Comparison of Exercise Mode on Disruptions in Calcium Homeostasis

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Subject Name: _____ **Date:** _____

Title of Study: Comparison of Exercise Mode on Disruptions in Calcium Homeostasis

Principal Investigator: [redacted] **VAMC:** 554

VA Investigator: [redacted] **COMIRB#** 21-2580

Key Information

- Your consent is being sought for research and your participation in this research is voluntary.
- This study is being done to understand how different types of exercise effect different bone markers in your blood. It is expected that your participation will last up to 12 weeks, including all screening tests. If you qualify for the study, you will complete 2 1-hour exercise sessions that include blood draws during exercise and during recovery. The exercise collection visits last approximately 6 hours.
- The risks of this study include bruising and infection from blood draws, cardiac events related to exercise, radiation exposure from the screening bone scan, and loss of confidentiality. These risks are explained in more detail in this form.
- This study is not designed to treat any disease or illness, so there is no direct benefit to you. The study is intended to add to the knowledge of exercise and bone health. Because this is not treating any disease, there are no alternative treatments or research.

You are being invited to take part in a research study that is being funded by the VA. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

Why is this study being done?

This study plans to learn more about if different types of exercise have a different effect on bone. Research has found that exercise can sometimes lead to an increase in bone breakdown, but it is not known if this breakdown is different between different kinds of exercise. This study will measure markers in your blood before, during, and after two different exercise sessions to understand how these markers change after treadmill walking versus cycling exercise.

You are being asked to be in this research study because you are a veteran who is aged 60 or older and are accustomed to regular cycling and walking exercise.

Other people in this study

Up to 60 people from your area will participate in the study.

What happens if I join this study?

If you decide to join the study, you will participate in a screening visit to the clinic to determine your eligibility. If you are eligible, you may be asked to participate in the full study.

This research study is expected to take approximately 2 years. Your individual participation in the project will take up to 12 weeks.

Consenting Visit:

You will be asked to fast (no food or drink for 8 hours; water only) overnight for this visit. If you choose to fast for your consenting visit, we will do all of these procedures in the same day. If you choose not to fast for your consenting visit, we will schedule a separate visit for your screening tests, which will require you to be fasting. During this visit:

- You will have the opportunity to review and discuss this consent form to present any questions you have and if you desire to sign it.
- You will have a physical exam and a review of your medical history.
- About 2 teaspoons of blood will be taken from a vein in your arm.
- You will also have a bone density test (DXA), which involves lying on an x-ray table for about 15 minutes.
- You will be asked to complete questionnaires at baseline and screening visits.

This visit will take place at the Clinical Trial Research Center (CTRC) Clinic on the University of Colorado Anschutz Medical Campus and will last about 1.5 hours.

Baseline Study Visits:

Exercise Tests: During this visit you will exercise on a treadmill for 10 to 15 minutes. It will be easy at the start and become gradually more difficult until you cannot continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal and you will breathe only through your mouth using a special mouthpiece. If you have any signs of a heart problem, such as certain ECG changes, we may ask you to follow-up with your doctor. If further evaluation by a cardiologist shows there is no problem, you may be able to continue in the study. If you choose not to follow-up with your primary care provider, you will not be allowed to participate in the study.

This visit will take place at the IMAGE Group Exercise Gym on the University of Colorado Anschutz Medical Campus and will last about 1 hour.

Exercise Familiarization:

If your ECG is normal and it is safe for you to participate, you will come back to the IMAGE Group Exercise Gym to become used to the equipment we will use during your exercise collection visits. Alternatively, you may complete these visits at Building P on at the Rocky Mountain Regional VAMC, if you prefer. You will exercise for 20 minutes on the treadmill at 70-80% of the highest heart rate we recorded during your treadmill exercise test. After a ~15-minute rest, you will exercise for 20 minutes on the stationary bike at the same intensity. You will provide a rating of how hard you feel like you are working every 5 minutes during exercise for both the treadmill and the bike. After 15 minutes exercise on each piece of equipment, you will be asked if you could complete 60 minutes at this intensity. This information will be used to select the intensity for your visits and to see if it is safe for you to continue with the study.

Exercise Collection Visits:

Before each visit, you will be asked to record what you ate for the night before you come to the clinic. You will bring this record with you to your visit and we will make you a copy. You will be asked to eat the same thing

before both exercise collection visits. The morning of your visit, a meal will be provided to you to eat 4 hours before you begin to exercise. You can come to the lab to eat it or pick it up the day before and eat it at home. You will be asked to eat the entire meal, which will be the same for both visits. After eating this meal, you will be asked not to eat or drink anything except for water until the end of exercise testing for that day. We ask that you engage in only light physical activity (i.e., walking to your vehicle) during this time. The exercise portion of each visit will last a little more than 1 hour.

