, headache, excess pain, unexpected hospitalization and minor infections occur in about 6-20% of marrow donors, and all resolve within a few to several days. Other rarely

seen potential complications include excessive bleeding, formation of a fluid pocket, and persistent pain at the site where the bone marrow was collected. In order to minimize these risks, bone marrow collection will be performed by a doctor who is experienced in the technique.

Concentrated Bone Marrow Delivery into the Leg

Although less likely, you may have some flu like symptoms for the first several days after your procedure such as a low-grade fever and body aches. Also, your leg may be tender, and you may experience bleeding associated with needle penetration, hematoma (a swelling filled with blood), bruising, cramping, fever, infection, rash, skin ulcer (skin breaks), redness, inflammation or swelling of muscle or skin (myositis, fasciitis, cellulitis), pain or pressure in the leg at the site of injection, and lack of blood flow and oxygen to the leg, or other discomforts around the injection sites. The most likely possible risk associated with the injections, though small, is an allergic reaction around the injection sites in your leg or a blood clot in the vein. To reduce these risks, this procedure is performed under sterile technique.

Complications that may occur from the injection of the study product may lead to a higher level amputation than planned. Less likely risks include nerve damage that may cause decreased sensitivity to touch, decreased blood volume due to bleeding, dizziness or fainting, chest pain, muscle spasms, seizures, and reduced body temperature in your study leg. In very rare cases, injections can cause excessive bleeding in your calf or lower thigh muscles leading to swelling in your lower leg, which could require surgery to correct. There may be an increased risk for harm or increase risk of disease or infection as a result of receiving multiple injections in the diseased leg, though this is less likely due to this procedure being performed by experienced staff who will use sterile technique during the surgical procedure.

Nerve Tissue Collection

The tissue being collected will be from the amputated portion of your leg. There are no known risks to you for collection of tissue from the portion of your leg that will be amputated.

Needle Biopsies

Risks associated with removing tissue via needle biopsy include bleeding and infection. However, the incision is small (about the width of a pencil tip) and the procedure will be performed by a skilled surgeon in a sterile operating room.

ECG

You may experience slight discomfort when the adhesive patches are removed. Care will be taken when removing the adhesive patches to reduce your discomfort.

Confidentiality

There is a risk of loss of confidentiality.

Reproductive Considerations for Women of Childbearing Potential

Being a part of this study while pregnant may expose the unborn child to significant risks. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a pregnancy test will be performed as part of your blood tests at the screening visit and it must be negative before you can enter this study. If sexually active, you must agree to use appropriate contraceptive measures for three months after receiving the BMAC injections. Medically acceptable contraceptives include: (1) surgical sterilization, (2) approved hormonal contraceptives (such as birth control pills, Depo-Provera, or Lupron Depot), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). If you do become pregnant during the 3-month time period following your procedure, you must inform the study physician immediately.

Contraceptive Measures for Men

The stem cells used in this study could affect your sperm and could potentially harm a child that you may father while in this study. If you are sexually active, you must agree to use a medically acceptable form of birth control for three months after receiving the MSC injections. Medically acceptable contraceptives include: (1) surgical sterilization, or (2) a condom used with a spermicide. If your partner becomes pregnant during the 3-month time period following your procedure, you must inform the study physician immediately.

Other Risks

Since there is limited experience with the investigational BioCue™ treatment, there may be unforeseen risks that we cannot predict, including but not limited to acceleration of the disease process and death.

If you feel that you are experiencing problems directly related to the study treatment, you should tell the study doctor immediately. If you cannot do this because it is an emergency, you should get treatment and tell the study doctor as soon as possible.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

The VA medical facilities shall provide necessary medical treatment to a research subject injured as a result of participation in a research project approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees in accordance with applicable federal regulations. This does not apply to (1) treatment for injuries due to noncompliance by a subject with study procedures; or (2) research conducted for VA under a contract with an individual or a non-VA institution.

By signing this form, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?

You may or may not benefit from taking part in this study. A possible benefit of your participation in this study is avoiding wound infection or more surgery to revise to your amputation; however, you may not benefit at all. The information that we gather will help us learn more about stem cell therapy and could help patients in the future. Participating in this study may lessen the symptoms of your disease. However, we don't know for sure. We are doing this research study to find out if this treatment helps or not.

WILL I BE PAID FOR PARTICIPATION?

You will not be paid for participating in this study.

WILL IT COST ME ANYTHING TO PARTICIPATE?

There will be no costs to you for any of the treatment or testing done as part of this research study. Research-specific costs include the BMAC injection procedure, all costs related to the procedure including, but not limited to hospital fees, anesthesia fees, medications, research blood draws, ECGs, and doppler testing. Eligibility for medical care at a VA Medical Center is based upon the usual VA eligibility policy and is not guaranteed by participation in a research study.

You will not be required to pay for medical care or services received as a subject in a VA research project except as follows:

> 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 VA that are **not** part of this study.

