Multi-frequency bioelectrical impedance analysis

Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

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Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

Foreword

This essay has been written as completion of the bachelor course Nutrition & Dietetics at the Hogeschool van Amsterdam. For the past twenty weeks I have worked on a research study of multi-frequency bioelectrical impedance analysis, using a new device, called the GAIA 359 PLUS. I have investigated the validity and reproducibility of this new device and also intended to examine its applicability in chronic wasting diseases, such as COPD.

Body composition measurements are very important to assess nutritional status, especially in patients with chronic wasting diseases, because of their high risk of (appendicular) skeletal muscle loss. The GAIA 359 PLUS is a device that is non-invasive, easy to use and results are rapidly obtained. Therefore it was a challenge to investigate its validity and reproducibility against a reference method and one other much applied bedside method.

I would have not been able to perform this research study and write my essay as a result of that, without the help of others. Therefore I would like to take this opportunity to show my gratitude to a couple of people.

First of all I would like to thank my practice supervisor and sponsor, Marielle PKJ Engelen and Nicolaas EP Deutz of the Center for Translational Research in Aging & Longevity for their guidance, support, involvement and feedback during my graduation period. Due to their broad expertise and experience with human and animal research I have been able to expand my knowledge. I am also very thankful for the opportunity they have given me to finish my bachelor course in the United States of America.

Second of all I really appreciate the support and help I have got from the research team, both in terms of participating as study subjects, as for their assistance in organizational matters for this internship.

I would also like to thank my teacher tutor, Peter JM Weijs for his time, guidance and feedback during this graduation period.

I am very grateful for the educational, exciting and challenging period.

Little Rock AR, June 2009

Renate Jonker
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

Abstract

Background – More research shows that a poor nutritional status is a systemic marker of disease severity in chronic wasting diseases. (Hidden) depletion of muscle mass negatively affects health-related quality of life and prognosis, and reduces exercise capacity due to a decrease in muscle strength. Multi-frequency whole-body and segmental bioelectrical impedance analysis is a potential method for a fast and easy clinical evaluation of body composition, giving insight in the nutritional status of these patients. (Early) detection of patients at risk for body and muscle wasting, would benefit treatment for this population, and make individualized dietary interventions possible.

Objective – The purpose of this study was to determine whether multi-frequency bioelectrical impedance analysis, by the GAIA 359 PLUS, provided valid and reproducible data for body composition in healthy subjects, and in patients with Chronic Obstructive Pulmonary Disease (COPD) characterized by muscle wasting. COPD was used as a model for chronic wasting disease.

Methods – In an exploratory research study in 21 healthy subjects (males (n=10), females (n=11)), age range from 21 to 56 y, the validity and reproducibility of a multi-frequency GAIA 359 PLUS 8-contact electrode bioelectrical impedance (BIA) system (Jawon Medical Co. Ltd., Shinsang, Korea) was evaluated. Whole-body fat-free mass (FFM), fat mass (FM), and total soft lean mass (SLM) and FM in the limbs (to derive total body skeletal muscle mass) and trunk were assessed by GAIA and compared to those values obtained by dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance spectroscopy (BIS).

Results – Highly significant correlations were found for whole-body FFM_{GAIA}, as compared to whole-body FFM_{DXA} and whole-body FFM_{BIS} (r = 0.96 and 0.92, respectively, \( P < 0.001 \)). The same applies to segmental and trunk SLM (r = 0.95 and 0.93, respectively, \( P < 0.001 \)). When calculating the FFM and FM on the basis of % body weight the difference between GAIA and DXA were -0.04% and 0.25%, respectively. For appendicular SLM, GAIA gave systematically higher values than DXA (2.7 kg; \( P < 0.001 \)). Bland-Altman analyses showed wide limits of agreement, with substantial bias between individuals for whole-body FFM and appendicular SLM. Bias was considerably different for the men, as compared to the women. Regarding comparisons for FM between GAIA and DXA, trunk FM was significantly higher for GAIA than DXA (1.3 kg; \( P < 0.01 \)). The between-day variation for GAIA was low (CV \leq 2.4%). Reproducibility of both ankle and plate electrodes was high (CV \leq 1.1%). Comparisons between postabsorptive and prandial state by GAIA resulted in significantly higher values for body weight and whole-body FM (0.2 kg and 0.4 kg, respectively, \( P < 0.05 \)).

