DOCUMENTATION

for

MUSCULOSKELETAL HEALTH and FUNCTION DATA

in

MIDUS REFRESHER BIOMARKER PROJECT (P4)

University of Wisconsin ♦ Institute on Aging
March 2018

INTRODUCTION

This document provides an overview of the musculoskeletal health and function data collected in the MIDUS-Refresher (MR) Biomarker Project (P4) data. This document describes the measures obtained and also provides comprehensive information regarding methods used to collect the data. Administrative and computed variables are also identified and information about the construction and usage of these variables is included.

Data users are also encouraged to review the Biomarker (P4) Readme Data File Notes. This document provides information about naming conventions, as well as administrative and filter variables included in the data file. It also includes information about how we handled missing values and other issues that arose over the course of the study. For example, there are instances when variables were added or sections of an instrument were expanded for data entry purposes to accommodate additional information provided by the respondent.

This document will be periodically revised and updated as more information is gathered, and researchers continue to work with the MIDUS Biomarker data. If there are suggestions or comments, please contact midus_help@aging.wisc.edu.

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SECTION A

OVERVIEW OF DATA FILE AND COLLECTION PROTOCOLS

OVERVIEW OF DATA FILE AND COLLECTION PROTOCOLS

The Biomarker Project (P4) includes multiple types of data regarding musculoskeletal health (from the indicated sources, some of which are new or expanded as follows:

- Bone Turnover measures from serum.
- Questionnaire Data
- Dual Energy X-ray Absorptiometry (DXA) Scans (EXPANDED)
- Bioelectrical Impedance Spectroscopy (NEW)
- Bioelectrical Impedance via BodyComp Scale (NEW)
- Muscle Function Assessments (Jump Mechanography/Balance) (NEW)

As described in the "MIDUS Refresher Biomarker Project (P4) Readme Data File Notes" the MIDUS naming convention organizes variables according to data type or the method used for data collection. We have followed this convention with respect to the musculoskeletal health data, thus analysts using bone turnover, DXA, impedance, and questionnaire data will need to pull variables from different sections of the data file. Details about these data appear below.

Questionnaire and blood assay data are obtained at all three sites as described below. Due to funding limitations, the DXA scans and muscle function assessments are only obtained at the University of Wisconsin (UW) and bioelectrical impedance is assessed via different methods at the UW and UCLA sites. The following text provides details about the development of the overall bone/musculoskeletal health protocol, as well as additional details about the measures.

Data Documentation

Bone Turnover:
The bone turnover assays use samples that are processed through the Biocore. Thus, these data can be found with the other blood assay result data. Details about the blood collection and processing protocols can be found in the "Documentation for Blood, Urine and Saliva Data."

Following the MIDUS variable naming convention, the first four characters of these variables are "RA4B."

Questionnaire Data:
At MIDUS 2 a standalone bone questionnaire was developed and administered by project staff during the clinic visit. For the MIDUS Refresher the items from the Bone Questionnaire were integrated into the Medical History Interview administered during the visit. See the Study Summary for information about how those items were integrated and other information about the interview. Since these items are now in the Medical History the variable names begin with the unique 4 character set "RA4H" used for that instrument.

Densitometry Scans:
DXA scans are performed using the GE Dual Energy X-Ray system (iDXA). Historically we used DXA to provide bone density assessments. However given the escalation of obesity in the population, we elected to also collect whole body scans to measure 3 compartment total body composition (bone, fat and lean), thus these data are included. Additionally, to better characterize skeletal status, lateral vertebral fracture assessment (VFA) scans have been added to complement self-report of clinical fracture. VFA data are reported as evidence of moderate or severe vertebral fracture, with number of effected vertebrae based on clinical interpretation of the scans.

Bone density scan data is only collected at UW for the MIDUS Refresher. The DXA scan protocol appears in Section B below.

The DXA variables appear in the data file immediately following the Medical History Interview data. The variable names begin with “RA4D” and include the following measures:

1. Bone Density:
    a. Spine - Bone mineral density (BMD) for L1-L4, T-score for L1-L4
    b. Femur (one side only) – BMD and T-score for the Femur Neck and Total Femur
        Note: BMD data from both hips is available for most of the subjects from UW. In those instances the lowest value was selected for inclusion in this dataset.
    c. Forearm – BMD for the 1/3 radius, T-score for 1/3 radius

2. Vertebral Fracture: based on review of lateral spine scan, approximately L5-T4, by trained clinician
    a. Moderate or severe vertebral fracture observed?
    b. If yes, how many fractures?

3. Body Composition – measures of bone, fat, and lean mass in grams for:
    a. Arms – right, left, both
    b. Legs – right, left, both
    c. Trunk – right, left, both
    d. Total – right, left, both
    e. Android
    f. Gynoid

The data set also includes the following more administrative variables:

- RA4DAVAIL – categorical variable indicating whether there are Bone Mineral Density data available for a given case.
- RA4DSTYPE -The scanner system (Lunar, Hologic) used to collect the data
- Region specific variables indicating the side (left or right) scanned for the individual femur areas and the radius.
    - RA4DFNSID - Femur Neck side scanned, 1=Right, 2 = Left
    - RA4DFTSID - Femur Total side scanned, 1=Right, 2 = Left
    - RA4DRSIDE - Radius side scanned, 1=Right, 2 = Left

- RA4DTBAVAIL – categorical variable indicating whether there are Body Composition data for a given case

<u>Bioelectrical Impedance Assessments (NEW):</u>
As noted above, the increase in obesity in the population and increasing interest in sarcopenia, prompted interest in total body composition assessment. DXA was selected, as it is a well-accepted method to assess body composition and is included in most consensus sarcopenia definitions, however, it is not without limitation. Specifically, DXA measured lean mass is largely a measurement of water, not true muscle mass. Although this is commonly used as a surrogate of muscle mass, it is truly a measure of the compartment not comprised of fat or bone mass, therefore DXA-lean mass provides an overestimation of muscle mass. Consequently, we sought to add an additional measurement that potentially may better assess muscle mass.

Single frequency bioelectrical impedance analysis (BIA) is often assessed in large national research studies, such as MESA (Multi-Ethnic Study of Atherosclerosis) using body comp scales. However, this single frequency measurement has a similar limitation to DXA, in that it does not differentiate muscle from lean mass. A multi-frequency approach, in the form of bioelectrical impedance spectroscopy (BIS) likely offers a better surrogate. In this approach, high frequency current travels through the fluid inside and surrounding the cell, taking a measurement of all fluid. The low frequency currents travel in the fluid surrounding the cells, generating a measure of

extracellular fluid (ECF). Therefore, this technology allows for assessment of both ICF (intercellular fluid) and ECF.