You will be asked to come to the clinic before 9AM for both exercise collection visits. You will exercise on either the bike or the treadmill, and which exercise you get at the first visit will be random. At your second visit, you will complete the other exercise. For example, if you walk on the treadmill at your first exercise collection visit, you will ride the stationary bike at your second collection visit. Each exercise will be 60 minutes in duration (plus a 5-minute warm-up at ~50% of your highest recorded heart rate) and your exercise collection visits will be at least 1 week apart.

When you first get to the clinic, we will take your heart rate and blood pressure, get your weight in a hospital gown, and then insert an IV into a vein in your arm. You will be resting when we get our first blood sample (~ 2 teaspoons) from the IV about 15 minutes before exercise. Once that sample is taken, you will move to the cycle ergometer or treadmill and remain seated or standing for 5 minutes before exercise. A second pre-exercise blood sample (~2 teaspoons) will be taken immediately before exercise. Once you start exercise, a blood sample will be taken from your IV every 15 minutes during exercise. All blood samples during exercise and recovery are approximately 2 teaspoons.

Once exercise is over, you will be asked to rest at the clinic, and we will continue to take blood samples from your IV. You will have samples taken 15, 30, 45, and 60 minutes after exercise. You will have another sample taken 4 hours after exercise. You cannot leave the facility during this time. You will be allowed to drink as much water as you want, and we will provide the water for you, but you cannot eat until after the last blood sample. After the blood sample taken 4 hours after exercise, you will be allowed to go home. A total of 20 teaspoons will be collected during exercise and recovery. You will be asked to come back to the clinic 24 hours after the end of exercise for another blood draw. You will need to be fasted for this blood draw. An additional blood sample 48 hours after exercise will be available as an optional procedure.

At your second exercise collection visit, all the steps will be the same, but you will complete the other exercise. The total amount of blood collected for both exercises is up to 48 teaspoons (1 cup).

What are the possible discomforts or risks?

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur.

Discomforts you may experience and possible risks of the study include:

- **Exercise and Increased Heart Rate**: The potential risks of exercise testing include irregular heartbeats, heart attack, cardiac arrest, and death, as well as the less serious problems of injury to joints and muscles. Exercise can also lead to excessive sweating and dehydration. There is also a minor risk of skin irritation from the electrodes we use to track your heart rate. These risks are minimized by a review of your medical history and physical exam prior to exercise testing, and by monitoring your heart and blood pressure before, during, and after exercise testing. If your heart or blood pressure responses are not normal, we may not perform the test, stop the test early, or complete the test but not enroll you in the study. The same risks are present during the exercise sessions (visits 3 and 4).

- **Blood Draw**: In visit 1 we will take about 2 teaspoons of blood from your vein. In visits 3 and 4 we will take about 24 teaspoons of blood from your vein at each visit. We will get blood on visit 1 by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin. You may feel faint during the blood draw.
- **Catheter:** For visits 3 and 4, blood will also be drawn by inserting a needle connected to a plastic tube into a vein in your arm. The plastic tube will stay in your vein during exercise so that we can take blood samples or give you fluids. You will feel some pain when we first inset the tube into your vein. You may have some redness, swelling, or bruising where the tube goes under your skin. In some cases this type of tube can cause an infection where it goes under the skin. In rare cases, it can cause a blood clot in the vein. You may feel faint when we insert the tube into your vein. You will have this tube in your vein for about two and a half hours.
- **DXA**: During visit 1 we will perform 2 sets of DXA scans of your whole body, spine, and hip (6 scans total). The second set of scans will be performed immediately after the first scan. DXA is a way of looking inside the body by using X-rays. X-rays are a type of radiation. Your natural environment has some radiation in it. These tests will give you about the same amount of radiation you would get from your environment in 4 days.
- **Confidentiality and Privacy**: There is a risk that people outside of the research team will see your research information. We will do all that we can to protect the privacy of your information, but it cannot be guaranteed.
- **Unknown Risks:** The study may include risks that are unknown at this time.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about exercise, calcium regulation, and bone health. This study is not designed to treat any illness or to improve your health. Also there are risks as mentioned in Discomforts and the Risks Section.

This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Who is paying for this study?

This research is being sponsored for by the VA Rehabilitation Research and Development Service (RR&D).

Will I be paid for being in the study?

You will be paid $100 for each of your exercise collection visits for a total of $200 for both visits. If you leave the study early, or if we must take you out of the study, you will only be compensated for the visits you have completed.