Conclusions – The GAIA 359 PLUS can be considered an easy applicable, fast and reproducible method for assessing body composition that is low in costs. Although highly significant correlations were found on whole-body level and for segmental values, the specific underlying causes for the substantial bias between individuals needs to be further examined. Because of the low between-day variance and high reproducibility GAIA can be considered a good method to follow individuals during weight losing and weight gaining periods. For clinical practice more research needs to show its accuracy, most importantly in disease specific populations and conditions.

KEY WORDS GAIA 359 PLUS, dual-energy X-ray absorptiometry, bioelectrical impedance analysis, skeletal muscle mass, chronic obstructive pulmonary disease
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1. Introduction

1.1 Background

Chronic wasting diseases, such as Chronic Obstructive Pulmonary Disease (COPD), Chronic Heart Failure (CHF), Cancer and Chronic Liver and Renal Failure are progressive disorders, which result in significant debilitation. There is increasing evidence that a poor nutritional status should be considered as a systematic marker of disease severity in chronic wasting diseases. A poor nutritional status initially results in (appendicular) skeletal muscle atrophy only, and in later stages also in cachexia (combination of weight loss and muscle wasting). The costs involved with managing the consequences due to a poor nutritional status (cachexia) are immense. Billions of dollars each year are spent on different complications, such as falls, hip fractures and pressure ulcers (1). Weight loss, due to a poor nutritional status, is also an important precursor for early hospital readmission (2). Muscle wasting is a serious complication in patients with chronic wasting disease as it negatively affects their health related quality of life and survival rates, independent of the local organ dysfunction, and is a strong predictor for skeletal muscle weakness, which negatively affects their exercise capacity (3,4, 5, 6, 7).

Aging is often accompanied by chronic wasting disease. Aging, independent of other factors, is already associated with a gradual loss of skeletal muscle mass (sarcopenia). Cross sectional data suggest that the loss of appendicular skeletal muscle mass (ASMM) is greater with aging than the loss of non-skeletal muscle mass. Furthermore, skeletal muscle mass loss in the elderly may be masked by weight maintenance (hidden depletion), due to a relative increase in total body fat mass (8). When aging is accompanied by a chronic wasting disease, such as COPD, a greater loss of skeletal muscle mass even occurs (9). In addition, many other health related conditions (like surgery, trauma and inactivity) often develop in the elderly, further compromising the amount of skeletal muscle (8). As appendicular (or limb) skeletal muscle mass (ASMM) accounts for > 75% of total skeletal muscle and is the primary portion of skeletal muscle involved in daily activities (10) a careful analysis will provide important information in the assessment of overall nutritional status in elderly with a chronic wasting disease, such as COPD (11).

For the assessment of overall nutritional status and body composition several methods have proven to be accurate and precise (ie. total body potassium, nitrogen and chloride by γ-counter, dual-energy X-ray absorptiometry, deuterium dilution techniques and underwater weighing). However, these techniques are often not well applicable in clinical practice due to high costs, laborious measurements, and the amount of time needed.

Recently, a new device has been brought on the market for measuring body composition, the GAIA 359 PLUS. The GAIA 359 PLUS determines body composition using multi-frequency bioelectric impedance and personal data (height, age, gender and weight). This device is able to make whole body and segmental analysis. Use of the GAIA 359 PLUS would make it easier, faster and less expensive to measure body composition in clinical practice and therefore might be a useful tool in (early) detection of (appendicular) skeletal muscle loss due to chronic wasting diseases.

Therefore, the purpose of the present study is to examine whether the GAIA 359 PLUS provides valid and reproducible data for body composition in healthy subjects, and in patients with COPD characterized by muscle wasting.

COPD will be used as a model for chronic wasting diseases.

Specific aims include:
- Specific aim 1: To test the hypothesis that the GAIA 359 PLUS provides valid and reproducible data for whole-body fat-free mass (FFM), fat mass (FM) and
appendicular and trunk soft lean mass (SLM) and FM, as compared to dual-energy X-ray absorptiometry, as a reference method, and bioelectrical impedance spectroscopy, in healthy adults

Specific aim 2: To test the hypothesis that the GAIA 359 PLUS provides valid data for whole-body fat-free mass (FFM), fat mass (FM) and appendicular and trunk soft lean mass (SLM) and FM, as compared to dual-energy X-ray absorptiometry, as a reference method, in COPD patients with muscle wasting

If the GAIA 359 PLUS is a valid and reproducible method for assessing body composition in chronic wasting diseases, patients characterized by and at risk for body and muscle wasting can be screened in clinical practice. Subsequently, individualized dietary interventions can be started and evaluated.
1.2 COPD and nutritional status

Around 30.5-34.5 million patients in the United States suffer from different chronic diseases associated with muscle wasting. Part of this group is COPD, with a prevalence of 15-16 million patients (1). As a world wide cause of death and in terms of disability-adjusted life years, COPD is expected to rise to the third place by the year 2020 (12).