The equipment and software for obtaining BIS data was available at the UW site, a BodyComp scale was available at UCLA. Thus both methods of measuring bioelectrical impedance were added to the Biomarker protocol at these sites, respectively, several months after data collection began. Details about these two bioelectrical impedance measurement procedures are provided below.

The BIS variables appear in the data file immediately following the DXA data, the BIA variables immediately follow the BIS variables. All the bioelectrical impedance variable names begin with "RA4I" regardless of method. In addition to the bioelectrical impedance variables described below the data file also includes the following flag/filter variables:

- RA4IELIG – categorical variable indicating whether a given case is eligible for the body impedance assessment, including reasons for not eligible (i.e. pacemaker, etc.).
- RA4IBISAVAIL – categorical variable indicating whether there is BIS data available for a given case
    - This variable will be INAPP for all Georgetown and UCLA participants as well as UW participants who completed the study visit before BIS was added to the protocol.
- RA4IBIAVAIL – categorical variable indicating whether there is BI data available for a given case
    - This variable will be INAPP for all Georgetown and UW participants, as well as the UCLA participants who completed the study visit before BIA was added to the protocol.

Bioelectrical Impedance Spectroscopy (NEW):
Bioelectrical Impedance Spectroscopy (BIS) is performed using the ImpediMed SFB7 (Eight Mile Plains, QLD, Australia). This data was collected only at UW and was added to the Biomarker protocol at that Refresher. Two measurements were acquired for each site (total body and left leg). The reported data is a mean of these measurements. When one of these measurements was excluded due to technical inadequacy, only the technically valid measurement was used. For segmental measurement of the left leg, leg length was measured from the most lateral point on the greater trochanter to the most distal tip of the tibia from the whole body DXA images using the ruler tool.

The BIS acquisition protocol appears in Section B below.

The BIS variables appear in the data file immediately following the DXA bone density and body composition data. The variable names begin with "RA4I" and include the following measures:

1. Whole Body Measurements:
    a. Software generated fat free mass (FFM)
    b. Percent fat free mass (FFM/total body mass)
    c. Instrument measured extracellular fluid (ECF)
    d. Instrument measured intracellular fluid (ICF)
    e. Calculated percent intracellular fluid (ICF/ICF+ECF)
    f. Calculated total body water (ICF+ECF)
    g. Calculated ICF proportion of weight (ICF/total body mass)

2. Left Leg Measurements: For purposes of these equations, ECF = instrument measured extra cellular resistance (Re) and ICF = instrument measured intracellular resistance (Ri).
    a. Extracellular fluid index (leg length^2/ ECF)

b. Intracellular fluid index (leg length^2/ICF)

Bioelectrical Impedance via BodyComp Scale (NEW):
Bioelectrical impedance (BIA) was assessed using the Body Comp Scale manufactured by Valhalla Scientific. This data was collected only at UCLA and was added to the Biomarker protocol at the Refresher. In contrast to BIA scales that might be found in health clubs, this scale is more standardized and has been employed by other large national research studies. Participants stand on the BodyComp scale (which looks like a weight scale) without shoes or socks and grip two metal handles, so that a safe, small, unnoticeable electrical current can pass through the body. The algorithms used by the BodyComp Scale calculations are proprietary according to the manufacturer Valhalla Scientific (http://www.bodycompscale.com/faqs/, section titled "What is Bioelectrical Impedance Body Composition Analysis and Ohms Modulation Logic?"). The results of the BIA are printed and the values subsequently entered in the study database. Note that if height or age are entered incorrectly, the subsequent BIA measures will not be correct and are flagged in the data.

The report produced by the device calculates the following:

- Current body weight (in 2 different units: pounds and kilograms)
- Total body fat (in 3 different units: pounds, kilograms, and percent of body weight)
- Fat-free mass (in 3 different units: pounds, kilograms, and percent of body weight)
- Total water (in 2 different units: liters and percent of body weight)
- Body mass index (BMI; kg/m^2)
- Target weight range (minimum)
- Target weight range (maximum)
- Resting Energy Expenditure (REE, calories/day)

All of these measurements are included in the data file, as different investigators may have preferences for which forms of the analysis variables they want to use. In particular, target weights and REE are proprietary calculations provided by the algorithms and are included here for completeness, although it is rare that these would be used in analyses. In addition, Investigators may choose to calculate other indices, such as muscle mass. Therefore, the ohms (RA4IOHMS) measured during the procedure (the values resulting from the electrical current that passes through the body) are also included in the file to support such calculations.

In addition, the manufacturer advises that BIA measurements be completed when the participant is fasting. Research staff collected information about the time and date the participant last ate (reported as number of hours since the participant last ate – RA4I7B) as well as what was eaten. This information is included for researchers who may want to use it in analysis, although this is not common. A copy of the tracking form with variable names added is included below with the BIA protocol. Note, responses to the eligibility questions (Q4-6) are incorporated into the filter variable RA4IELIG (see above).

<u>Muscle Function (NEW):</u>
Muscle power and function is assessed via two tasks (jump, balance) performed on a force plate and assessed via the Leonardo mechanography software. These tasks were added to the protocol about 6 months after data collection began.

1. Jump assessment: participants complete three trials in which they jump as high as possible using both legs and attempt to reach the ceiling. The software generates the following measures:
    a. For each trial
        i. Measured Jump Height (meters)

ii. Raw Jump Power (watts)
iii. Relative Jump Power – raw jump power corrected for body weight as measured by the mechanography software (Watts/kg)

b. Summary Measures (for use in analysis)
i. Maximum Height selected from the 3 trials
ii. Raw jump power associated with the selected maximum height
iii. Relative jump power associated with the selected maximum height

2. Balance Assessment: participants complete two sets of trials. Subjects stand with feet about a shoulder's width apart, the first trial is completed with eyes open and the second with eyes closed. The amount of sway and the relative path are assessed for each condition to provide the following variables:
   a. For each condition (eyes open or closed) and trial
      i. Relative path length
      ii. Standard ellipse area
   b. Summary Measures (for use in analysis)
      i. Average path length (2 trials)
      ii. Average ellipse area (2 trials)

The jump and balance protocols appear in Section B below. The muscle function variables appear in the data file immediately following the body impedance variables described above. The variable names begin with "RA4D".

