Study protcol and Statistical Analysis plan:

Semi-Recumbent Vibration in Older Adults

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Protocol Objectives and Hypotheses:

Impaired physical function causes dependency and reduces quality of life. Sarcopenia, the age-related decline in muscle mass and function, is increasingly being appreciated as a cause of falls, injury, disability and fracture. Sarcopenia is common, costly, and a major risk factor for impaired physical function and reduced quality of life. Approaches to improve function in older are sorely needed but no approved therapies currently exist to treat sarcopenia. Exercise and nutrition have shown some promise in improving physical function. However, many older adults do not or cannot routinely exercise; approaches providing exercise benefits to such individuals will substantially enhance quality of life for many older adults. Moreover, even following exercise prescription, a major limitation is adherence. Vibration exercise is a training approach that is time efficient, effective and safe in older adults. This proposed prospective study will evaluate whether a novel exercise approach, seated vibration therapy, can improve function in our target population of older adults.

Our specific aims and hypotheses are as follows:

Specific Aims/Hypothesis:

Specific Aim: The primary aim of this pilot is to examine the effect of vibration therapy on muscle function (balance, muscle power and strength) and muscle mass. Relative (weight corrected jump power will be the main outcome variable Our hypothesis is that vibration therapy will improve jump power as measured by jumping mechanography and other muscle function parameters as well as muscle mass and mobility/independence (measured through the AM-PAC questionnaire) compared to sham exercise.

Exploratory Aim/Hypothesis:

Exploratory Aim: Examine adherence and factors that influence adherence, specifically subjective health benefit, exercise enjoyment (5-point Likert scales), pain (Comprehensive Pain Assessment Form), exercise related self-efficacy (Self-Efficacy for Exercise Scale), mood (Geriatric depression scale), and social support network (Lubben Social Network Scale). Our hypothesis is that vibration exercise will be well liked, not cause pain, and found to be beneficial by participants. Further more adherence will be influenced by parameters such as mood, social support network and exercise self-efficacy.

Background:

Sarcopenia: Definition, Prevalence and Consequence

With advancing age, a decrease in muscle function and mass occurs; a phenomenon known as sarcopenia. Although sarcopenia definitions have been proposed, no single consensus definition exists. As such, it is not surprising that studies evaluating sarcopenia prevalence and consequences have used different methodologies to evaluate muscle mass and/or to quantitate function. Despite variable definitions, it is apparent that sarcopenia becomes common with advancing age. Our own data in a small sample of community dwelling older adults demonstrated this variation in sarcopenia prevalence (from 11 to 34%) depending which definition was used. In a much larger cohort (NHANES III) sarcopenia prevalence was estimated to be 7-11% in older adults. Using definitions that include muscle mass and function the prevalence tends to be higher, particularly in older populations. Sarcopenia is associated with increased disability and reduced ability to perform activities of daily living, increased risk of falls and fractures, increased morbidity/mortality and is associated with substantial healthcare costs estimated at $18.5 billion annually. In summary, sarcopenia is common, costly and associated with adverse health consequences. It is apparent that clinical recognition of sarcopenia and therapies to prevent or correct this common condition, will have major societal and personal benefit including reduction of falls/fractures and loss of independence.

Vibration

Exercise improves mobility, reduces falls and injury risk and can maintain and improve mobility, independence and healthy aging. As such, exercise is an attractive non-pharmacologic intervention for those with sarcopenia. However, many older adults do not, or cannot, routinely exercise. Moreover, even following exercise prescription, adherence is often poor. As such, new approaches to provide exercise benefits to older adults are sorely needed. In this regard, vibration exercise is a training approach that is effective, time efficient and safe in older adults. Vibration exercise activates skeletal muscle via linear accelerations transmitted by the vibration device into the musculoskeletal system. These stimuli not only increase muscle function but might also be beneficial for bone health and balance. Vibration exercise requires less time than other exercise regimens, and can be performed by

older adults with comorbidities that often limit the ability to perform conventional exercise. Importantly, vibration training modalities differ; most vibration exercise systems require individuals to stand on a platform. Exercising in a standing position requires greater concentration and musculoskeletal coordination than sitting and may be too difficult for some individuals with physical function impairments or other co-morbidities, e.g., cardiac and/or pulmonary disease. The novel vibration system recently been developed by VibeTech located in Sheboygan, WI obviates this problem by providing semi-recumbent vibration exercise. Initial experience with the VibeTech chair is promising in frail adults. The proposed research will begin to examine whether this vibration modality can improve muscle function in older adults with physical function impairment.

