Protocol Title: Exploration of potential alterations in bone perfusion after spinal cord injury

Principal Investigator: J. Andrew Taylor, Ph.D.

Site Principal Investigator:

Description of Subject Population: Healthy male and female volunteers between the ages of 18 and 40

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Partners now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn more about blood flow control in bone.

How long will you take part in this research study?

If you decide to join this research study, it will take you about **3 hours** to complete the study. During this time, we will ask you to make **1** study visit to **Spaulding Hospital Cambridge.**

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen: we will measure blood flow in your leg with an ultrasound and with light. During these recordings, you will be asked to lie down on a table while your calf is lowered with the knee flexed at 90deg. Also, we will inflate a cuff above your knee that will stop blood flow below the cuff level for 10 minutes. After releasing the cuff, blood flow will return to your calf. We will also give you one tablet of sublingual nitroglycerin. You will also have your leg placed in a boot while sitting with a strap placed over your knee. With the leg in the boot and the knee flexed at 90deg, we will apply load to your shin using the strap placed over your knee.

Why might you choose to take part in this study?

You will not benefit from taking part in this research study. Others with osteoporosis or other bone related medical conditions may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include: inconvenience and discomfort of multiple attachments to your body; possible muscle discomfort, leg numbness, and pins and needles sensation during cuff inflation and/or immediately after cuff release, but this sensation will shortly go away; headache, dizziness, lightheadedness, nausea and flushing shortly after ingesting the sublingual nitroglycerin tablet , but these sensations will shortly go away; bone and muscle injury during leg loading, but the amount of loading poses minimal risk.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

Other things to consider are that the study requires 1 visit at Spaulding Hospital Cambridge and about 3 hours for the study protocol.

What other treatments or procedures are available for your condition?

This research investigates human physiology, focusing on regulation of blood flow to bone, and does not involve any diagnosis or treatment.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. J. Andrew Taylor, M.S., Ph.D. is the person in charge of this research study. You can call him/her at **617-758-5503, M-F 9-5**. You can also call **Dr. Adina E. Draghici, Ph.D. at 617-758-5508, M-F 9-5** with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call **Dr. Adina E. Draghici, Ph.D. at 617-758-5508**.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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.

Why is this research study being done?

We are doing this research to examine key mechanisms of blood flow regulation to bone. Bones need blood flow like other important organs in the human body. Without adequate blood flow, bone cannot maintain its integrity. In fact, reductions in bone blood flow have been associated with bone loss. After a spinal cord injury (SCI), there are many changes in the paralyzed legs which might result in reductions in bone blood flow and may relate to post injury bone loss. We are doing this research to examine the changes in the paralyzed legs on bone blood flow in those with SCI compared to able-bodied individuals. Additionally, we are examining bone blood flow response to different shin loading conditions in those with SCI compared to-able-bodied individuals. This research may provide important insights into potential causes of bone loss post SCI and could open new clinical avenues for treating osteoporosis.

Who will take part in this research?

We are asking you to take part in this research study because you are a healthy male or female. About 29 people (men and women) will take part in this research study. About 29 subjects will take part at Spaulding Hospital Cambridge. The National Institutes of Health is paying for this research to be done.

What will happen in this research study?

To participate in this study, you must be between the ages of 18 and 40 years of age. You must not have a history of cardiovascular problems or neurological conditions.

Exclusion criteria:

You are not eligible for this study if you have:

- clinical signs or symptoms of heart disease, hypertension, coronary disease
- diabetes
- other neurological disease
- cancer
- take medicine for erectile dysfunction
- abnormal resting ECG
- pregnant women
- tibial fracture or tibial stress fracture in the past 2 years
- underweight or obese (body mass index between 18.5 and 29.9)

- have recent weight changes ≥ 15 pounds
- are allergic to nitroglycerin patches, capsules, tablets, ointments, or spray.

SCREENING PROCEDURES

Screening: about 30 minutes (Spaulding Hospital/Cardiovascular Research Laboratory)

Medical History: We will ask you questions about your medical history. This will help us check for disease or other reasons you would not qualify for this study.
Weight: Your weight will be measured.
Tibial Length: Your shin will be measured.

Instructions:
- Do not drink caffeine for 24-hours before your visit.
- Do not take part in any heavy physical activity /exercise for 24-hours before your visit
- You will need to wear shorts or loose sweatpants during the testing session

STUDY PROCEDURES

Study Visit about 3 hours, following screening (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

1) **Popliteal Artery Structure.** An ultrasound device will be used to measure the thickness and diameter of an artery in your leg under your knee.

2) **Bone Blood Flow.** We will measure the content of the blood in your bone (tibia, or the shin bone) by placing a probe on the skin. The probe is housed in a material sleeve with flexible plastic backing. The probe has three holes: one to shine light into the bone and two to measure the light that comes back out of the bone. We will shine the light into your shin and we will measure the light that comes out for the entire duration of the experiment.