COPD is a chronic lung disease characterized by irreversible airway obstruction and chronic inflammatory response in the airways. It can be classified into two general categories: emphysema and chronic bronchitis. Dominant symptoms are shortness of breath and impaired exercise capacity. Furthermore, COPD is a progressive disease with systemic features that include chronic inflammatory processes and altered protein metabolism, which eventually can result in body wasting (ie. cachexia). Multi-organ consequences, like skeletal muscle loss, osteoporosis, cardiovascular disease and diabetes mellitus are well known co-morbidities in COPD (13).

Body composition parameters, such as chronic weight loss and a low BMI, have been associated with poor outcomes in COPD, independent of impaired lung function (FEV1) (6). The association between BMI and mortality, in patients with severe COPD, decreases as BMI increases. Overweight or obese COPD patients (BMI between 25 to 29.9 kg/m2 and above 30 kg/m2) therefore have a better prognosis than patients with a BMI below 25 kg/m2. In mild to moderate COPD the best prognosis is found in normal-weight or overweight subjects (14). Between 25 and 40% of all COPD patients with severely impaired lung function (FEV1<50%) experienced clinically relevant weight loss (5% of actual weight within three months or 10% within 6 months) (15).

Muscle wasting, defined as fat-free mass index (FFMI) < 16 kg/m2 (males) and < 15 kg/m2 (females), was found in 27% of 389 patients with moderate COPD (mean FEV1: 51%) (16). Using the same cut-off points to define muscle wasting, the prevalence was much higher (40-50%) in severe COPD (FEV1: < 35%) (17). Furthermore, a higher percentage of muscle wasting was found in COPD patients eligible for rehabilitation than in the outpatient population (18, 19). Muscle wasting is a serious complication in COPD, as fat-free mass index (FFM divided by %IBW) is associated with a reduction in submaximal exercise performance (18). Muscle wasting is also a strong predictor of skeletal muscle weakness (3) and research has shown that this muscle weakness is related to peripheral muscle atrophy (20, 21). More ensuing effects of muscle wasting are negative effects on health related quality of life and survival rates, independent of the impaired lung function (3, 4, 5, 6).

Depletion of muscle mass is not always accompanied by weight loss (hidden depletion). A French cross-sectional survey in 300 COPD outpatients showed that lean body mass (LBM) depletion was present in 38% of the patients, whereas low BMI levels (< 20 kg/m2) were found in only 17% (22). Therefore LBM or the fat-free mass index could be considered a more accurate indication of overall nutritional status and body composition than body weight. Research by Soler-Cataluna and Marquis has indicated the importance of segmental body assessment, as lower and upper extremity mass was better correlated with mortality than BMI in patients with COPD (23, 24).

To prevent or delay muscle wasting in COPD or other chronic wasting diseases an improvement of the anabolic response to feeding is crucial. Enteral nutrition in combination with exercise and anabolic pharmacotherapy has the potential to improve nutritional status and function in patients with COPD (15).
1.3 Body composition and methods for analysis

The body can be divided into two or four chemically distinct compartments. In the two-compartment model, according to a view developed by Keys and Brozek (25), the body consists of fat mass (FM) and fat-free mass (FFM) (Figure 1). Fat mass is described as all the solvent-extractable lipids contained in both adipose tissue and other tissues, and the residual is the fat-free mass. The fat-free mass is composed of muscle, water, bone, and other tissues free of fat and lipid. Adipose tissue contains about 14% water, whereas the chemically less homogenous, but relatively constant fat-free compartment has a water content of 72 to 74%, at normal body temperature (26). Several techniques are available for determining body composition based on the two-compartment model such as anthropometry (skin fold measurements), determination of whole-body density (underwater weighing), electrical conductance and impedance (bioelectrical impedance analysis).