Measurement of Muscle Function in Older Adults

No consensus sarcopenia definition exists, however, all proposed definitions include assessing parameters of both muscle mass and physical function. Thus, it is important to have valid and reproducible methods to assess muscle mass and function. Additionally, these tools need to be sensitive to change, in order to prospectively monitor age-related decline or intervention response to sarcopenia treatments. A number of traditional methods are currently used to assess muscle function; these include grip strength, gait speed, Timed Up and Go, repeated chair-rise and balance tests such as Romberg stance, semi-tandem and tandem stance. There is good evidence that these methods predict health outcomes such as mobility, physical function, morbidity and mortality. However, these tests vary in their reproducibility, likely in part due to human variability in collecting measurements. This is particularly true for tests that involve a starting and stopping time (e.g. gait speed, Timed Up and Go, repeated chair rise) and a subjective decision whether an individual has passed or failed a balance test such as the Romberg or tandem stance. Compared to human assessment, it is logical that computerized measures will have less variability. Unfortunately, there are only very limited data comparing widely utilized muscle function tests as measured by a human to computerized methods.

Additionally, but importantly, computerized tests have other advantages in that they allow collection of information that cannot be measured with traditional testing. For example, computerized methods assessing balance generate continuous variables instead of the qualitative "normal/abnormal" results often obtained with classical testing. As another example, chair rise performed on a computerized force plate can be analyzed not only by time (i.e. speed) but the software also reports power and force, if needed, for each leg separately. We will be using the Leonardo Force Platform (Novotec, Pforzheim, Germany) will be used for jumping mechanography (JM). JM uses a force platform to collect bilateral leg power, force and velocity from individuals performing a countermovement jump. We, and others, have demonstrated this to be a safe method to measure leg function in older adults that correlates well with other muscle function tests and exhibits good reproducibility. Importantly, even the very old and those with significant limitations can safely perform JM, as long as they can stand independently. JM has potential advantages in function assessment; the two-legged countermovement jump is a high intensity, complex movement that integrates neural, muscle and joint function. Moreover, it is less prone to have a ceiling effect. The system used (Leonardo, Novotec, Pforzheim, Germany) cannot only measure JM parameters but also balance parameters and chair rise time and power. Furthermore, we will use Mobility Lab™ (APDM, Portland, OR) to examine gait and balance. Mobility Lab uses wearable wireless sensors, that can be used to measure not only gait speed and Timed Up and Go but also variables such as stride variation and cadence. Additionally, it can measure several parameters that assess postural control. The hardware design allows analysis without the need for expensive and bulky gait laboratories. This method has been validated in older adults with gait abnormalities such as Parkinson's patients.

Measurement of Muscle Mass in Older Adults

In addition to physical performance, all current sarcopenia definitions include some assessment of muscle mass. Gold standard approaches to assess skeletal muscle mass, such as whole-body MRI, do exist, however these are both time and cost intensive. Consequently, they are not widely utilized. A potential method is body impendence spectroscopy (BIS) which will be utilized in this study. BIS measures the dynamic resistance across a spectrum of electrical frequencies to distinguish between intra- and extracellular water and thereby is able to measure muscle mass (intracellular water), not simply lean mass (mostly intra- + extracellular water). BIS is used in a variety of settings and is accepted as safe. It measures the impedance to the flow of a very small (<1 mA) alternating electrical current across a spectrum of frequencies through the body. The low frequency currents pass only through extracellular water, while the high frequency currents pass through both intra- and extracellular water because the cells act as capacitors. Currents at the frequencies utilized do not stimulate electrically excitable tissues such as

nerves or cardiac muscle. Consistent with this, there are no reports of untoward events caused by BIS despite thousands of individuals undergoing this procedure.