3) **Calf Blood Flow.** An ultrasound device will measure the blood flow in an artery in the same leg. A small device will be placed under your knee and strapped into place with a band around your leg.

4) **Leg Dependency.** While lying down, we will measure bone blood flow and calf blood flow in your shin while your leg is supine and when we lower your leg below heart level such that you your knee is bent at 90 degrees. Dropping the leg will increase arterial pressure, causing blood to pool in your leg.

5) **Cuff Inflation.** While lying down, we will place a pressure cuff above the knee. We will inflate the cuff for 10 minutes. The cuff will be inflated at a level that will stop blood flow below the cuff level for the 10 minutes duration. After releasing the cuff, blood flow will return in your calf. This will allow us to measure the shin blood content and leg blood flow before, during, and after cuff inflation.

6) **Nitric-Oxide Response.** While lying down, we will give you 1 nitroglycerin tablet to put under your tongue until it gets dissolved. This will allow us to measure the shin blood content and leg blood flow in response to a nitric-oxide donor – a medication that dilates your blood vessels briefly.

7) **Shin Loading.** With the leg still in the boot used for determining maximal calf force, we will load your shin. A 2 inch strap will be secured over your thigh. The knee will be bent at 90degrees for the entire loading protocol. Wires will pull vertically down on the strap, loading your shin. We will load your leg four times for five minutes each time, at three different loads corresponding to about 10% of your body weight, 30%-of your body weight, 50% of your body weight. This loading is much smaller than during walking. For example, during walking a person loads their legs with about 3-4 times their body weight. During loading we will measure shin blood content.

Protocol:
You will be asked to not drink caffeine for 24-hours before your visit. In addition, you will be asked to not participate in any heavy physical activity for 24-hours before testing. You will need to wear shorts or loose sweatpants during the testing session.

You will be connected to the monitoring equipment described above. At the beginning of the study procedure, we will measure arterial diameter and thickness in your leg using an ultrasound. Throughout the study procedure, we will monitor continuously shin blood. We will also measure calf blood flow in the same leg using an ultrasound device during leg dependency and cuff inflation. First, after 5 minutes of lying supine on an exam table, you will be asked to lower your shin for 5 minutes. After 10 minutes of rest, we will place a pressure cuff above your knee and inflate it for 10 minutes as described above. We will record date for 5 minutes before cuff inflation, during 10 minutes of cuff inflation, and 5 minutes after cuff release. Following another 5 min of rest, we will give you one tablet of sublingual nitroglycerin and we will continue collecting data for an additional 15 minutes. Afterwards, in a sitting position we will place your leg in the boot of the loading device. We will determine your maximal calf contraction as described above. After 10 minutes of recovery, we will load your bone three times; each cycle of loading will consist of 5 minutes of rest, 10 minutes of loading, and 5 minutes of recovery.

We will remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples to share with our research collaborators at Northeastern University.

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study. A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, weight).

You may be asked to repeat any of the above testing if there is difficulty obtaining results that meet our quality standards or there are equipment issues that arise. If any of the above testing may be repeated, you may be asked to attend an additional study visit for this purpose.

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

At the completion of this research study, we would like to store and be able to use and share your identifiable samples and health information with researchers at Partners for other research related to regulation of blood flow to bone and/or bone health. If we share your samples and/or health information with other researchers outside of Partners, we will label the samples and information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your sample and/or information. We will keep the code in a password protected computer at Spaulding Hospital Cambridge.

Because these samples and/or health information are identifiable, we are asking your permission to store, use and share them for other research. You can still take part in the research study whether or not you give permission for the storage, use, and sharing of the samples and health information for other research.

Do you agree to let us store and use your samples and health information for other research related to regulation of blood flow to bone and/or bone health?

☐ YES ☐ NO Initial _____

Will you get the results of this research study?

You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. We and the researchers involved in this study will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning. There is a small chance that we or the researchers could find out something from the study that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

You can choose to get a newsletter that will tell you about the research studies we are doing. This newsletter will not announce your results or anyone else's, but it will tell you some information about what we are learning about bone health. We will also publish what we learn in medical journals. In the future, when research results are published, they may show that certain groups (for example, racial or ethnic groups, or men/women) have genes that are associated with increased risk of a disease. If this happens, you may learn that you are at increased risk of developing a disease or condition.

What are the risks and possible discomforts from being in this research study?

General

The measurements of thickness and diameter and blood flow of the artery involve the inconvenience and discomfort of multiple attachments to your body, but do not have any risk.

Specific

Bone Blood Flow. The system is non-invasive and there are no known associated risks. Previous trials with the blood flow activity measurement showed minor reddening due to the plastic holder; however, this was temporary and it quickly went away. During the experiment, we will ask you if you feel any discomfort or heating effect. If you have any discomfort we will stop and turn off the light source immediately.