Some individuals are able to perform the balance tasks, but not the jump tasks due to an injury or some other physical problem. Thus, this section of the data begins with the categorical variable RA4DJBAVAIL which indicates whether jump and/or balance are available.

- This variable will be INAPP for all Georgetown and UCLUA participants, as well as the UW participants who completed the study visit before jump/balance was added to the protocol.

Analysis Notes:

For users who combine MIDUS Refresher with MIDUS 2 data please note, the following site specific idiosyncrasies.

1. The University of Wisconsin (UW, Site 2) is the central coordinating site and is responsible for all QC tasks.

2. At MIDUS 2 UW had been collecting bone densitometry data for the lumbar spine (L1-L4, both hips, and the non-dominant forearm) for several months when funding became available at the other two sites. To accommodate differences among the three sites the protocol described in the manual includes just scans of the *lumbar spine* (L1-L4) and *left femur*. All 3 sites follow the protocol in the manual for these 2 scan sites. To maintain consistency locally, however, the protocol already in use at Site 2 (UW) continues to include the right femur and the non-dominant forearm.

3. Sites 1 (UCLA) and 3 (Georgetown) use the Hologic system, while Site 2 uses the GE Healthcare Lunar system. Due to significant known differences in BMD as measured by the two systems we created two sets of mutually exclusive variables, one for Hologic data and one for Lunar data. Thus, UW cases only have Lunar data, while UCLA and Georgetown cases only have Hologic data.

IMPORTANT: The BMD values from Lunar and Hologic systems are not directly comparable, as they generate different values (grams/cm^2) for the same amount of bone, but there is good

agreement between the T-scores generated by these systems. Thus, it is recommended BMD values from the two systems not be combined as a variable, but instead that T-scores be used in analyses involving the full set of bone scan data. For more information see the following citations.

Hanson, J. (1997). "Letter to the Editor Standardization of femur BMD." Journal of Bone and Mineral Research 8:1316-1317.

Kiebzak, G., E. M. Lewiecki et al. (2004). "Good diagnostic agreement using T-scores between Delphi and Prodigy." Journal of Clinical Densitometry 7:229.

Kiebzak, G.M, N. Binkley et al (2007). "Diagnostic agreement at the total hip using different DXA systems and the NHANES III data base." Journal of Clinical Densitometry 10:132-137.

For data analysts interested in using *just* proximal femur data the following citation provides equations for converting Lunar data to Hologic for *women*.

Lu, Y., T. Fuerst, et al (2001). "Standardization of bone mineral density at femoral neck, trochanter and Ward's triangle." Osteoporosis International 12:438-444.

For body composition data, conversion equations are available for BMC, BMD and percent fat in the citation below.

Shepherd J, Fan B et al (2012). "A multinational study to develop universal standardization of whole-body bone density and composition using GE Healthcare Lunar and Hologic DXA systems."

SECTION B

DUAL ENERGY X-RAY ABSORPTIOMETRY (DXA) SCAN PROTOCOL

BIOELECTRICAL IMPEDANCE PROTOCOLS:

1. SPECTROSCOPY (UW)
2. BODY COMP SCALE (UCLA)

BALANCE & JUMP PROTOCOL

DXA PROCEDURES

MIDUS REFRESHER
BIOMARKER
(PROJECT 4)

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CONTACT INFORMATION

DXA/IQC Related Issues:

1. _____

2. _____

3. _____

Study Specific Protocol Issues:

DXA OPERATOR'S SIGN-OFF

This is to insure that all DXA technologist read and fully understand what will be expected from their site for the DXA procedures portion of the MIDUS study. The material in this manual should be read and understood prior to scanning the first subject. All DXA technologists directly involved with the study must sign and date this form to acknowledge and confirm understanding of DXA requirements for the MIDUS biomarkers supplement study.

Please fax a copy of this form to designated staff. The original is to be kept with the study DXA binder at the site.

DXA Technologist (s):

Printed Name and Date (First and Last)	Signature	Initials

INTRODUCTION TO QUALITY ASSURANCE

The purpose of this manual is to standardize DXA scanning procedures among clinical centers participating in the MIDUS study. Bone mineral density and body composition parameters are an important endpoint in this study. As such, excellence in obtaining these data are critical. Success will depend on several factors, including qualifications and dedication of the DXA technologists, clear understanding of the study requirements and good communication between the clinical sites, study investigators and UW Osteoporosis Research DXA QA Center.

Site Responsibilities

- Monitor DXA scanner performance throughout the study duration.
  1. Daily QA
  2. Phantom QA
  3. Notify UW DXA center of all hardware problems or replacements
  4. Notify UW DXA center of all software problems or upgrades

- Ensure that BMD measurements are skillfully and consistently acquired for each subject, following the procedures in the Manufacturer's Operator's manual and this manual.
  1. Subject demographic entry
  2. Subject BMD scan modes
  3. Subject BMD positioning and acquisition
  4. Subject BMD data back-up and archived

- Data transmission to the UW Osteoporosis Research DXA QA Center
  1. Subject BMD scans
  2. Instrument Quality Control data

UW Osteoporosis Research DXA QA Center

- Monitor the performance of all densitometers used for acquisition of BMD data in this study and provide a summary of scanner performance at the study conclusion
  1. Collect all QA data from study sites
  2. Analyze, maintain and validate QA data
  3. Assure that sites submit all QA and study participant data in a timely manner

- Assure consistent acquisition and analysis of subject scans among individual densitometry sites
  1. Analyze and retain all images for every subject
  2. Retain DXA data in an orderly fashion for the duration of the study

- Assure that study sites have proper supplies needed for DXA data transmission
  1. Study specific DXA forms

CROSS CALIBRATION

The purpose of cross calibration is to ensure that bone mineral density (BMD) measurements at different clinical study sites may be compared. Your site cannot start scanning subjects until cross calibration has been completed. Your site will be contacted as to when you may start scanning subjects.

You will receive a BoneFide® encapsulated phantom before the study begins. You will be contacted to determine a time that this phantom will arrive at your site; please have the cross calibration done in a timely manner. Each site will scan the phantom ten times on the same day without repositioning. A courier service will be used to deliver and forward the phantom to the next study site after cross-calibration scan completion. You will need to send media with the electronic copies and the cross calibration form to the UW DXA Center when completed.