Study Design

This study will evaluate community dwelling women and men ≥ 70 years recruited from the Jewish Home and Care Center in Milwaukee, WI. Based on power calculations, to meet our primary specific aim, 32 study volunteers are necessary.

Following informed consent, at the screening visit exclusion/inclusion criteria will be reviewed. Those volunteers meeting eligibility criteria will be enrolled.

Inclusion criteria

1.) Men and women age ≥ 70 years
2.) Able and willing to sign informed consent
3.) Able to stand without assistance
4.) Able and willing to train for 10 minutes, 3 times per week
5.) Total SPPB score of ≤ 9 or ≤ 2 in any of the three tests included in the SPPB

Exclusion criteria

1.) Cognitive impairment to the degree that it limits the ability of signing informed consent
2.) Unable to sit upright for 10 minutes
3.) History of injury or surgery within the prior six months which limits the ability to ambulate
4.) Major illness that might cause missed training sessions or visits.

Study Flow Chart

Study visit	**Screen**	**Baseline**	**8 Weeks – Training 3x/week**	**Visit 1**	**4 Week Washout**	**Visit 2**	**8 Weeks – Training 3x/week**	**Visit 3**
Consent	X							
Medical history	X							
Hand grip strength		X		X		X		X
Jumping mechanography		X		X		X		X
BIS		X		X		X		X
Timed Up and Go (TUG)		X		X		X		X
SPPB	X	X		X		X		X
AM-PAC questionnaire		X		X		X		X
Comprehensive Pain Assessment Form		X		X		X		X
Geriatric Depression Scale		X		X		X		X
Self-Efficacy for Exercise Scale		X		X		X		X
Lubben Social Network Scale		X		X				X
Physical Activity Scale for the Elderly		X		X		X		X
Falls Assessment		Will be done on a weekly basis						
Adverse event recording and safety survey		Will be done at every training session						

Study Procedures

The study consists of five visits; screening, baseline followed by eight weeks of training three times a week, visit 1 at eight weeks followed by 4 weeks of washout, Visit 2 at 12 weeks followed by eight weeks of training three times a week, and a final Visit 3 at 20 weeks.

The following will occur at the screening visit after obtaining consent. Volunteers will be asked to perform tests included in the SPPB (gait speed, chair rise, balance). If their score is ≤ 9 or or ≤ 2 in any of the three tests included in the SPPB they will be eligible for the intervention phase. Included participants will be asked information about their medical history including personal history of osteoporosis, fragility fractures and falls within the last 12

months. At the baseline visit several questionnaires will be obtained and participants then will proceed with muscle function tests (SPPB, jumping mechanography, grip strength, timed-up-and-go test).

Participants will then be randomized into one of two groups. The first group will receive vibration + loading treatment for the first 8 weeks, the second group will receive sham treatment (loading only). After 8 weeks both groups will go through a 4 week wash-out period and then crossover will occur. The first group will now receive sham treatment (loading only) while the second group will receive vibration + loading treatment. The participants will train for 10 minutes, 3 times a week, during the active 16 total weeks.

Vibration Training

VibeTech One, a semi-recumbent strength training and vibration therapy system (VibeTech, Inc., Sheboygan, WI), while performing leg presses against the system's vibrating footplate. The footplate supplies low-level vibrations comfortably from the feet through the legs and into the low back at 30 Hz. This frequency is commonly reported in the vibration therapy literature in association with a variety of musculoskeletal benefits. Moreover, vibrations supplied to the legs near this frequency induce the tonic vibration reflex (TVR), which results in the affected muscles contracting in a controlled, but involuntary manner when the muscles are stimulated with appropriately delivered vibration. The vibration supplied through the footplate is considered safe according to ISO2631 (ISO2631-1:1997). The vibration amplitude produced by the VibeTech One has an adjustable range from 0.05 to 0.5 mm. The higher the vibration amplitude, the higher the alternating force supplied to the muscle at 30 Hz. For example, a vibration amplitude of 0.05 mm peak-to-peak produces an alternating force of +/-4 lbs. A vibration amplitude of 0.5 mm peak-to-peak produces an alternating force of +/-22 lbs. This alternating load is absorbed by the muscles, tendons, ligaments, bones, cartilage, and other tissues of the affected region. While it is not known how much vibration reaches each tissue, it is hypothesized that larger amplitude vibrations result in a larger amount of force being absorbed by the muscles through the TVR. In clinical use with the VibeTech One (where over 400 treatments have been supplied to nursing home residents to date), therapists typically apply a larger vibration amplitude when a higher leg pressure is selected. As such, vibration amplitude and leg pressure will increase in a linear fashion as patients progress in this study.