Cuff Inflation. The cuff inflation may result in muscle discomfort, leg numbness, and pins and needles sensation in the leg during cuff inflation and/or immediately after cuff release. This sensation will shortly go away.

Shin Loading. There is a risk of bone or muscle injury during loading. However, the loading should pose little risk since the device applies loads at less than full body weight (maximum weight will be about half your body weight). For example, during walking a person loads their legs with about 3-4 times their body weight.

Nitric Oxide Response. The sublingual nitroglycerine might result in headache, weakness, dizziness, lightheadedness, nausea, and flushing (warmth, redness, or tingly feeling under your skin) as your body adjusts to the medication, mild burning or tingling with the tablet in your mouth. Some serious but unlikely side effects include fainting and fast and irregular heart rate. Blood pressure and heart rate will be monitored continuously.

There may be other risks that are currently unknown.

What are the possible benefits from being in this research study?

You will not directly benefit from your participation in this study. This research may help physicians and scientists to better understand how blood flow is controlled in bone.

Can you still get medical care within Partners if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will receive $100 as a check for participating in this study. The study is a 1 time visit and you will receive the full amount if the study has been started. The check should arrive in your mailbox about 3-4 weeks after the study. In order to reimburse you, we will need your social security number.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Partners to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Partners researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)

- Other researchers within or outside Partners, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter	Date	Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name	Date	Time (optional)

Consent Form Version Date: 06/10/2022

Subject Identification

Protocol Title: Exploration of potential alterations in bone perfusion after spinal cord injury

Principal Investigator: J. Andrew Taylor, Ph.D.

Site Principal Investigator:

Description of Subject Population: Volunteers with SCI ages 18-40

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Partners now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn more about blood flow control in bone.

How long will you take part in this research study?

If you decide to join this research study, it will take you about **3 hours** to complete the study (for entire protocol, with shin loading) or 1.5 hours if you are a volunteer with time since injury between 3 and 24 months complete only the first part of the protocol. During this time, we will ask you to make **1** study visit to **Spaulding Hospital Cambridge.**

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen: we will measure blood flow in your leg with an ultrasound and with light. During these recordings, you will be asked to lie down on a table while your calf is lowered with the knee flexed at 90deg. Also, we will inflate a cuff above your knee that will stop blood flow below the cuff level for 10 minutes. After releasing the cuff, blood flow will return to your calf. You will also have your leg placed in a boot while sitting with a strap placed over your knee. With the leg in the boot and the knee flexed at 90deg, we will apply load to your shin using the strap placed over your knee.

Why might you choose to take part in this study?

You will not benefit from taking part in this research study. Others with osteoporosis or other bone related medical conditions may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include: inconvenience and discomfort of multiple attachments to your body; possible muscle discomfort, leg numbness, and pins and needles sensation during cuff inflation and/or immediately after cuff release, but this sensation will shortly go away; tingling, pins and needles sensation on the skin, skin irritation, increased spasticity and autonomic dysreflexia during cuff inflation and leg loading, but the amount of loading poses minimal risk.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

Other things to consider are that the study requires 1 visit at Spaulding Hospital Cambridge and about 1.5 hours or 3 hours (with shin loading) for the study protocol.

What other treatments or procedures are available for your condition?

This research investigates human physiology, focusing on regulation of blood flow to bone, and does not involve any diagnosis or treatment.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. J. Andrew Taylor, M.S., Ph.D. is the person in charge of this research study. You can call him at **617-758-5503, M-F 9-5**. You can also call **Adina E. Draghici, Ph.D. at 617-758-5508 M-F 9-5** with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call **Adina E. Draghici, Ph.D.** at **617-758-5508**.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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.

Why is this research study being done?

We are doing this research to examine key mechanisms of blood flow regulation to bone. Bones need blood flow like other important organs in the human body. Without adequate blood flow, bone cannot maintain its integrity. In fact, reductions in bone blood flow have been associated with bone loss. After a spinal cord injury (SCI), there are many changes in the paralyzed legs which might result in reductions in bone blood flow and may relate to post injury bone loss. We are doing this research to examine the changes in the paralyzed legs on bone blood flow in those with SCI compared to able-bodied individuals. Additionally, we are examining bone blood flow response to different shin loading conditions in those with SCI compared to able-bodied individuals. This research may provide important insights into potential causes of bone loss post SCI and could open new clinical avenues for treating osteoporosis.

Who will take part in this research?

We are asking you to take part in this research study you had a spinal cord injury. About 29 people (men and women) will take part in this research study. About 29 subjects will take part at Spaulding Hospital Cambridge. The National Institutes of Health is paying for this research to be done.

What will happen in this research study?

To participate in this study you must be an adult with spinal cord injury (American Spinal Injury Association Impairment Scale A or B or C. You must be between the ages of 18 and 40 years of age.