INSTRUCTIONS FOR CROSS CALIBRATION

Patient Biography

The first patient in the new database for this study will be the cross calibration phantom. Please create the patient biography in a new database if possible for the GE Lunar phantom as follows:

MANDATORY INFORMATION
LAST NAME: Cross-Calibration Phantom
FIRST NAME: MIDUS
MIDDLE INITIAL: Leave blank
ETHNICITY: White
SEX: F
BIRTHDATE: 11/11/1951
PATIENT ID: Leave blank
IDENTIFIER 2: Site location (e.g.: UW, UCLA, Georgetown)
REFERRING PHYSICIAN: Leave blank
MENOPAUSE AGE: Leave blank
WEIGHT: 130 lbs or 60 kg
HEIGHT: 65 inches or 164 cm
PATIENT COMMENT: Cross Calibration / Technologist initials

Scan Acquisition

Please set the parameters to the default mode and use array, if applicable.

Position the phantom on the scanner pad after the machine's scan arm has moved to the approximate start position. Position the phantom so that the laser light is on the start position indicated on the phantom. **DO NOT move the laser light, move the phantom to the laser light.** Make sure that the phantom is parallel to the scanner's long axis with the starting mark pointing toward the foot end of the table. The phantom should be approximately in the center of the scanner table.

Begin scanning the phantom. The phantom image should appear in the first 6-10 lines or 1 swipe of the scan. If no phantom image appears in the first 10 lines or the 2 swipes, stop the scan. Reposition the phantom and restart the scan.

Please allow the scan to finish on its own, do not stop it prematurely.

Scan the phantom nine more times. The starting point for subsequent scans will be correct as long as the operator does not move the scanner arm or the phantom between scans.

Scan Analysis

Please use "Auto Analysis" to analyze the spine phantoms. **DO NOT alter bone edges or baselines.** Analyze the L1-L4 region. Do not accept the default analysis. Use the scan image and the histogram to place the intervertebral marker defining L1-L4. Use the compare function to analyze the remaining nine scans, using the first scan as the reference.

DXA SCANNER PERFORMANCE

DAILY QA

Quality assurance should be done at least three times per week and on all days that patients are scheduled to insure stable scanner performance. QA must be done before study patients are scanned.

If the QA does not pass on the first try, please repeat. Make sure that the QA block is positioned correctly. If QA fails twice, please refer to your manufacturer's manual for instructions. DO NOT scan study participants; if QA fails reschedule or cancel the appointment.

PHANTOM QA

Phantom QA should be done at least three times per week using your site's phantom, and on all days that study patients are scheduled. When analyzing phantom scans please use the copy/compare function.

If a phantom baseline is not established at your site, please scan your phantom a total of 25 times in two or more days (e.g. 13/12 scans on two days, 8/8/7 scans on three days or five scans on five days) to establish a baseline. Please follow the instructions below to calculate the mean and 1.5% acceptable range.

Calculating the Phantom Baseline BMD

- Record the results of the 25 phantom scans onto the QA phantom form.
- Add the total of *L1-L4 BMD* values from the 25 baseline phantom scans to determine the sum.
- Divide the sum by 25 to determine the BMD mean.
- Record the mean. The BMD mean will not change unless you recalculate the baseline for your densitometer.
- Determine the acceptable range. This range should be ± 1.5% of the BMD mean.
- Mean = the sum of 25 phantom scans divided by 25.
  +1.5% = mean + (.015 x mean)
  -1.5% = mean - (.015 x mean)

The phantom BMD value should not differ from your mean by > 1.5%. If two consecutive values exceed this, it is recommended that you contact the manufacturer's service department.

HARDWARE PROBLEMS OR REPLACEMENTS

Please notify the UW DXA center by fax if there are any scanner hardware problems during the study and include a copy of the service reports. The UW DXA center must be notified when hardware changes are required. If possible, please scan your QA phantom 10 times before hardware changes are made and 10 times after replacement or service has been done. This is to determine if changes in machine calibration occur.

SOFTWARE PROBLEMS ORUPGRADES

Please notify the UW DXA center if there are any scanner software problems during the study. Ideally, no software upgrades should occur during the study. However, if software changes are scheduled to occur, please notify the UW QA center prior to making this change. Additionally, please scan the QA phantom 10 times before and after such changes are made. This is to determine changes in machine calibration.

ACQUIRING SUBJECT DXA SCANS

SUBJECTS

All premenopausal women will have a urine pregnancy test performed on the GCRC prior to DXA scan performance

Eligible respondents will be given a Whole Body Scan in addition to the standard spine and femur scans. The screening questionnaire will be administered by project staff before the participant arrives for the bone scan. The technician should review the screening questions with the respondents to confirm eligibility prior to beginning the scan.

SUBJECT DEMOGRAPHIC ENTRY

Subject ID numbers will be assigned by your local site study coordinator. Please fill in the subjects demographic as follows:

Last Name: Subject Initials
First Name: MIDUS
Middle Initial: Leave Blank
Ethnicity: Fill in
Sex: Fill in
DOB: Fill in
Patient ID: (Subject ID – obtain from study coordinator)
Identifier 2: (Site location - e.g.: UW, UCLA, Georgetown)
Referring Physician: (Investigator's Name)
Menopause Age: Leave blank
Weight (kg): Fill in
Height (cm): Fill in
Patient Comment: (MIDUS Study)
(Technologist Initials)

SUBJECT BMD SCAN MODES

Subjects should be scanned in the same modes as routinely done at your site, unless the densitometer defaults or suggest that the scan be done in a specific mode.

SUBJECT POSITIONING AND SCAN ACQUISITION

General Guideline for Subject Scanning

- Describe the scanning procedures to the volunteer.
- Assure that recent GI contrast or nuclear medicine scans have not been done.
- Check to make sure that volunteer does not have any metal around the scanning area (e.g., zippers, belts, coins/keys in pockets, etc.).
- The volunteer should be positioned using the manufacturers positioning devices.
- Ask the volunteer to remain still for the scan duration.

SPINE SCAN PROCEDURES

For spine scans, please include at least half of L5 and T12 and assure that the lowest ribs are visible. All volunteers should be positioned as straight as possible, with a sponge positioner under subject's legs in a 90 degree angle and their hands to the side. The starting location should be approximately two fingers below patients navel, place the laser there. Reposition the volunteer and restart the scanner as necessary.

FEMUR SCAN PROCEDURES

For femur scans, the LEFT femur will be measured. Volunteer's shoes should be removed, the femoral shaft straight, hip optimally rotated using the positioner routinely used at the facility, such that only a small amount of the lesser trochanter is visualized. Palpate the greater trochanter, and align the laser with the knee and the pubis area (laser should be positioned on the individuals thigh at about 1.5 inches below the pubis). The scan should start about five cm below the lesser trochanter and the ischium should be seen within 20 scan lines or two swipes.