It is important to know that payments for participation in a study are taxable income.

The VA will be disbursing your payments. Your SSN will be collected and used to report this taxable income to the IRS.

The payment will be made via a Mastercard debit type card called a "Clincard" and is provided by Greenphire. Your funds will be available to you via this card usually within 24 hours following your scheduled visit or phone call, but no more than 48 hours (possible exceptions are weekends or holidays). Greenphire and its customer support members will have access to your name, address, and date of birth. Instructions and terms of use are included with the card upon receipt.

Will I have to pay for anything?

You will be responsible for your transportation costs to and from the research facility.
Otherwise, there will be no cost to you for participation in this study. However, some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by the VA that are not part of this study. If you decide to participate in this study, you cannot be charged nor your insurance billed, for research-related interventions or procedures that are required by the protocol.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission, if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?

Every reasonable safety measure will be used to protect your well-being. The VA Eastern Colorado Health Care System (ECHCS) will provide necessary medical care and treatment for any injury that is a result of participation in this study for veterans, in accordance with applicable federal regulations (38 CFR 17.85). Compensation for such an injury may be permitted by applicable federal laws and/or regulations. The VA is not required to provide treatment for injuries in research studies if the injuries are caused by your non-compliance with study procedures.

You should inform your care provider(s) if you decide to participate in this research study. If you have questions about an injury related to the research, call [redacted] between 8AM and 5PM.

If you have an injury while you are in this study, you should call [redacted] immediately. Her phone number is [redacted]. Emergency and ongoing medical treatment will be provided as needed.

Who do I call if I have questions?

The researcher carrying out this study at the VA is [redacted]. You may ask any questions you have now. If you have any questions, concerns, or complaints later you may call [redacted]. You will be given a copy of this form to keep.

If you have questions regarding your rights as a research subject, concerns or complaints about this research study, please call the [redacted]. This is the Board that is responsible for overseeing the safety of human participants in this study. If you want to verify that this study is approved or if you would like to obtain information or offer input, please contact the [redacted].

How will my private information be protected?

Taking part in this study will involve collecting private information about you. We will keep all research records that contain your identifiable health information, confidential to the extent allowed by law. Records about you will be kept in locked filing cabinets in a locked office or on password-protected computers accessible by study personnel.

We will try to keep your medical records confidential, but it cannot be guaranteed. Records that identify you (including your medical records and the consent form signed by you), may be looked at or portions of your records copied that identify you by others.

There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the VA Institutional Review Board (IRB), our local Research and Development Committee, and other study monitors may look at or copy portions of records that identify you. (If the study involves a product regulated by the FDA, the Food and Drug Administration should be included in the above list)

The data and blood and collected from you are important to this study and to future research. Future tests will not include any DNA, RNA, or genetic analysis. If there is any unused blood left at the end of this study, we will store it for potential future measurements related to the biology of aging tissues in response to exercise. Only the investigators involved in this study will be allowed to use these samples for research, which may include some experiments not directly related to this study. Samples will be stored using a unique code that cannot be used to personally identify you until they are used up or no longer of good quality. There are no known commercial benefits related to your banked samples.

We will include information about your study participation in your medical record.

The data we collect will be used for this study but may also be important for future research. Your data may be used for future research or distributed to other researchers for future study without additional consent if information that identifies you is removed from the data.

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

Who will see my research information?

We will try to keep your medical records confidential, but it cannot be guaranteed. Records that identify you (including your medical records and the consent form signed by you), may be looked at or portions of your records copied that identify you by others. These include:

- Federal agencies such as the Food and Drug Administration (FDA), the General Accountability Office (GAO), the Office of the Inspector General, Office for Human Research Protections (OHRP), and the Office of Research Oversight (ORO) that protect research subjects like you, may also copy portions of records about you.
- People at the Colorado Multiple Institution Review Board
- The investigator and research team for this study
- The sponsor (VA Rehabilitation Research and Development group paying for the study), study monitors or agents for the sponsor
- Officials at the institution where the research is being conducted, and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research
- Our local VA Research and Development Committee
- UCDenver and its Clinical Trials Management System
- BuildClinical, a social media recruitment company
- Denver Research Institute (DRI, the VA's affiliated non-profit corporation) for payment purposes

I understand that by signing this consent form, a copy of limited data about me, restricted to (list data elements or state "all research data") that is collected as part of this specific VA research study will be stored in the REDCap database (or Data Storage System) at the University of Colorado Denver's (UCD's) Colorado Clinical and Translational Sciences Institute (CCTSI). This data will be used solely for the purposes defined in this consent form and for this specific study. Data collected about me for this study placed on the CCTSI REDCap Database will not be accessed or used for any other study or purposes and will only be accessed by VA-credentialed personnel. The CCTSI REDCap Database is a highly secure, nationally-utilized data management system, and it is housed within the highly-secure environment at the University of Colorado Denver.