Exclusion criteria:

You are not eligible for this study if you have:

- clinical signs or symptoms of heart disease, hypertension, coronary disease
- diabetes
- other neurological disease
- cancer
- abnormal resting ECG
- pregnant women
- tibial fracture or tibial stress fracture in the past 2 years
- extreme spasticity to avoid spontaneous contractions
- are taken baclofen due to its potential autonomic effects

SCREENING PROCEDURES

Screening: about 30 minutes (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

Medical History: We will ask you questions about your medical history. This will help us check for disease or other reasons you would not qualify for this study.

Weight: Your weight will be measured.

Tibial Length: Your shin will be measured.

Instructions:

- Do not drink caffeine for 24-hours before your visit.
- Do not take part in any heavy physical activity /exercise for 24-hours before your visit
- You will need to wear shorts or loose sweatpants during the testing session

STUDY PROCEDURES

Study Visit about 1 hour (no shin loading) or 2.5 hours (with shin loading), following screening (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

1) **Popliteal Artery Structure.** An ultrasound device will be used to measure the thickness and diameter of an artery in your leg under your knee.

2) **Bone Blood Flow.** We will measure the content of the blood in your bone (tibia, or the shin bone) by placing a probe on the skin. The probe is housed in a material sleeve with flexible plastic backing. The probe has three holes: one to shine light into the bone and two to measure the light that comes back out of the bone. We will shine the light into your shin and we will measure the light that comes out for the entire duration of the experiment.

3) **Calf Blood Flow.** An ultrasound device will measure the blood flow in an artery in the same leg. A small device will be placed under your knee and strapped into place with a band around your leg.

4) **Leg Dependency.** While lying down, we will measure bone blood flow and calf blood flow in your shin while your leg is supine and when we lower your leg below heart level such that you your knee is bent at 90 degrees. Dropping the leg will increase arterial pressure, causing blood to pool in your leg.

5) **Cuff Inflation.** While lying down, we will place a pressure cuff above the knee. We will inflate the cuff for 10 minutes. The cuff will be inflated at a level that will stop blood flow below the cuff level for the 10 minutes duration. After releasing the cuff, blood flow will

return in your calf. This will allow us to measure the shin blood content and leg blood flow before, during, and after cuff inflation.

6) **Shin Loading.** With the leg still in the boot used for determining maximal calf force, we will load your shin. A 2 inch strap will be secured over your thigh. The knee will be bent at 90degrees for the entire loading protocol. Wires will pull vertically down on the strap, loading your shin. We will load your leg three times for five minutes each time, at three different loads corresponding to about 10% of your body weight, 30% of your body weight, 50% of your body weight. This loading is much smaller than during walking. For example, during walking a person loads their legs with about 3-4 times their body weight. During loading we will measure shin blood content. This part of the protocol will be completed only in volunteers with injuries between 3 and 24 months post injury.

Protocol:
You will be asked to not drink caffeine for 24-hours before your visit. In addition, you will be asked to not participate in any heavy physical activity for 24-hours before testing. You will need to wear shorts or loose sweatpants during the testing session.

You will be connected to the monitoring equipment described above. At the beginning of the study procedure, we will measure arterial diameter and thickness in your leg using an ultrasound. Throughout the study procedure, we will monitor continuously shin blood. We will also measure calf blood flow in the same leg using an ultrasound device during leg dependency and cuff inflation. First, after 5 minutes of lying supine on an exam table, you will be asked to lower your shin for 5 minutes. After 10 minutes of rest, we will place a pressure cuff above your knee and inflate it for 10 minutes as described above. We will record date for 5 minutes before cuff inflation, during 10 minutes of cuff inflation, and 5 minutes after cuff release. Afterwards, in a sitting position we will place your leg in the boot of the loading device. We will load your bone three times; each cycle of loading will consist of 5 minutes of rest, 10 minutes of loading, and 5 minutes of recovery.

We will remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples to share with our research collaborators at Northeastern University.

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study. A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, weight).

You may be asked to repeat any of the above testing if there is difficulty obtaining results that meet out quality standards or there are equipment issues that arise. If any of the above testing may be repeated, you may be asked to attend an additional study visit for this purpose.

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

At the completion of this research study, we would like to store and be able to use and share your identifiable samples and health information with researchers at Partners for other research related to regulation of blood flow to bone and/or bone health. If we share your samples and/or health information with other researchers outside of Partners, we will label the samples and information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your sample and/or information. We will keep the code in a password protected computer at Spaulding Hospital Cambridge.

Because these samples and/or health information are identifiable, we are asking your permission to store, use and share them for other research. You can still take part in the research study whether or not you give permission for the storage, use, and sharing of the samples and health information for other research.

Do you agree to let us store and use your samples and health information for other research related to regulation of blood flow to bone and /or bone health?

☐ YES ☐ NO Initial _____

Will you get the results of this research study?