The footplate is force driven with a robotic loading mechanism that supplies between 5 and 100 lbs of force to the user's legs depending on the ability level of the participant. This force is increased as tolerated by the user. Clinical use of the equipment has shown that an initial force on the order of 40 lbs is appropriate for most nursing home therapy patients, while specific conditions may warrant a lower starting force (e.g., 25 lbs has worked well as a starting load for knee replacement patients according to therapy staff using the equipment). The therapist carefully monitors patient progress and increases the force in 5 lbs increments over the course of treatment as the patient progresses. The same approach will be used in this study by our training supervisors.

The footplate moves slowly, taking between 20 and 30 seconds to complete one leg press depending on the range of motion of the participant. This encourages the participant to apply slow and controlled pressure while vibrations are transmitted through the major muscle groups of the legs (quads and hamstrings) while the muscles traverse throughout their physiological range of motion (0-90 degree knee flexion). If a participant wishes to take a break, they are allowed to hold their legs in a fixed position while the load is maintained. If a participant becomes fatigued during treatment, the therapist will stop treatment and record the length of the session endured. Treatment sessions are prescribed to be 10-minutes in duration, and will be applied as often as deemed fit by the therapy staff (the target is 3x per week).

The VibeTech One Rehab Chair allows vibration exercise while being semi-recumbent. This is a major advantage for older adults with co-morbidities as fear of falling, fatigue, chronic pain or cardio/respiratory disease in older adults thus preventing them from standing vibration exercise. The VibeTech One Rehab Chair is configured to allow users to receive vibration training to their legs while seated, removing concerns of balance and fear of falling and does not require substantial cardio/respiratory effort. The applied load simulates the weight of standing (or partial bodyweight) by applying a force on a footplate, while restraining movement of the knees and back. This design requires no effort from the user, which makes it accessible to people who are too weak or otherwise unable to use standing vibrating platforms or participate in traditional exercise. Participants will be asked to train for 10 minutes 3 days per week. In the "loading + vibration group" (intervention group) vibratory acceleration will be 30Hz and the applied load will be 50% of body weight up to a device maximum applied load of 100 lbs. Vibration intensity will initially be set to 0.2 g and will increase by 0.2 g every other week, as tolerated by the participant, and max out at 1.0 g. In the "loading only" group (control group) participants will be seating in the vibration device and will experience loading of their leg muscles through the device. Participants will be screened

for discomfort during every treatment. If an increase in vibration intensity causes any discomfort, that participant will maintain the same vibration exercise dosing as the prior 2 weeks.

During training sessions participants will be able to stop exercising whenever they chose to. They will be encouraged to continue their training session after a short break to finish 10 minutes of exercise, but if they decline the session will be ended. The participant will be asked why they stopped and these comments will be recorded. After that an appointment for the next session will be offered.