WHOLE BODY SCANPROCEDURES

On Hologic machines, choose the Whole Body of HP Whole Body mode (for obese participants) in the Scan Type list.

Positioning:

Lie the participant oh his/her back with the head at the right end of the table, looking up at the ceiling, arms at the sides with palms down, separated from the thighs, and feet pointing up. Move the table and C arm to the center. Check that

- the body is straight, using the center lines at the head and foot of the table as gauge
- the body (including feet) are within the scan limit border line
- arms are within the scan limit border

Rotate the participants' legs inward 25 degrees till toes touch, then BIND the feet USING A SOFT COTTON STRAP (EG, GAUZE BANDAGE) to maintain position.

Instruct the patient to lay still and breathe normally.

Scan Procedure:
Make sure that the entire body and both arms are in the scan field. If the person is taller than 6 feet, 6 inches, exclude the feet. If the person is wider than the scan width, exclude THE LEFT ARM COMPLETELY AND CAPTURE THE RIGHT ARM. BE SURE THERE IS AIR BETWEEN THE PPTS TRUNK AND THEIR ARMS. Make sure that the participant remains still until the last pass of the C arm.

VERTEBRAL FRACTURE ASSESSMENT SCAN PROCEDURES

Positioning:
Lie the participant on his/her left side with their head at the top of the table. Their back should be parallel to the edge of the scanner table, it is recommended to use the positioner provided with the instrument. Open the positioner so the side is locked perpendicular to the base, and place against the back of the table and behind the subjects. The participant should be instructed to press their back against the positioner. Subjects should then place their left arm through the dual femur positioner and their right elbow should rest on the top of the positioner. Finally, ask participants to bend their legs so their thighs are perpendicular to their torso and calves perpendicular to their thighs. Their lower back and hips should remain pressed against the VFA positioner and a foam wedge should be placed between their knees to level their right leg. Check that

- the body is straight and back is a parallel to the table as possible
- the hips and shoulders will clear the scanner arm (do not perform this exam if the arm will not move uninhibited)
- the right arm and leg are as level as possible

Instruct the patient to lay still and breathe normally.

Scan Procedure:
Make sure that the entire spine is in the scan field. Start the scan just below the sacrum. Allow the scanner to keep imaging either until the end of the scan field is reached, or the thoracic spine has been imaged. Make sure that the participant remains still until the last pass of the scanner arm.

DATA BACK UP AND ARCHIVING

If possible, please create a separate database for this study. Please backup and archive all study DXA scans daily.

ANALYSIS OF DXA SCANS

Please DO NOT send analyzed patient scans. All patient scans should be sent to the UW DXA center unanalyzed.

SUBJECT DXA SCANS

Subject DXA scans should be sent by FTP Secure FX

- Please ensure that all patient information is accurate
- Subject scans labeled by Hologic software with date and time sent, with an extension containing subject ID;
  - i.e. 0606061122-1456 (datetime-subID)
- Complete and properly filled out BMD Logsheet,
  - label 'Subj' your site scan date, i.e. 'Subj UC 042606.doc'
  - emailed to designated staff
  - Not to be included on FTP site

INSTRUMENT QUALITY CONTROL (IQC) DATA

IQC data should be sent monthly in a timely manner. The following should

be enclosed in each shipment:

- A complete QA spine phantom form
- DXA service record form (if applicable)
- DXA technologist information sheet if new technologist acquiring scans

BIOELECTRICAL IMPEDENCE: SPECTROSCOPY PROTOCOL

MIDUS REFRESHER BIOMARKER (PROJECT 4)

Bioelectrical Impedance Spectroscopy (BIS) Procedure

Preparation: Participants should:

- be supine for at least 10 minutes, consequently, this will be performed following the DXA scans (performed in the order of VFA, FA, LS, PF & TB)
- void bladder prior to performing procedure
- not be wearing or touching any metal
- report their last meal- when and what they last ate
- remove socks prior to DXA scans, right knee will need to be exposed for BIS
- not have the BIS test if they have a pacemaker
- be positioned so arms and legs are separated from the body- if necessary, use foam wedges

Procedure:

- Unplug the BIS equipment prior to performing procedure and connecting the leads
- Run the test cell on all days the equipment is used
- Turn power on
- Hit "Measure" on the screen
- The "Measurement Setup" screen will appear.
    - Touch "File Name" to bring up the edit box with a keypad. Label this with "Three Subject Initials" [space] "Subject ID #" [space] and which test is being performed ("TB" for total body, "LG" for leg and "LL" for lower leg measurement). If no filename is listed- the measurement data will NOT be saved.
    - Touch "Patient Details Edit." This is where the gender, height, weight, and age are updated. This is done by touching the arrow buttons located next to the detail (gender, height, weight, etc.) This can also be done manually by touching the box itself, and a keypad will appear.
- Clean the sites where electrodes will be placed with alcohol
- Apply the electrodes (Figs 1 - 2)
    - Left hand - Feel the protruding bones (distal ulnar styloid and radial tip) of the wrist, draw a line spanning straight across the wrist from the top of the protruding bones. Place the first electrode so that the edge of the electrode rests on, and is placed distal to, that line. Place the second electrode edge proximal to the knuckle aligned with the index and middle fingers, no less than 5 cm from the first lead.
    - Left foot - Feel the protruding ankle bones (malleolus bones) and draw a line spanning from level with the protruding bones, across the ankle. Place the first electrode so that the edge of the electrode rests on, and is

placed distal to, that line. Place the second electrode edge proximal to the base of the toes aligned with the second and third toes, no less than 5 cm from the first lead.
    - Right foot - Place one electrode so that the bottom edge is edge proximal to the base of the toes aligned with the second and third toes. There is no second electrode on the right foot.
    - Left knee – One electrode is placed on left side of the body on the articular cleft between the femoral and tibial condyles. The placement can be found when the participants bent the left knee fully. A wrinkle is made on the lateral side of knee when the participants bent the left knee fully. Place one electrode on the wrinkle.
- Attach the leads - Attach an alligator clip to each of the probe tips of the four leads. (Fig 1)

- **Total body measurement (Figs 1, 3):**
    - Yellow (Sense lead) - Attach to the electrode placed at the wrist of the left hand
    - Red (Current source lead) - Attach to the electrode placed distal to the yellow lead on left hand
    - Blue (Sense lead) - Attach to the electrode placed at the left ankle joint
    - Black (Current lead) - Attach to the electrode placed distal to the blue lead in the on the left foot.
- Once all leads are connected, touch the "Measure" button on the opening screen OR press the large green button on the front of the device. The "Begin measurement" screen will show; summarizing the subject information you have entered. Press "Start" or the large green button. The device will take the measurement, and results will immediately appear.
- The data is saved, just hit back to get to the measure screen, then push "Start" or the green button again to perform the same measurement a second time
- Next, to switch measurement areas, go back to the patient information screen and edit the filename to say "subject initials," "subject ID number," "LG"