You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. We and the researchers involved in this study will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning. There is a small chance that we or the researchers could find out something from the study that might be important to your

health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

You can choose to get a newsletter that will tell you about the research studies we are doing. This newsletter will not announce your results or anyone else's, but it will tell you some information about what we are learning about bone health. We will also publish what we learn in medical journals. In the future, when research results are published, they may show that certain groups (for example, racial or ethnic groups, or men/women) have genes that are associated with increased risk of a disease. If this happens, you may learn that you are at increased risk of developing a disease or condition.

What are the risks and possible discomforts from being in this research study?

The measurements of thickness and diameter and blood flow of the artery involve the inconvenience and discomfort of multiple attachments to your body, but do not have any risk.

Specific

Bone Blood Flow. The system is non-invasive and there are no known associated risks. Previous trials with the blood flow activity measurement showed minor reddening due to the plastic holder; however, this was temporary and it quickly went away. During the experiment, we will ask you if you feel any discomfort or heating effect. If you have any discomfort we will stop and turn off the light source immediately.

Cuff Inflation. The cuff inflation may result in muscle discomfort, leg numbness, and pins and needles sensation in the leg during cuff inflation and/or immediately after cuff release; also, it may result in autonomic dysreflexia (signs include: headache, nausea, rise in blood pressure, sweating, and goosebumps).

Shin Loading. There is a risk of bone or muscle injury during loading. However, the loading should pose little risk since the device applies loads at less than full body weight (maximum weight will be about half your body weight). For example, during walking a person loads their legs with about 3-4 times their body weight. This part of the protocol will be completed only in volunteers with injuries between 3 and 24 months post injury.

There may be other risks that are currently unknown.

What are the possible benefits from being in this research study?

You will not directly benefit from your participation in this study. This research may help physicians and scientists to better understand how blood flow is controlled in bone.

Can you still get medical care within Partners if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will receive $100 (for those that complete the entire protocol, with shin loading) or $50 (no shin loading) as a check for participating in this study. The study is a 1 time visit and you will receive the full amount if the study has been started. The check should arrive in your mailbox about 3-4 weeks after the study. In order to reimburse you, we will need your social security number.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Partners to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Partners researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other researchers within or outside Partners, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate

does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.

- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter | Date | Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name | Date | Time (optional)

Consent Form Version Date: 05/13/2022

Partners HealthCare System
Research Consent Form

Clinicaltrials.gov # NCT04083794

General Template
Version Date: August 2016

Subject Identification

Protocol Title: Exploration of blood flow regulation to bone in humans

Principal Investigator: J. Andrew Taylor, Ph.D.

Site Principal Investigator:

Description of Subject Population: Healthy male and female volunteers between the ages of 18 and 40

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Why is this research study being done?

The purpose of this research study is to learn more about how the nervous system controls blood flow in bone. You are being asked to participate as a healthy male volunteer or as a healthy female volunteer. About 68 people (34 men, 34 women) will take part in this research.

How long will I take part in this research study?

Your total time will be approximately 4 hours and will require 1 or 2 visits to Spaulding Hospital Cambridge. For all volunteers, screening and consenting and the study will take place on the same day or on different days at Spaulding Hospital Cambridge.

IRB Protocol No: 2018P000156
Consent Form Valid Date: 11/21/2023
IRB Expiration Date: 11/21/2024
IRB Submission: CR6/AME22

What will happen in this research study?

To participate in this study, you must be between the ages of 18 and 40 years of age. You must not have a history of cardiovascular problems or neurological conditions.

SCREENING PROCEDURES

Screening: about 30 minutes (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

Medical History: We will ask you questions about your medical history. This will help us check for disease or other reasons you would not qualify for this study.

Height and Weight: Your height and weight will be measured.

Instructions:

- Do not drink caffeine for 24-hours before your visit.
- Do not take part in any heavy physical activity /exercise for 24-hours before your visit.
- Do not take any amphetamines such as Ritalin, Adderal, Concerta for 48-hours before the visit.

STUDY PROCEDURES

Study Visit about 3.5 hours, following screening (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

1) **Blood Pressure, Heart Rate, and Breathing**. Blood pressure will be recorded by placing a small cuff around your middle finger and cuff around your upper arm. Heart rate will be measured by placing electrodes on your chest. Your breathing will be measured from a band around your lower chest.

2) **Bone Blood Flow.** We will measure the content of the blood in your bone (tibia, or the shin bone) by placing a probe on the skin. The probe is housed in a material sleeve with flexible plastic backing. The probe has three holes: one to shine light into the bone and two to measure the light that comes back out of the bone. We will shine the light into your shin and we will measure the light that comes out for the entire duration of the experiment.

3) **Nerve Activity.** We would like to learn more about how your nervous system controls your blood content in the bone. The measurement of nervous system activity involves measuring the activity of the nerve located on the side of your leg below the knee. The nerve will be located by touching your skin with a probe, which is about the size of a pen. When the probe touches your skin it will give off a mild electric current, causing your leg to twitch. This can cause mild discomfort. This gives us information on where your nerve lies.