In the four-compartment model, the body is divided into four chemical groups: water, protein, mineral, and fat (Figure 1). Assumptions are that 100% of the FFM is 6.8% bone, 73.8% water (44.3% ICW and 29.5% ECW), and 19% protein (with virtually all the protein in the cell and the cell is 30% protein and 70% water), and 0.4% protein in the ECW. When bone mineral is subtracted from the FFM only muscle mass or in other words soft lean mass (SLM) are left. SLM consists of total body water and protein and some internal organs. Methods for estimating body composition based on this four-compartment model include neutron activation analysis and isotope dilution techniques. Four-compartmental model analysis using several sophisticated body composition techniques is considered to be the gold standard, however this makes it inapplicable for use in clinical practice.

FIGURE 1. Body composition compartments, a two- and four-compartment model

When relating body composition to physical activity in COPD, application of a 2-compartment model appears to be appropriate (27).

To prevent or delay muscle wasting in patients at high risk, it is therefore necessary to measure body composition serially. The different screening methods all have different benefits and disadvantages.
1.4 Dual-energy X-ray Absorptiometry (DXA)

Dual-energy X-ray Absorptiometry commonly referred to as DEXA or DXA was originally developed as a tool to assess bone mineral density for the diagnosis of osteoporosis. However, in recent years it has become one of the most widely used approaches for determining fat mass and fat-free mass.

DXA divides the body into three compartments. It directly assesses bone mineral content (28) and the soft tissue surrounding the bone (26) by measuring the amount of fat and lean tissue. By many it is considered the most accurate method for assessing FFM (29).

The basic principle of DXA data acquisition is based on the different bone and soft tissue attenuation characteristics at two pulsed X-ray levels (a high intensity and low intensity level). As the beam passes through the body it measures the amount of X-ray absorbed by the tissue it passes through. The higher tissue density, the greater the reduction in X-ray intensity. For that purpose the subject has to lie in supine position on a scan table for ≈ 6 minutes (duration depends on type of device that is used), while the pencil- or fan-beam X-rays pass through the subject and are interpreted by a mechanical arm above the subject (Figure 2). The resultant value is translated into a density value for bone, lean, and fat tissue.

Benefits and disadvantages of DXA

Several advantages of the DXA as a tool for assessing body composition are little subject cooperation, relatively quick measurement, and low radiation dose. Because density values are derived from a direct assessment of tissue density, no (population specific) predictive equations have to be used. DXA also allows regional assessment, and therefore assessment of the lower limb FFM separately from trunk FFM. DXA also has the advantage of measuring the actual shape of a each body part, instead of assuming an overall cylindrical shape. However presence of bone or calcified soft lean tissues may affect the accuracy of body composition measurements. Also the thickness of the body part being scanned, may result in systematic differences between thin and obese persons or affect the accuracy of serial measurements in persons losing or gaining weight (30, 31, 32). Practical problems due to a subject’s height, weight, thickness and surface area of the table are also important.

Research by Engelen et al. has shown that Dual-energy X-Ray absorptiometry (DXA) when compared to deuterium dilution (Deu), is a clinically valid method for the assessment of whole body composition in COPD patients. However, DXA did give systematically higher values for FFM than Deu (33). Recent research by Miller and others concludes that DXA is the best instrument for assessing body composition in COPD, as compared to several other methods based on the two- and four compartment model. (34).

FIGURE 2. DXA, Hologic QDR 4500W
1.5 Bioelectrical impedance analysis (BIA)

The establishment of BIA was founded in the 1970s. From that time on a variety of single frequency BIA analyzers and multi-frequency analyzers became available on the market.

Principles

Bioelectrical impedance analysis is a method based on the difference in electrolyte content between fat and fat-free tissue. Electrolytes (like sodium, chloride, potassium and bicarbonate) are able to conduct electricity. They are found primarily in the fat-free tissues, because of its high water content, and not in adipose tissue. Therefore the fat-free mass is more capable of conducting electricity and it has a lower resistance \((R)\), than adipose tissue (35).

The resistance of a length of homogenous conductive material of uniform cross-sectional area is proportional to its length and inversely proportional to its cross-sectional area. The combination of the two different types of resistance (capacitive \((R_c)\) and resistive \((R)\)) is described by impedance \((Z)\). An empirical relationship can be established between the impedance quotient \((\text{Length}^2/R)\) and the volume of water. In human research length is described by height and volume of water reflects the lean body mass (73% water). Because the body is not a homogenous cylinder an appropriate coefficient \((\rho)\) is necessary to match the real geometry of the human body (volume \((V) = \text{pHt}^2/R\)). However this coefficient varies due to different factors (anatomy of the body segments, ratio height to conductive length and shape of the body).