- **Total leg measurement (Fig 3)**
    - Do not change the lead placement on the left ankle and foot.
    - Move the yellow (sense lead) from the left wrist and attach it to the electrode on the right foot, leave the red lead in place on the left hand.
- Perform 2 measurements with this lead positioning
- Next, to switch measurement areas, go back to the patient information screen and edit the filename to say "subject initials," "subject ID number," "LL"

- **Lower leg measurement (Fig 2)**
    - Do not change the lead placement on the left ankle, foot or hand.
    - Move the yellow (sense lead) from the right foot and attach it to the electrode on the left knee.
- Perform 2 measurements with this lead positioning
- Hit "back" to get back to the main screen.
- Remove the leads from the subject
- Remove the electrodes from the subject, wipe the area with alcohol to remove residual glue

Figure 1 - Whole Body Lead Placement
(Left)

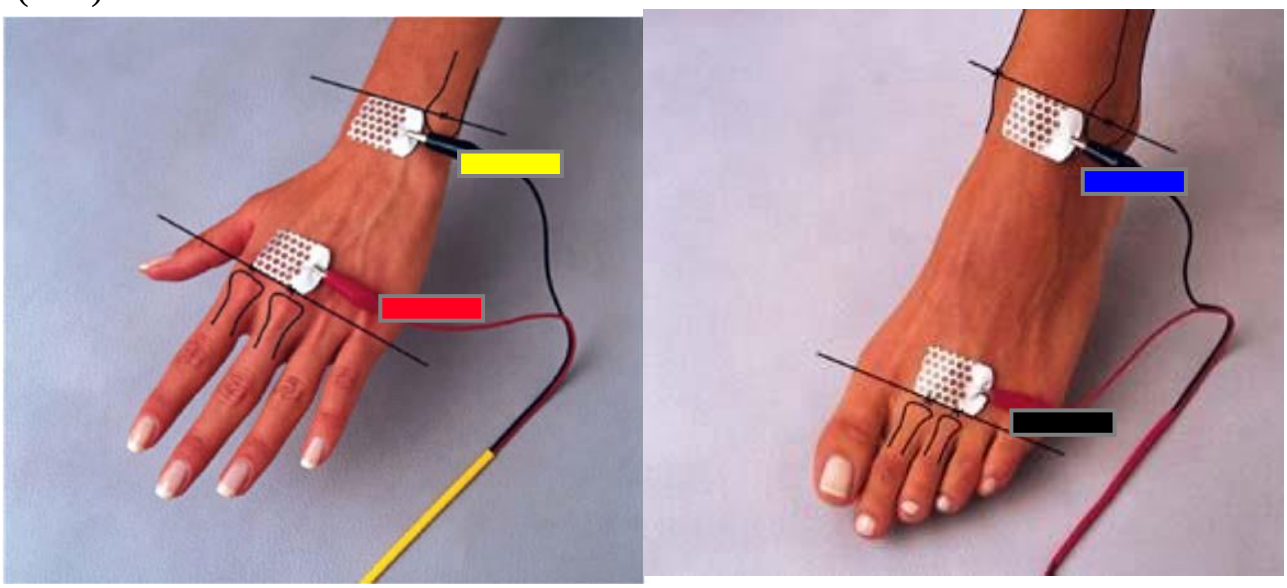


Figure 2 – Lower Leg Lead Placement
(Right)

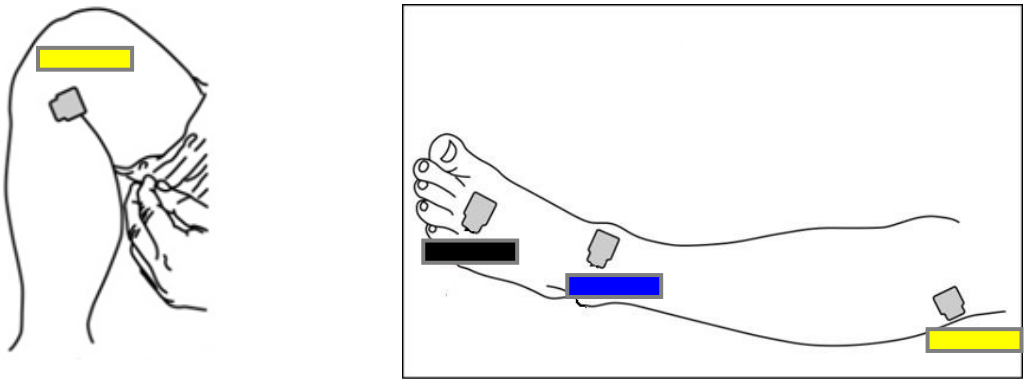
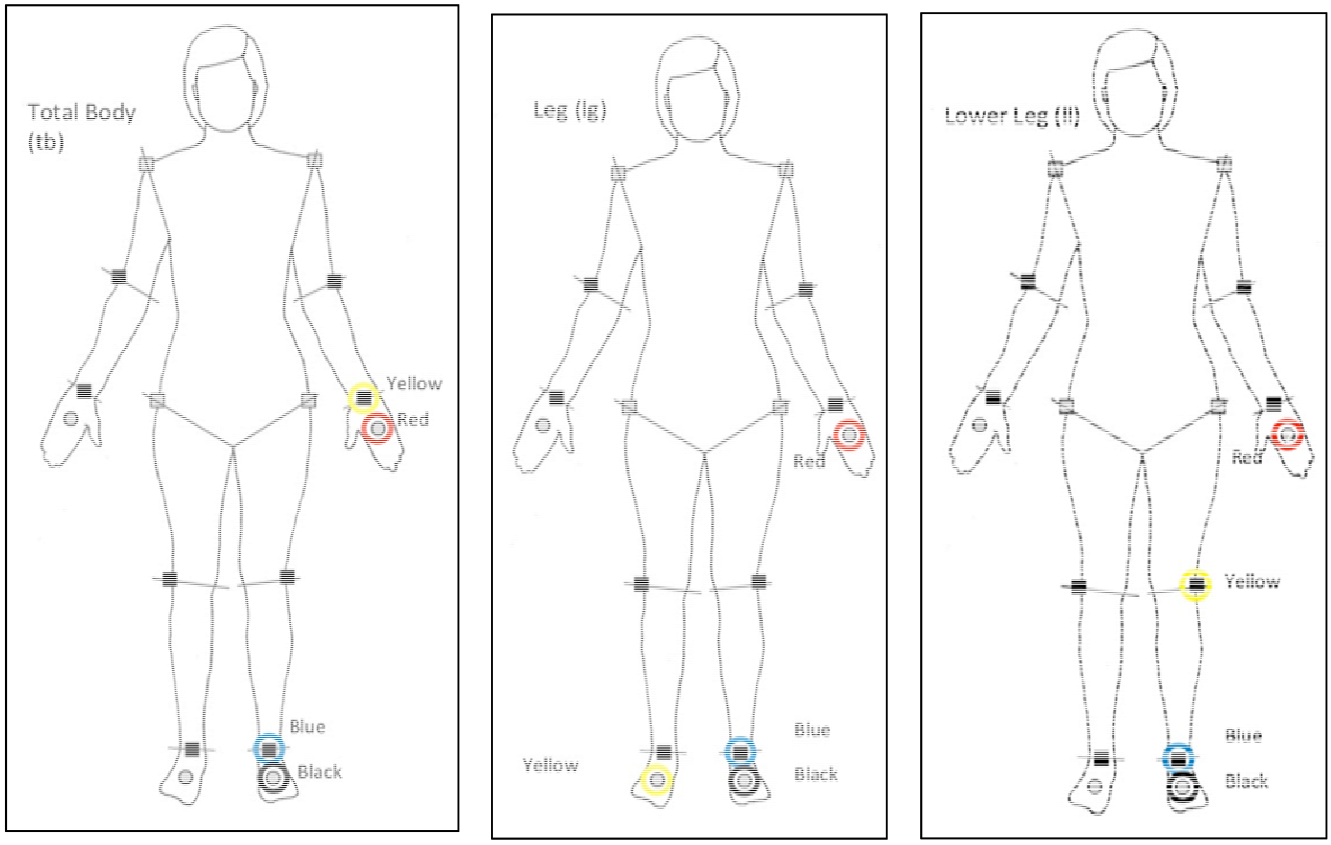