   Next two tiny wire-electrodes will be placed in your skin on the side of your leg below the knee. The position of one of the wire-electrodes will be moved slightly while a very mild electric current is passed through the electrode. While the wire-electrode is moved you may feel temporary muscle twitches, pins and needles sensations and/or a dull aching sensation. This procedure will take between 5-60 minutes depending on how easy it is to find where your nerve lies.

4) **Calf Blood Flow.** An ultrasound device will provide the blood flow in an artery in your other leg. A small device will be placed under your knee and strapped into place with a band around your leg.

5) **Valsalva maneuver.** You will breathe out into a tube forcefully for 15 seconds. This maneuver is similar to bearing down when in the bathroom. This will allow us to assess if we obtained a good nerve activity recording. You will do this three times.

6) **Tilt Test.** A tilt table is used to move you into downright and upright position in a controlled manner without having you sit up. Only a low tilt angle will be used, comparable to the angle when reclining in a chair.

7) **Ice Water Test.** We would like to know more about how your body controls blood flow in response to cold sensation. You will place your hand in a bucket of ice water up to your wrist for 3 minutes. This will cause a slowly increasing amount of mild to moderate discomfort. This test will allow us to measure the shin blood content, leg blood flow, and leg nerve activity responses to cold sensation.

8) **Handgrip Exercise.** You will perform brief, sustained exercise by squeezing a handgrip device for several minutes. You will be asked to maintain a constant handgrip tension until your arm is tired. This will allow us to measure shin blood content, leg blood flow, and leg nerve activity in response to exercise.

Protocol:
You will be asked to not drink caffeine for 24-hours before your visit. In addition, you will be asked to not participate in any heavy physical activity for 24-hours before testing.

You will be connected to the monitoring equipment described above. You will rest quietly on the tilt table set at 0 degrees tilt. Your heart rate, blood pressure, and respiration will be monitored the entire time. The shin blood flow device will measure blood content in your shin the entire time. The nerve activity of your leg will be monitored the entire time. The ultrasound device will measure blood flow in an artery in your other leg. First you will be asked to perform a Valsalva maneuver as described above. After 2 minutes of rest, there will be a 25 minutes session with different levels of tilt as follows: downright 10 degrees, 0 degrees, upright 10 degrees, and upright 20 degrees. After you will be brought back to the initial position at 0 degrees tilt. After 10 minutes of rest, you will be asked to perform the ice water test described above for 3 minutes. Following a 3 minutes recovery, you will perform a handgrip exercise. When finished, your heart rate and blood pressure will be monitored until they return to normal levels.

You may be asked to repeat any of the above testing if there is difficulty obtaining results that meet our quality standards or there are equipment issues that arise. If any of the above testing may be repeated, you may be asked to attend an additional study visit for this purpose.

What are the risks and possible discomforts from being in this research study?

General
The measurements of blood pressure, heart rate, breathing, and blood flow of the artery involve the inconvenience and discomfort of multiple attachments to your body, but do not have any risk.

Specific
Nerve Activity.
You will feel discomfort when we insert the wire-electrodes into your skin. We will show you the wire-electrode before you start the study. It is much thinner than a needle used for shots from a doctor. You may get muscle twitches, "pins and needles" feelings and or a dull aching sensation while we search for your nerve. If you do feel them, they should only last for a short time. Some individuals have experienced these feelings for up to three days after the test. Most people who had these feelings after the test said they felt them once or twice. They usually lasted only a couple of seconds and went away spontaneously.

Bone Blood Flow.
The system is non-invasive and there are no known associated risks. Previous trials with the blood flow activity measurement showed minor reddening due to the plastic holder; however this

was temporary and it quickly went away. During the experiment, we will ask you if you feel any discomfort or heating effect. If you have any discomfort we will stop and turn off the light source immediately.

Valsalva Maneuver.
You may feel dizzy or faint. There are some serious risks with this maneuver, including detachment of blood clots, bleeding, and heart attack. These risks are very rare in young individuals without cardiovascular disease.

Tilt Test.
You may feel dizzy, nauseous, sweaty, or become pale. Your heart rate may increase and your blood pressure may decrease during the tilt test. If you have any discomfort you will be immediately be put back in a lying down position and you should feel better in a couple of minutes.

Ice Water Test.
You will feel mild to moderate discomfort, much like if you put ice on an injury, while your hand is in the ice-cold water.

Handgrip Exercise.
You will feel mild to moderate discomfort while performing the handgrip exercise as your hand and arm get tired.

At the completion of the study, we will ask you to complete a short questionnaire monitoring for symptoms from the nerve recording about 4 days after the study.

What are the possible benefits from being in this research study?

You will not directly benefit from your participation in this study. This research may help physicians and scientists to better understand how the nervous system controls bone blood flow.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

You will receive $150 at the completion of the study. In order to reimburse you, we will need your social security number.