Information about you will be combined with information from other people taking part in the study. We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

We will ask you to sign a different form that talks about who can see your research records. That form is called a HIPAA Authorization form. It will mention companies and universities who will seel your research records.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study has been completed.

The HIPAA Authorization form that you will also be asked to sign will state when or if it expires. However, you may withdraw this authorization for use and disclosure of your personal health information by providing written request to the Investigator. If you withdraw the HIPAA Authorization form, the Institution, the Investigator, the research staff, and the research Sponsor will no longer be able to use or disclose your personal health information from this study, except so far as that they have already relied on this information to conduct the study.

Agreement to be in this study

I have read this form. A member of the research team has explained the study to me. I have been told about the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

By signing this form below, I voluntarily consent to participate in this study. I will receive a copy of this consent after I sign it. A copy of this consent form will be placed in my medical record.

Subject's Signature: _____ Date:_____

Print name: _____

Consent form explained by: _____ Date: _____

Print name: _____

OPTIONAL ADDITIONAL PROCEDURES

Optional Consent for Data and Specimen Banking for Future Research

The Investigations in Metabolism, Aging, Gender, and Exercise (IMAGE) group would like to keep some of the blood and serum that is taken during the study but is not used for other tests. The PI ([redacted]) is a member of this research group, which includes approximately 30 researchers and staff on the University of Colorado Anschutz Medical Campus and many are affiliated with the VA Eastern Colorado Healthcare System. If you agree, the blood and serum will be kept and may be used in future research to learn more about how bone responds to exercise. The research that is done with your blood and serum samples is not designed to specifically help you. It might help people who have osteoporosis and other diseases in the future. Reports about research done with your blood and serum samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your blood and serum samples will not affect your care.

The choice to let the IMAGE group keep the blood and serum samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your blood and serum samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want the IMAGE group to use your blood and serum samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until the IMAGE group decides to destroy them.

When your blood and serum samples are given to other researchers in the future, [redacted] and the IMAGE group will not give them your name, address, phone number or any other information that will let the researchers know who you are. Sometimes blood and serum samples are used for genetic research (about diseases that are passed on in families). Even if your blood and serum samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your blood and serum samples will only be used for research and will not be sold. The research done with your blood and serum samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your blood and serum samples include learning more about what causes osteoporosis and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. The IMAGE group will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by the IMAGE group.

Please read each sentence below and think about your choice. After reading each sentence, check “yes” or “no” and initial. If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data and blood to be stored in a central tissue bank at the Rocky Mountain Regional VA for future use by the study investigators:

1. I give my permissions for my data and blood samples to be kept by IMAGE Group for use in future research to learn more about how to prevent, detect, or treat diseases or conditions related to aging.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my data and blood samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   ☐ Yes ☐ No _____Initials

3. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials

Re-contact. If you are interested in being recontacted for future research, please indicate below. You will be contacted from within the VA.

☐ Yes, I am interested in being contacted to participate in future studies. ____Initials

☐ No, I am not interested in being contacted to participate in future studies. ____Initials

Optional Additional Blood Draw

Please note: This section of the consent form is about optional research that is being done with people who are taking part in this study. You may volunteer for this optional research if you choose. You can still be a part of this study even if you choose to not take part in any of the optional research.

These are additional procedures that ask you to complete two visits. After each exercise collection visit, you will be asked to return to the clinic for another blood draw (~2 teaspoons).

These procedures will be used to provide more information on how the markers in your blood responded to each type of exercise.

Please take as much time as you need to decide. You may ask any questions that you may have and discuss this with the study team (your study doctor and her staff).

You will have a fasted blood draw (~2 teaspoons) taken from a vein in your arm approximately 48 hours after the end of each exercise collection visit. Like the other blood draws, you may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin. You may feel faint during the blood draw.

Taking part in this part of the study is voluntary. You can change your mind at any time about participating in these optional procedures.

You will not be paid for completing the additional blood draws beyond what you will receive as part of your normal participation.

Consent for optional procedures

Select your choice below:

☐ Yes, I agree to have an additional blood sample collected 48 hours after each exercise collection visit. _____ Initials

☐ No, I do not agree to have an additional blood sample collected 48 hours after each exercise collection visit. ____ Initials