WHAT ARE THE OTHER TREATMENT OPTIONS?

The alternative to participating in this research study is to continue with supportive measures that include medications to relieve discomfort, wound care for areas of ulceration or gangrene, and antibiotics for infection; all of which are routine standard of care. Your doctor will discuss these alternatives with you.

HOW WILL MY INFORMATION BE PROTECTED?

Efforts will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study or in databases in which results may be stored. The results of this study may be published, but your records or identity will not be revealed unless required by law. You will be told about new information that may affect your health, welfare, or willingness to stay in the study.

Audio/Video Recording and Photography

Your amputation site and any wounds present will be photographed, which will be used for research purposes. At any time, you may tell the researcher that you feel uncomfortable or do not wish to continue. The photograph files will be stored on a password-protected computer at VA Medical Center. The photographs will not have any information on them that can identify you.

Research records will be maintained by the investigator in accordance with the VHA Records Control Schedule. Personal health information about you will be stored on a secured, protected database called OnCore, and on VA REDCap. Information will be stored at Indiana University in both paper and electronic files. Paper records will be stored by Dr. Murphy's research team in the office of Dr. Murphy's study coordinator and electronic records will be stored on Indiana University computers. This data will be stored in accordance with the VHA Records Control Schedule. Any research information in your medical record will be kept indefinitely. Information that could identify you will not be used if the results of this study are published.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the investigator and their research associates, the Indiana University Institutional Review Board or its designees, Zimmer Biomet Biologics, Inc., the Indiana CTSI Clinical Research Center (CRC), the Data Safety Monitoring Board (DSMB), the VA Research and Development Committee's designees, and federal agencies, including but not limited to the Office for Human Research Protections (OHRP), the Office of Research Oversight (ORO), VA Office of the Inspector General (OIG), and the Food and Drug Administration (FDA),etc., who may need to access your medical and/or research records. When you sign this form, you will be giving permission for these groups to see your confidential information when it is necessary. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

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

WILL MY INFORMATION AND SPECIMENS BE USED FOR RESEARCH IN THE FUTURE?

Information and specimens collected for this study may be used for other research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

Specimens collected from you for this research may be used to develop products which could be sold in the future. The investigator does not plan to share any profits or losses from the sale of those products with you.

WHAT WILL YOU DO WITH MY GENETIC INFORMATION?

We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

In case there are medical problems or questions, Dr. Murphy can be called at 317-988-2353 during the day. After business hours, please call (317) 554-0000 and ask for the vascular surgery physician on call to be paged (24 hours a day). If any medical problems occur in connection with this study, the VA will provide emergency care.

Please direct questions about the consent process and the rights of research subjects to the VA Customer Service Office at (317) 988-2602. For questions about your rights as a research subject or complaints about a research study, contact the Indiana University Human Research Protection Program at 800-696-2949 or at irb@iu.edu. If you have any questions about the research study or want to check the validity, discuss problems, concerns or obtain information or offer input, please call the VA Research Personnel Office at 317-988-3032.

WHAT IF I DO NOT PARTICIPATE OR CHANGE MY MIND?

After reviewing this form and having your questions answered, you may decide to sign this form and participate in the study. Or, you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your usual medical care or treatment or relationship with Roudebush VAMC.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw, leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your decision whether or not to participate in this study will not affect your current or future relations with the VA Medical Center. If you withdraw from the study, no new information about you will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. If you choose to withdraw from the study, we ask that you do so in writing to Dr. Michael Murphy, VA Medical Center, 1481 W. 10th Street, C3125 (151), Indianapolis, Indiana 46202 . However, if you choose to withdraw from the study by telling us on the phone or in person, we will honor that as well.

The researchers may stop your participation in the study even if you do not want to stop, if the study doctor feels that it is in your best interest to do so. Your participation will be stopped if you need a revision of your below-the-knee amputation to an above-the-knee amputation. In addition, Indiana University or the FDA could discontinue further enrollment of people into this study. If this happens, a full explanation and possible alternatives will be discussed with you. You will be told about new information that may affect your health, welfare, or willingness to stay in the study.

Re-contact for Future Use

If you agree, we may contact you after your participation is over to request additional information or biospecimens. Please **initial** one of the following options:

_____ Yes, I agree to be contacted for the purpose of collecting additional health information and/or possibly additional biospecimens.

_____ No, I do NOT agree to be contacted for the purpose of collecting additional health information and/or possibly additional biospecimens.

The study has been explained to me and all of my questions have been answered. The risks or discomforts and possible benefits of the study have been described. Other choices of available treatment have been explained.

PARTICIPANT'S CONSENT

In consideration of all of the above, I agree to participate in this research study. I will be given a copy of this document to keep for my records.

Participant's Printed Name: _____

Participant's Signature: _____Date: _____

Printed Name of Person Obtaining Consent: _____

Signature of Person Obtaining Consent: _____Date: _____