What will I have to pay for if I take part in this research study?

Participation in this study will cost you nothing.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.
Dr. J. Andrew Taylor, M.S., Ph.D. is the person in charge of this research study. You can call him/her at 617-758-5503 M-F 9-5.

If you have questions about the scheduling of appointments or study visits, call Glen Picard at 617-758-5511.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study

- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter	Date/Time

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name	Date/Time

Consent Form Version: 03/24/21

Subject Identification

General Consent Form Template
Version Date: January 2019

Protocol Title: Exploration of blood flow regulation to bone in humans

Principal Investigator: J. Andrew Taylor, Ph.D.

Site Principal Investigator:

Description of Subject Population: Volunteers with SCI ages 18-40

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

IRB Protocol No: 2018P000156
Consent Form Valid Date: 11/21/2023
IRB Expiration Date: 11/21/2024
IRB Submission: CR6/AME22

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Partners now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn how the nervous system controls bone blood low.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 3 hours to complete the study. During this time, we will ask you to make 1 or 2 study visits to Spaulding Hospital Cambridge.

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen: we will measure blood pressure, heart rate, breathing, and blood flow in your leg. During these recordings, you will be asked to breathe forcefully. Also, you will be asked to place your hand in a bucket of ice water. After, you will be asked to maintain a constant handgrip tension by squeezing a handgrip device until your arm is tired. Afterwards, we will move you into downright and upright position without having you sit up.

Why might you choose to take part in this study?

You will not benefit from taking part in this research study. This research may help physicians and scientists better understand how the nervous system controls bone blood flow.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully. Important risks and possible discomforts to know about include: inconvenience and discomfort of multiple attachments to your body. You may feel dizzy or faint during the Valsalva maneuver, there are some serious risks with this maneuver, including detachment of blood clots,

bleeding, and heart attack, but these risks are very rare in young individuals without cardiovascular disease. During the tilt test, you may feel dizzy, nauseous, sweaty, or become pale; your heart rate may increase and your blood pressure may decrease; however, if you have any discomfort you will be immediately be put back in a lying down position and you should feel better in a couple of minutes. You will feel mild to moderate discomfort while your hand is in the ice-cold water and while you are performing the handgrip exercise.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

Other things to consider are that the study requires 1 visit at Spaulding Hospital Cambridge and about 3 hours for the study protocol.

What other treatments or procedures are available for your condition?

This research investigates human physiology, focusing on regulation of blood flow to bone, and does not involve any diagnosis or treatment.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. J. Andrew Taylor, M.S., Ph.D. is the person in charge of this research study. You can call him/her at **617-758-5503 M-F 9-5**. You can also call **Dr. Adina E. Draghici, Ph.D at 617-758-5508 M-F 9-5** with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call **Dr. Adina E. Draghici** at **617-758-5508**.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

Who will take part in this research?

We are asking you to take part in this research study you had a spinal cord injury. About 17 men with spinal cord injury (with ages between 18 and 40 years old) will take part in this research study at Spaulding Hospital Cambridge.

What will happen in this research study?

SCREENING PROCEDURES

Screening: about 30 minutes (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

Medical History: We will ask you questions about your medical history. This will help us check for disease or other reasons you would not qualify for this study.

Weight: Your weight will be measured.

Instructions:

- Do not drink caffeine for 24-hours before your visit.
- Do not take part in any heavy physical activity /exercise for 24-hours before your visit
- You will need to wear shorts or loose sweatpants during the testing session

STUDY PROCEDURES

Study Visit about 2.5 hours, following screening (Spaulding Rehabilitation Hospital/Cardiovascular Research Laboratory)

1) **Blood Pressure, Heart Rate, and Breathing.** Blood pressure will be recorded by placing a small cuff around your middle finger and cuff around your upper arm. Heart rate will be measured by placing electrodes on your chest. Your breathing will be measured from a band around your lower chest.

2) **Bone Blood Flow.** We will measure the content of the blood in your bone (tibia, or the shin bone) by placing a probe on the skin. The probe is housed in a material sleeve with flexible plastic backing. The probe has three holes: one to shine light into the bone and two

to measure the light that comes back out of the bone. We will shine the light into your shin and we will measure the light that comes out for the entire duration of the experiment.

3) **Calf Blood Flow.** An ultrasound device will provide the blood flow in an artery in the same leg. A small device will be placed under your knee and strapped into place with a band around your leg.

4) **Valsalva maneuver.** You will breathe out into a tube forcefully for 15 seconds. This maneuver is similar to bearing down when in the bathroom. This will allow us to assess if we obtained a good nerve activity recording. You will do this three times.

5) **Ice Water Test.** We would like to know more about how your body controls blood flow in response to cold sensation. You will place your hand in a bucket of ice water up to your wrist for 3 minutes. This will cause a slowly increasing amount of mild to moderate discomfort. This test will allow us to measure the shin blood content, leg blood flow, and leg nerve activity responses to cold sensation.