Figure 3 Lead Placement Overview



BIOELECTRICAL IMPEDANCE: BODYCOMP SCALE PROTOCOL

MIDUS REFRESHER BIOMARKER (PROJECT 4)

Body Composition (Impedance)

MIDUS Refresher Study

Manual of Procedures

Overview

As part of the MIDUS Refresher Biomarker project clinic visit, body composition was measured using bioelectrical impedance analysis. This procedure assesses body composition – primarily total lean body mass (i.e., total muscle mass in the body) - using the Body Comp Scale manufactured by Valhalla Scientific. Portable bioelectrical impedance meters are used by physical therapists, exercise trainers, and gyms to tell clients what proportion of their body weight is made up of muscle and fat. MIDUS is using more standardized equipment that has been employed in large national research studies, such as the 'Multi Ethnic Study of Atherosclerosis'.

Muscle contains 70% water and conducts electricity. The greater the muscle content relative to fat, the lower the electrical resistance (or impedance). The measured impedance in ohms is used to determine the amount of muscle mass (also called fat-free, lean mass) in the body using calibration equations created using the magnetic resonance imaging gold standard [Janssen et al. 2000].

A higher lean body mass relative to total weight typically means less fat content in the body, which translates to lower metabolic and cardiovascular risk [Pouliot et al., 1992; Janiszewski et al. 2008]. Such measures of relative fat content in the body are superior to anthropometric measures such as body mass index (body weight relative to height) and waist size in assessing metabolic and cardiovascular risk [Segal et al., 1987; Bigaard et al., 2005]. In fact, individuals who do not meet obesity criteria based on relative weight can still be at increased metabolic risk because of inadequate muscle mass [Stephen &Janseen 2009; Srikanthan et al. 2010]. New research has shown that muscle tissue has a key, independent role in health maintenance [Wolfe 2006], and that level of muscle mass is an important independent indicator of metabolic health, and not simply because high muscle mass reflects low fat mass [Srikanthan et al., 2011].

Visit Preparation

In preparation for the visit, ensure that the following supplies are available:

- Body Comp Scale
- Printer
- MIDUS Refresher BI Procedure Tracking form
- Lysol disinfectant spray
- Dry wipes
- USB drive designated for this measurement

Disinfect the scale prior to each participant's use. Use the Lysol disinfectant spray and wipe down the machine with a dry wipe. Also, ensure that the scale is on a firm, level surface. Ensure that the scale and printer are connected at that the printer has paper.

Measuring BI

1. Administer the eligibility questionnaire. If there is an indication that the participant is not eligible for BI measurement, do not proceed.

2. Ask the participant to remove socks and shoes. The participant must have bare feet and hands for this procedure.

3. Instruct the participant to stand in the middle of the balance scale platform with head erect and eyes looking straight ahead.

4. Once the participant is correctly positioned, enter information about the participant in the device:

    - Height display will flash. Selected English measurements by pressing LBS/KGS button on right hand side of display face
    - Enter height in feet (first digit), inches (two digit format), and fractional inch (0 for full inch, 5 for ½ inch), *ex. 5 ft. 9 in.: enter 5 09 0, 5 ft. 9 ½ in.: enter 5 09 5*: Press enter.
    - Enter Gender: Press one of the gender buttons (MALE or FEMALE)
    - Enter Age.

5. When GRIP appears on display, ask participant to grip the metal handles on each side of the BCS drive. Thumbs should rest comfortably on the top metal handle and fingers should be in firm contact with the lower metal handle.
6. Participant must remain still with hands in contact with handles and feet in contact with metal surface of the base until Body Weight and Body Fat % results are displayed AND results are sent to the printer.

7. Ask participant to get off the scale.

8. Using the device touchpad, select PLAIN and select ENTER in order to print results.

9. Record the following information from the printout to the Tracking form:
    - Ohms
    - Current body weight
    - Total body fat
    - Fat-free mass
    - Total body water

Calibrating the BCS Scale

Calibrate machine once a month at the end of the month. The admitting RA should record the date the machine was calibrated on the Excel sheet on the shared drive.

Special Consideration for Titanium in Body

(Per Dr. Karlamangla on 4/27/2015):

Metal in limbs can falsely reduce BI and overestimate muscle mass. But metal in the neck should not be a concern since the neck is not on the shortest pathway from hands to legs.