Impedance can be measured over a range of frequencies, from zero (or low) frequency to infinite frequency (or very high frequency). Depending on the frequency the body behaves as an insulator (at very low frequencies) or capacitor (at very high frequencies) (36).

Single frequency BIA (SF-BIA)

In single frequency BIA, 50 kHz is the standard frequency used by BIA body composition analyzers (50 kHz has the highest reactance). With most devices an electrical current is passed between surface electrodes placed on hand and foot (Figure 3). At 50 kHz it is possible to measure a weighted sum of extracellular water (ECW) and intra-cellular water (ICW) resistivities (~25%). The electrical current is capable of partly penetrating the cell membrane. It is therefore possible to predict TBW and FFM, but SF-BIA is not capable of determining differences in ICW. The prediction of TBW is based on mixture theories and empirical equations. The applicability of these empirical equations depends on the population, age or pathology examined. (36, 37)

Multi frequency BIA (MF-BIA) and bioelectrical impedance spectroscopy (BIS)

MF-BIA measures the impedance at different frequencies (0, 1, 5, 50, 100, 200, 500 kHz). Frequencies over 200 kHz are able to penetrate the cellular membrane and therefore MF-BIA is capable of measuring ECW as well as ICW. Resistances at all different frequencies are then used to calculate total body water (TBW) (37). BIS measures the impedance at a series of mostly 50 frequencies, the data is then applied to a theoretical model, the Cole-Cole model, where the resistance is extrapolated to a frequency of zero \((R_0)\) to infinity \((R_\infty)\). These values are then used to calculate fluid compartments (ECW and ICW) based on regression analysis (37).
When direct segmental analysis are performed using BIA it is possible to reflect different metabolic characteristics of trunk and extremities. Direct segmental analysis uses 8 electrodes to send a small electrical current through the body and measure electrical voltage drops. The body is comprised of 5 cylinders, the trunk and four limbs. Each cylinder has its own impedance value.

Several predictive equations by BIA for FFM and ASMM have been developed. General and COPD specific equations are summarized in Table 1.

Benefits and disadvantages of BIA
BIA has several benefits for analyzing body composition. It is a good bedside method, because the equipment is portable and safe, the procedure is non-invasive, results are reproducible and rapidly obtained.

One of the primary weaknesses of BIA is the assumption that the body is a single conducting cylinder with uniform resistivity. The major part of the body mass (~ 46%) is contained in the trunk, while whole body (WB) impedance is dominated by the impedance of the arm, which contains only approximately 4% of the body mass (38). Another weakness is the use of prediction equations to calculate TBW. Prediction equations for different populations, ages and pathologies should be validated against a reference method in a sufficiently large number of subjects. Relevant equations for this research study are named in table 1.

Furthermore BIA assumes that subjects are normally hydrated. Dehydration caused by insufficient water intake, excessive perspiration, heavy exercise, or caffeine or alcohol use will result in an overestimation of fat mass.

### Table 1
Predictive BIA equations for fat-free mass (FFM), appendicular soft lean mass (ASMM) and skeletal muscle mass (SMM) according to population

<table>
<thead>
<tr>
<th>Population</th>
<th>Source</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects, 18-94 y</td>
<td>FFM</td>
<td>-4.104 + 0.518 Ht^2/R_{50} + 0.231 * weight + 0.130 * Xc + 4.229 * sex</td>
</tr>
<tr>
<td>Healthy subjects, &gt; 16 y</td>
<td>FFM</td>
<td>-12.44 + 0.34 Ht^2/R_{50} + 0.1534 * height + 0.273 * weight – 0.127 age + 4.56 * sex</td>
</tr>
<tr>
<td>Elderly</td>
<td>FFM</td>
<td>11.78 + 0.499 Ht^2 / R_{50} + 0.134 * weight + 3.449 * sex</td>
</tr>
<tr>
<td>Elderly</td>
<td>FFM</td>
<td>5.741 + 0.4551 Ht^2 / R_{50} + 0.1405 * weight + 0.0573 * Xc + 6.2467 * sex</td>
</tr>
<tr>
<td>COPD</td>
<td>FFM</td>
<td>8.383 + 0.465 (length * length)/R + 0.213 * weight (males) + 0.184 * weight (females)</td>
</tr>
<tr>
<td>COPD</td>
<td>FFM</td>
<td>7.610 + 0.747 (length * length)/R + 0.012 * age + (0.058 * reactance)</td>
</tr>
<tr>
<td>Healthy adults and heart, lung and liver transplant patients, 22-94 y</td>
<td>ASMM</td>
<td>-4.211 + (0.267 * height^2/R) + (0.0095 * weight) + (1.909 * sex) + (-0.012 * age) + (0.058 * reactance)</td>
</tr>
<tr>
<td>Healthy adults, 18-86 y</td>
<td>SMM</td>
<td>(height^2/resistance * 0.401) + (sex * 3.825) + (age * -0.071) + 5.102</td>
</tr>
</tbody>
</table>