SPPB

The short physical performance battery (SPPB) consists of gait speed as determined by a four meter walk, timed repeated chair rise and standing balance. Gait speed will be measured by instructing participants to walk four meters at their normal pace; they are timed with a stopwatch. This test will be repeated twice. The walk performed in the least time will be utilized for SPPB scoring purposes. The timed repeated chair rise has participants stand up from a chair five times without the use of their arms, if possible. Specifically, participants are seated on a firm seat at knee level with their arms crossed over the chest and are asked to stand up from and sit back down five times as quickly as possible. Time to complete five stands is measured. Standing balance is assessed by having the participants stand in three positions of increasing difficulty for 10 seconds each. Standardized instructions will be given to all participants and the test performed twice. This initially consists of the feet being placed side by side, subsequently the heel of one foot is placed alongside of the big toe of the other foot and finally a tandem position is utilized with one foot directly in front of the other. In summary, the SPPB will be conducted and scored in standard manner. Participants will be wearing MobilityLab™ (APDM, Portland, OR) sensors on their chest, lower back, wrists and feet during these tests to collect computerized data (cadence, stride length, arm swing, sway, stance velocity) for these standardized tests.

Jumping Mechanography

Countermovement jumps are performed on a Leonardo force plate (Novotec Medical, Pforzheim, Germany) following standard procedures. Standardized instructions will be given to all participants. Jumping mechanography uses maximal countermovement jumps to quantitatively measure muscle strength in the legs. Participants will be asked to perform three countermovement jumps. Participants are asked to try to jump as high as possible using both legs, attempting to touch the ceiling with their head. Three jumps are performed; the jump with the highest jump height is used for analysis. The software computes instantaneous power by multiplying force and velocity. Vertical velocity is calculated by integrating acceleration over time and jump height by integrating vertical velocity over time. The acceleration is the result of dividing measured force and the participants body weight. To assure participant safety, two staff will be present during performance of all jumps to increase security.

Grip Strength

Grip Strength will be acquired using a JAMAR hand dynamometer in the routine clinical manner. Measurements will be recorded using participants' non-dominant hand and repeating the test 3 times.

Timed-Up-and-Go test

The Timed-Up-and-Go (TUG) test will be performed twice; participants will be seated in an armless chair, upon instruction, they will be asked to stand, which starts the timing, they will walk 3 meters past a mark on the floor at their normal pace, turn around and return to a full seated position, at which time the test will end. Participants will be wearing MobilityLab™ (APDM, Portland, OR) sensors on their chest, lower back, wrists and feet during this test to collect additional computerized data such as peak velocity, cadence, stride length, turn time, number of steps during turn etc. for this standardized test.

Bioelectrical Impedance Spectroscopy

An ImpediMed SFB7 device (Eight Mile Plains, Queensland, Australia) will be used to obtain these measurements. Participants will be positioned supine for a minimum of 10 minutes prior to acquisition; adequate separation of their legs will be obtained to allow for accurate BIS measurement. Measurements will be obtained by placing four EKG-like electrodes on the skin of the participant's hand, feet and knee. Wires will be attached from the BIS device to these skin electrodes. Painless electric waves will be sent through the tissues as noted above. Each measurement lasts only a few seconds. This method will generate measurements of whole body, leg and lower leg lean mass.

Study Duration

We estimate that a minimum of eight volunteers will be enrolled every 8 weeks. Assuming some lead-time for start up, IRB approval, etc., we project that the study recruitment and conduct will require 2 years.

Analytical Considerations and Data and Statistical Analysis

Overview of Data Management

All data will be entered into an Excel spreadsheet; data that cannot be electronically exported will have duplicate data entry performed to validate accuracy. This database will reside on the UW Osteoporosis Clinical Research server located at 2870 University Ave. All OCRC computers are password protected the UW OCRP private LAN is connected to the campus fully redundant Ethernet backbone network. The backbone spans three super nodes, 12 nodes and approximately 180 radial buildings. Communication speeds are 10 Gbps between super nodes and a minimum of 1 Gbps between nodes. Devices connected to the UW OCRP LAN, are protected by a Cisco Pix Firewall appliance at the building level as well as, personal firewall software on each desktop and server computer. The computer systems on the UW OCRP network, have a remote back up performed daily, with off-site media storage for data security. Additionally, BIS results will be shared with Dr. Yosuke Yamada with the National Institute of Health and Nutrition in Tokyo, Japan. Dr. Yamada will receive electronic files UW e-mail or FTP.