6) **Handgrip Exercise.** You will perform brief, sustained exercise by squeezing a handgrip device for several minutes. You will be asked to maintain a constant handgrip tension until your arm is tired. This will allow us to measure shin blood content, leg blood flow, and leg nerve activity in response to exercise.

7) **Tilt Test.** A tilt table is used to move you into downright and upright position in a controlled manner without having you sit up. Only a low tilt angle will be used, comparable to the angle when reclining in a chair.

Protocol:
You will be asked to not drink caffeine for 24-hours before your visit. In addition, you will be asked to not participate in any heavy physical activity for 24-hours before testing. You will need to wear shorts or loose sweatpants during the testing session.

You will be connected to the monitoring equipment described above. You will rest quietly on the tilt table set at 0 degrees tilt. Your heart rate, blood pressure, and respiration will be monitored the entire time. The shin blood flow device will measure blood content in your shin the entire time. The ultrasound device will measure blood flow in an artery in your other leg. First you will be asked to perform a Valsalva maneuver as described above. Afterwards, you will be asked to perform the ice water test described above for 3 minutes. Following a 3 minutes recovery, you will perform a handgrip exercise. After 2 minutes of rest, there will be a 20 minutes session with different levels of tilt as follows: downright 10 degrees, 0 degrees, upright 10 degrees, and upright 20 degree. After you will be brought back to the initial position at 0 degrees tilt. When finished, your heart rate and blood pressure will be monitored until they return to normal levels.

We will remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples to share with our research collaborators at Northeastern University.

You may be asked to repeat any of the above testing if there is difficulty obtaining results that meet our quality standards or there are equipment issues that arise. If any of the above testing may be repeated, you may be asked to attend an additional study visit for this purpose.

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, weight).

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

At the completion of this research study, we would like to store and be able to use and share your identifiable samples and health information with researchers at Partners for other research related to regulation of blood flow to bone and/or bone health. If we share your samples and/or health information with other researchers outside of Partners, we will label the samples and information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your sample and/or information. We will keep the code in a password protected computer at Spaulding Hospital Cambridge.

Because these samples and/or health information are identifiable, we are asking your permission to store, use and share them for other research. You can still take part in the research study

whether or not you give permission for the storage, use, and sharing of the samples and health information for other research.

Do you agree to let us store and use your samples and health information for other research related to regulation of blood flow to bone and/or bone health?

☐ YES ☐ NO Initial _____

Will you get the results of this research study?

You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. We and the researchers involved in this study will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning.

You can choose to get a newsletter that will tell you about the research studies we are doing. This newsletter will not announce your results or anyone else's, but it will tell you some information about what we are learning about bone health. We will also publish what we learn in medical journals. In the future, when research results are published, they may show that certain groups (for example, racial or ethnic groups, or men/women) have genes that are associated with increased risk of a disease. If this happens, you may learn that you are at increased risk of developing a disease or condition.

What are the risks and possible discomforts from being in this research study?

General

There is inconvenience and discomfort due to multiple attachments to your body, but do not have any risk.

Specific

Bone Blood Flow. The system is non-invasive and there are no known associated risks. Previous trials with the blood flow activity measurement showed minor reddening due to the plastic holder; however, this was temporary and it quickly went away. During the experiment,

we will ask you if you feel any discomfort or heating effect. If you have any discomfort we will stop and turn off the light source immediately.

Valsalva Maneuver. You may feel dizzy or faint. There are some serious risks with this maneuver, including detachment of blood clots, bleeding, and heart attack. These risks are very rare in young individuals without cardiovascular disease.

Tilt Test. You may feel dizzy, nauseous, sweaty, or become pale. Your heart rate may increase, and your blood pressure may decrease during the tilt test. If you have any discomfort you will be immediately be put back in a lying down position and you should feel better in a couple of minutes.

Ice Water Test. You will feel mild to moderate discomfort, much like if you put ice on an injury, while your hand is in the ice-cold water.

Handgrip Exercise. You will feel mild to moderate discomfort while performing the handgrip exercise as your hand and arm get tired.

There may be other risks that are currently unknown.

What are the possible benefits from being in this research study?

You will not directly benefit from your participation in this study. This research may help physicians and scientists to better understand how the nervous system controls bone blood flow.

Can you still get medical care within Partners if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will receive $100 as a check for completing this study. The study is a 1 or 2 times visits and you will receive the full amount if the study visit has been started. The check should arrive in your mailbox about 3-4 weeks after the study. In order to reimburse you, we will need your social security number.

What will you have to pay for if you take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Partners to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Partners researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records

- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other:

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

_____	_____	_____
Hospital Medical Interpreter	Date	Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____	_____	_____
Name	Date	Time (optional)

Consent Form Version: 03/24/2021