R, resistance; Xc, reactance; 1 for men, 0 for women; weight in kg; height in cm (9, 29, 39, 40, 41, 42, 43, 44)
1.6 GAIA 359 PLUS

In the past several years contact electrode systems have replaced the need for stainless-steel paste-on gel electrodes (45, 46). Several BIA systems are now available that measure impedance across the arms and legs.

Recently a new device has been brought on the market to measure body composition, GAIA 359 PLUS (Figure 4). This device measures the impedance through BIA method and personal data (height, age, gender, weight) and then performs various analysis about body composition such as mass of body fat, lean body mass, soft lean mass, total body water, protein mass, mineral mass, BMI, percent body fat, BMR, W.H.R., age matched of body, segmental soft lean mass and mass of body fat.

GAIA 359 PLUS measures the impedance via tetra-polar electrode method, with 8 touch electrodes. The touch electrodes measure impedance with light touch namely by grasping the soft handle electrodes and by standing on plate electrodes. The GAIA 359 PLUS measures through (segmental) multi-frequency BIA, at frequencies of 5, 50 and 250 kHz and at a current of 500µA. It indicates the average value of 50 kHz in the result.

<table>
<thead>
<tr>
<th>Measuring time</th>
<th>30 seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applicable height</td>
<td>100 – 200 cm</td>
</tr>
<tr>
<td>Measuring weight</td>
<td>10 – 250 kg</td>
</tr>
<tr>
<td>Applicable age</td>
<td>5 – 89 years old</td>
</tr>
</tbody>
</table>

Based on Lukaski formula, GAIA 359 PLUS’s analyzing formula for Total Body Water (TBW) was developed of which constants were determined by isotope dilution. The formula of Lukaski uses 5 factors such as height, weight, gender, age and impedance when calculating TBW. The TBW formula of the GAIA 359 PLUS has a 98% correlation ratio with dilution method (47).

To calculate segmental values for arms, legs and trunk different measuring routes are used for different body parts. Measuring routes are 6 in total: right palm to left palm, right palm to left sole (passes through trunk), right palm to right sole (passes through trunk), left palm to left sole (passes through trunk), left palm to right sole (passes through trunk) and left sole to right sole. After measuring by various measuring routes, segmental impedance values and total impedance can be derived.

Lukaski formula 1988  
0.377 $Ht^2/R + 0.14 Weight – 0.08 Age + 2.9 Gender + 4.65$

GAIA 359 PLUS formula  
$A Ht^2/IMP + B Weight + C Age + D Gender + E$

Measurements can be done using plate or ankle electrodes. From hygienic point of view one could choose to use the ankle electrodes, because shoes and socks can be worn. Another reason for using the ankle electrodes is the fact that under the feet there can be corn that intervenes with the ability to measure impedance.

FIGURE 4. GAIA 359 PLUS (ankle electrodes installed)
2. Materials & methods

2.1 Study population

During a 4-mo period research subjects were measured by three different body composition techniques. The study population was split up in two target groups. In the first group, determination of the validity, reproducibility of the GAIA 359 PLUS was performed. Applicability was also studied. The second group was used to investigate the applicability of the GAIA 359 PLUS for clinical use in chronic wasting diseases.

- Group 1: healthy volunteers
- Group 2: COPD patients with weight/muscle loss (as a model for chronic wasting diseases)

Group 1 consisted of 21 healthy volunteers, recruited at the Center on Aging (D.W. Reynolds building, UAMS). All were part of the research team. The intention for group 2 was to recruit 10 COPD patients, at the UAMS clinics or in response to distributed flyers in the COPD community. The COPD patients were to be recruited via direct contact with the Principal Investigator (PI) or research staff followed by a telephone contact.