Moreover, titanium (although a metal) is a very poor conductor of electricity. So, it is fine to measure BI in a person with titanium in the neck.

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MIDUS-REFRESHER BIOMARKER STUDY

BODY COMPOSITION (BI) PROCEDURE TRACKING FORM

ID: #_____ AGE:_____y/o HEIGHT:_____'_____" Ft.

Q1. DAY COLLECTED: (CHECK ONE) ☐ DAY 1 ☐ DAY 2
[RA4I1]

Q2. VISIT DATE: __ __ / / __ __ __ _

Q3. TIME: __ __ : __ _ AM / PM(CIRCLE ONE)

ELIGIBILITY QUESTIONS:

Q4. Do you have a pacemaker or other medical device? ☐ YES ☐ NO **[RA4I4]**

IF "YES" TO Q4. CHECK METAL TYPE FOR ELIGIBILITY TO PERFORM BI

Q5. Are you currently pregnant? ☐ YES ☐ NO **[RA4I5]**

Q6. Do you have a prosthetic limb? ☐ YES ☐ NO **[RA4I6]**

IF "YES" TO ONE OF Q4~Q6, GO TO Q9. AND Q10. IF "NO" TO ALL Q4~Q6 CRITERIA: PROCEED WITH BODY COMPOSITION PROCEDURE, ASK Q7 AND CONTINUE.

LAST TIME ATE/DRINK

Q7. What time and date did you last eat and/or drink anything including water, candy and chewing gum?

a. DATE: __ __ / / __ __ __ _

b. TIME: ____ : __ _ AM / PM(CIRCLE ONE)

Q8. What did you last eat or drink?
(CHECK ONE BELOW) **[RA4I8]**

a. ☐ SNACK: 12OZ. BEVERAGE OR LESS AND/OR SMALL AMOUNT OF FOOD (≤12 OZ, ie-BAGEL, APPLE, YOGURT, COOKIE, etc)
b. ☐ MODERATE: ≤ 16OZ. BEVERAGE WITH FOOD INTAKE TOTALING ~12-20 OZ. (SALAD, SANDWICH, SOUP)
c. ☐ FULL: ≥ 20 OZ. ALL FOOD COMBINED

Q9. WAS BI COMPLETED? ☐ YES ☐ NO (GO TO Q.9a)
[RA4I9]

Q9a. IF NO, EXPLAIN:_____

Q10. ANY MISSING DATA? ☐ YES (GO TO Q10.a) ☐ NO
[RA4I10]

Q10a. IF YES, EXPLAIN:_____

JUMP MECHANOGRAPHY PROTOCOL

MIDUS REFRESHER BIOMARKER (PROJECT 4)

QUALITY ASSURANCE

The jump platform should be calibrated weekly using certified calibration weights. Create a test subject in your database. With gloved hands, stack three 20 kg weights on one corner of the platform and record the measured weight. Repeat this process for each of the other three corners. Additionally, place two weights side by side in the middle of the platform and place the third weight on top to get a central measurement. Each measurement should be ± 0.5 kg. If any of the measurements are outside of these limits, consult manufacturer guidelines for recalibration.

SUBJECTS

Participants should feel comfortable performing jump and balance tests. These are safe activities that can be performed by anyone that can stand independently. However, if a subject has a condition impacting the lower limbs, such as amputation, recent surgery or injury, and is consequently not comfortable performing the test, omit the test and document the circumstances. If the participant would like to try, or perform fewer trials, this is acceptable and the test can be performed at the discretion of the study staff.

Eligible respondents will perform two balance tests, one with eyes open and one with eyes closed, two trials for each condition. Additionally, they will perform one countermovement jump test consisting of three trials.

SUBJECT DEMOGRAPHIC ENTRY

Subject ID numbers will be assigned by your local site study coordinator. Please fill in the subjects demographic as follows:

Patient ID: (Subject ID – obtain from study coordinator)
First Name: MIDUS
Last Name: Subject Initials
Date of Birth: Complete as appropriate
Gender: Complete as appropriate
Leave rest of fields blank

SUBJECT POSITIONING AND TEST ADMINISTRATION

General Guideline for Exam

- Briefly explain the jump and balance tests
- Reassure that you will evaluate the subject during the exams for safety and the gait belt and spotters will reduce the risk of injury
- Ask the subject if they are comfortable performing the tests
- Fasten a gait belt to subjects that are at risk for falling, in your opinion
- Perform the balance tests before the jump test
- Read the instructions to participants before performing each test and make sure they understand what they are to do.

Balance Tests

Perform these tests with subjects standing on the platform, facing forward with one foot on each platform. Collect two trials for each test, repeat any trial that has acquisition errors. Read the following instructions for each condition; always perform the eyes open test first:

Balance Eyes Open

1) We are going evaluate your balance while you stand with your eyes open; we will conduct two measurements.
2) Stand as still as possible with one foot on each half of the platform and arms down at your sides.
3) This test will last for 30 seconds. The single beep tells you the test has started.
4) After 30 seconds you will hear two beeps; this tells you the test is over.
5) We will stand nearby to help in case you become unsteady.

Balance Eyes Closed

1) We are going evaluate your balance while stand with your eyes closed; we will conduct two measurements.
2) Stand as still as possible with one foot on each half of the platform and arms down at your sides.
3) This test will last for 30 seconds. The single beep tells you the test has started.
4) Keep your eyes closed for the entire duration of the test.
5) After 30 seconds you will hear two beeps; this tells you the test is over.

6) We will stand nearby to help in case you become unsteady.

Jump test

Perform three countermovement jumps for each test, repeat any trial that has acquisition errors. Ensure the platform is collecting an accurate weight by resetting the measurement to zero just before the subject steps on the force plate. Read the following instructions:

1) Jump as high as possible using both legs; attempt to touch the ceiling with you head.
2) Stand upright with your arms at your side, feet a shoulder width apart, one foot on each half of the force plate. Stand still for 2 seconds.
3) Once the single beep occurs you should jump
4) Start the jump by bending your knees slightly to gain momentum
5) Then push off the force plate and jump as high as you can
6) Remember that you must land on the platform with one foot on each half. It is ok not to land on the exact spot you jumped from as long as one foot is on each half of the plate.
7) Land on your forefoot and then stand as still as possible on both feet.
8) Step off the force plate once you hear two beeps.
9) Landing on your heels might cause some pain in your heels and lower back.
10) Do not bring your knees up to your chest when you jump because it will make it look like you jumped higher than you really did.
11) We will stand nearby to help in case you become unsteady
12) Do you have any questions?