Multisite Conduct Plan

The UW-Madison will be serving as the lead site and the data coordinating center, as Dr. Buehring is the primary investigator and has secured funding for the project. In this capacity, Dr. Buehring and the UW Osteoporosis Clinical Research Program study staff will be in regular communication with study staff at Jewish Home and Care Center (JHCC). This will be either through conference calls, site visits or correspondence initiated by JHCC staff, and will include information regarding changes in protocol and general study conduct.

The OCRP staff will manage all regulatory activities, data cleaning/ housing and will conduct the functional assessment visits described in this protocol. The primary JHCC coordinator will be responsible for all aspects of study conduct to include recruitment, consent, scheduling exercise sessions and coordinating testing visits with the OCRP. Informed consent will be obtained per OCRP SOP and determination of ability to consent will be assessed by the person obtaining consent based on their interaction with a subject. This person will also be in close contact with Dr. Buehring to ensure appropriate conduct of this trial. All subjects will be recruited at the JHCC through newsletters, flyers and community talks.

Staff at the JHCC will register adverse events and report directly to Dr. Buehring for causality assessment. All serious adverse events will be reported to OCRP staff by telephone within 24 hours for JHCC staff learning of the event. Monitoring of data collection, adverse event reporting and protocol/regulatory compliance will occur by OCRP staff in conjunction with functional testing visits.

Data and source documents will be stored at the UW in locked cabinets and on password protected computers only accessible by OCRP staff. Similarly, JHCC staff will securely store source documents in an area limited to research staff. Consequently, UW and JHCC staff will have access to non-anonymized data, however, stored master data files will be coded with ID numbers, initials and birthdates.

The protocol will only be amended by Dr. Buehring. When approval is obtained by UW HS-IRB, updated protocols and consent forms will be provided to study staff at JHCC and changes will be discussed via conference call or live meeting prior to initiation.

Data Management

The information collected from the participants will be handled confidentially to the extent provided by the law. The participants' information will be assigned a code number and identified by their initials. The list connecting their name to these identifiers will be kept in a locked file. Only researchers directly involved with the project will have access to the list. Participant names will not be used in any report. At the conclusion of the study, participants will be asked if they would like to have their treatment charts transferred to their designated medical professional. Data transferred to designated medical professionals will be handled confidentially to the extent provided by the law.

Data generated for this study will be managed by Dr. Buehring's staff. UW data managers will enter data 100% twice, independent of the initial entry, preferably by a different individual. Should it be necessary to have the same individual enter data, at least seven days will transpire between entry cycles. Any discrepancy between entries will be verified and corrected.

Statistical Analysis

ICTR biostatisticians will do the randomization and subsequent data analysis of the primary and exploratory aims, in concert with the study investigators and consultants. Repeated measures ANOVA will be used to test the primary hypothesis. Descriptive analyses and correlation analyses and regression models will be used to test the exploratory aim.

Power Analysis

Sample size estimation was conducted based on the primary outcome variable of weight corrected jump power. To detect a 10% difference in maximum jump power between control and intervention groups, 26 subjects are needed per group (alpha=0.05; 80% power; 2-sided) assuming a standard deviation of 2.6 and control group mean of 21 W/kg. These values are based on data previously collected by our group involving 81 older adults. Accounting for up to 20% subject withdrawal brings the required enrollment to 32 subjects per group (64 total). Due to budgetary constraints we are proposing a simple AB/BA crossover design (i.e. participants treated with the intervention also serve as the control group, and a washout period is provided to ensure that no training effects exist between the treatment and control periods) to reduce the number of needed participants to 32 patients."

Adverse Experience Reporting

All study participants will be questioned regarding adverse experiences at the conclusion of both the screening and subsequent follow up visits and will be asked to call and report significant events in the interim. Adverse events, including Serious Adverse Events, will be reported to the lead study site. The PI will evaluate all adverse events and determine relationship to study activities. SAE reports will be shared with the IRB according to the applicable reporting requirements and timeframes.

Safety

The risks of study participation are low.