Study subjects were enrolled (males and females of all races) based on the inclusion/exclusion criteria described below (Table 2 and 3). All subjects had to be able to walk, sit and stand up on their own. Measurements and data collection were performed at the nutrition clinic at the 1st floor and metabolic study rooms at the 2nd floor of the Center on Aging. Measurements on the own research team did not need any approval, but for measurements on COPD patients approval was obtained by the Institutional Review Board (IRB) of UAMS.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Inclusion and exclusion criteria group 1: healthy volunteers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Exclusion criteria</td>
</tr>
<tr>
<td>Age &gt; 21 years</td>
<td>Subjects with implants of metallic material (ie. pacemaker)</td>
</tr>
<tr>
<td>Free from acute or chronic diseases</td>
<td>Pregnant women</td>
</tr>
<tr>
<td></td>
<td>Women with contraceptive devices</td>
</tr>
<tr>
<td></td>
<td>Subjects with demonstrable abnormalities in fluid balance (ie. edema)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Inclusion and exclusion criteria group 2: COPD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Exclusion criteria</td>
</tr>
<tr>
<td>Age &gt; 50 years</td>
<td>Established diagnosis of malignancy or Diabetes Mellitus</td>
</tr>
<tr>
<td>Diagnosis of chronic airflow limitation (FEV1 &lt; 70%)</td>
<td>Other chronic metabolic diseases (ie liver, renal, disease)</td>
</tr>
<tr>
<td>Shortness of breath on exertion</td>
<td>Unstable heart disease requiring therapy or recent myocardial infarction</td>
</tr>
<tr>
<td>Clinically stable for at least 4 weeks (no respiratory infection)</td>
<td>Subject with implants of metallic material (ie. pacemaker)</td>
</tr>
<tr>
<td>Cachexia based on the criteria: Body mass index &lt; 23 kg/m² and/or FFM-Index: FFM/height² &lt; 17 (males), 15 (females) kg/m² and/or recent involuntary weight loss (&gt; 5% in preceding 3 months or &gt; 10% in preceding 6 months)</td>
<td>Pregnant women or women with contraceptive devices</td>
</tr>
<tr>
<td></td>
<td>Subjects with demonstrable abnormalities in fluid balance (ie. edema)</td>
</tr>
</tbody>
</table>
2.2 Data collection

2.2.1 Assessment of body weight and composition

Body weight in both groups was measured using the scale function of the GAIA 359 PLUS with readout to the nearest 0.1 lbs, with subjects standing barefoot and wearing light indoor clothing. In group 1 (healthy volunteers), height was obtained by self reported height. In the COPD group, during screening for eligibility, height of each subject was measured to the nearest 5 mm using a wall-mounted stadiometer (Novel Products Inc.)

Whole-body fat-free mass (FFM), fat mass (FM) and appendicular and trunk soft lean mass (SLM) and FM were determined by scanning each subject on a QDR bone densitometer (DXA, Hologic QDR 4500W; Bedford, MA) (voltage: 140/100 kVp; current: 10 µA; collimation: 2.40 x 0.04 mm). For that purpose, the subject lay in supine position on a scan table for ≈ 6 min., while the DXA scanner performed multiple, fast-speed, transverse scans from head to toes. Data were collected in 7 passes. Total tissue mass, bone mineral mass, fat mass, and lean tissue mass were derived according to computer algorithms (Hologic QDR Software for Windows version 11.2). Percentage body fat was calculated as fat mass relative to total body mass. FFM\(_{\text{DXA}}\) was defined as the sum of SLM and bone mineral mass. Appendicular skeletal muscle mass (ASMM) of DXA was defined as the sum of SLM in arms and legs. Quality-assurance tests were run daily. Each day DXA performed a scan of an anthropomorphic spine phantom, provided by the manufacturer, closely reflecting the attenuation characteristics of bone. DXA continuously self calibrated using HOLOGIC Automatic Internal Reference system. DXA, in this study was considered the reference method.