Potential Risks

Assessment: Over the last years we have conducted several studies using the muscle function tests included in this study. Participants who volunteered were often frail and up to 96 years old. We have not had any reports of increased pain or caused any injuries with the testing. We feel this is because we have many safety mechanisms in place that prevent adverse events. The risk of falling during SPPB assessments will be minimized by having the tester standing or walking next to the subject on each test. Similarly, given our and other's data documenting safety of jumping mechanography in older adults the risks are similar to those for SPPB and include losing balance, falling or trauma that could lead to musculoskeletal injuries such as sprains and fractures. These risks will be minimized by familiarizing and instructing each volunteer on the correct method to perform the jumps and practicing submaximal jumps before performing the maximal jumps. Additionally, two trained staff members will stand next to the jumping individual to assist in the case of loss of balance. Individuals will wear a physical therapy belt to enhance security. The only potential adverse effect may be slight muscle fatigue associated with the repetitive chair rise tests. This discomfort is not expected to last more than a few minutes. The Bio-Impedance analysis requires EKG electrodes to be placed on the skin to measure fat and muscle mass in the body. This could lead to skin irritation at the site of the electrodes if participants have an adhesive intolerance there could be skin irritation. Participants will be asked if they had adverse reaction to EKG electrodes in the past before the BIS is performed. If so they test will not be done.

Treatment: As mentioned above the vibration parameters selected for this study are within the range of values used for a number of vibration therapy studies performed on older adult subjects that reported no adverse events, thus no major risks are anticipated. Furthermore, the maximum magnitude of acceleration due to vibration applied to participants (1 g) and the duration of application is within the guidelines for vibration exposure recommended by ISO2631-1, an international standard used to govern human exposure to vibration. Vibration therapy may result in onset of muscle soreness that can be delayed for up to 4 days following the treatment as would be expected of other protocols involving physical activity. The risk involved with the VibeTech One intervention is no greater than performing squats on a squat machine. The seated position minimizes fall risk during treatment. Participants will be screened for discomfort during every treatment. If an increase in vibration intensity causes any discomfort, that participant will maintain the same vibration exercise dosing as the prior 2 weeks.
During training sessions participants will be able to stop exercising whenever they chose to. They will be

encouraged to continue their training session after a short break to finish 10 minutes of exercise, but if they decline the session will be ended. During treatment, the treatment supervisor will assist the participant in and out of the VibeTech One as needed and will operate the device. The treatment supervisor will remain in close proximity to the participant throughout the duration of treatment and can stop the treatment at any time if necessary. The participant and treatment supervisor will have access to an emergency stop button that will stop vibration delivery and remove load from the patient's legs within 1 second of pressing the emergency stop button.
Psychological Risks: Risk of psychological harm from study participation is low. We do not propose to collect sensitive information or to ask questions anticipated to cause distress. The questionnaires used in this study are all validated in older adults and have been safely used previously. Some participants could perceive filling out the questionnaires as burdensome. However, each tool is brief and most questions are not complex or abstract. The estimated time to complete all questionnaires will only be 20-25 minutes per visit. Additionally, two strategies will be used to reduce burden: 1) Staff will administer the tools by interview; and 2) after 10 minutes the person will be asked if they are fatigued and want to finish the questionnaires after a one-hour break or on another day. Participants will be asked to provide a medical history, the discussion of which could potentially result in psychological anxiety. As this is a research study, all volunteers reserve the right to decline participation in any aspect of the study for any reason. We expect subjects to exercise this right should we broach issues of a personally sensitive nature.

Financial, Legal and Other Risks: No financial legal or other risks are anticipated due to participation in this study. An additional potential risk of study participation is breach of confidentiality. To minimize this risk, all data will be coded by subject initials and ID numbers, thereby assuring confidentiality. Moreover, all information collected in this research study will be stored on password-protected computers or in locked cabinets at the University of Wisconsin-Madison Osteoporosis Clinical Research Program.

Any injuries or caused distress will be treated in the customary manner and the subjects referred to appropriate medical personnel as appropriate. Additionally, volunteers with clinically significant abnormalities will be called by Dr. Buehring to discuss the clinical relevance of their results.