Whole-body FFM and FM, and appendicular and trunk SLM and FM were also determined in each subject using Jawon’s Medical’s device, the GAIA 359 PLUS (output power: 500 µA/1 kHz, 50 kHz and 250 kHz). Before the actual measurement took place, input of height, age and gender was required, using the software program Bodypass PLUS (version BPGAIA.US.1.2.01). Each subject was measured in standing position (barefoot, using plate electrodes) with arms stretched out at about 30° to the body line, holding the hand piece electrodes lightly. SLM, FM and bone mineral content were derived according to computer algorithms (Bodypass PLUS version BPGAIA.US.1.2.01).

Measurements of whole-body FFM, intracellular fluid (ICF), extracellular fluid (ECF), and total body water (TBW) were carried out using the Xitron Hydra 4200 (Xitron Technologies, Inc. San Diego, CA) (Figure 5). This single-channel, tetra polar BIS device scanned the body at 50 frequencies between 5 kHz and 1 MHz. Resistance was measured with subjects lying in supine position, on the left side. Sticky gel adhesive Ag/AgCl tab electrodes (Medline) were placed on the dorsal surface of the left hand/wrist and at the left foot/ankle. Data acquisition was done using Hydra S Data Acquisition Utility rev. 1.0e and HydraUtility version 2.2. ECW, ICW and FFM for group 1 were calculated from Xitron equations (49, 50). For calculating FFM in COPD patients the predictive equation of Steiner et al (2002) was selected (29). Quality assurance tests were run every 2 weeks.

![Xitron Hydra 4200](image-url)
2.2.2 Measurement conditions
In order to make comparison between DXA, GAIA and BIS in group 1 and 2, certain conditions were standardized:
- Subjects had to be in fasted state (after 10 pm the day before) and no use of alcohol or caffeine was allowed for at least 12 hours;
- Measurements had to be done before or 3-4 hours after respiratory actions (like exercise, sauna or bath);
- Subjects were asked to wear clothing lightly as possible;
- Measurements had to be done at normal room temperature;
- Subjects were asked not to touch their sides with arms and the inner thighs were separated during measurements with all three devices;
- All devices and/or accessories, like cell phones and jewelry were removed before each measurement. Subjects were asked not to wear clothing with metal parts.

2.3 Study design specific aims

Specific aim 1: To test the hypothesis that the GAIA 359 PLUS provides valid and reproducible data for whole-body FFM, FM, and appendicular and trunk SLM and FM, as compared to dual-energy X-ray absorptiometry, as a reference method, and bioelectrical impedance spectroscopy, in healthy adults.

Specific aim 2: To test the hypothesis that the GAIA 359 PLUS provides valid data for whole-body FFM, FM and appendicular and trunk SLM and FM, as compared to dual-energy X-ray absorptiometry, as a reference method, in COPD patients with muscle wasting.

Specific aim 1 and 2: GAIA 359 versus DXA and BIS in healthy volunteers and COPD patients

Timeframe

<table>
<thead>
<tr>
<th>Day before</th>
<th>t = 0</th>
<th>t = 1 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPO (except water) after 10 pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAIA, BIS, DXA</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Breakfast</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>GAIA, BIS, DXA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To detect any differences in body composition, measurements by GAIA, BIS and DXA were done in postabsorptive and prandial state in group 1 “healthy volunteers” (n = 21). Breakfast (~ 300-400 kcal) consisted of a self brought meal and was taken right after the measurement. No foods or drinks were excluded. On average, one hour after breakfast the prandial measurement was done.

The intention was to measure patients of group 2 “COPD patients” by GAIA and DXA at t = 0 in the postabsorptive state, but no measurements would be carried out in the prandial state.

Order of measurements from first to last: GAIA, BIS, DXA in healthy volunteers and GAIA, DXA in COPD patients.
Specific aim 1: Within and between day variation of the GAIA 359 PLUS

**Timeframe**

<table>
<thead>
<tr>
<th></th>
<th>day 1</th>
<th>day 2</th>
<th>day 3</th>
<th>day 4</th>
<th>day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of measurement</td>
<td>1 2 3</td>
<td>1 2 3</td>
<td>1 2 3</td>
<td>1 2 3</td>
<td>1 2 3</td>
</tr>
</tbody>
</table>

The precision of the GAIA 359 PLUS was determined by measuring body composition three times a day for five consecutive days in one study subject (female). The measurement times were:

1: ≈ 8.45 am (before breakfast)
2: ≈ 11.45 am (before lunch)
3: ≈ 15.45 pm

Specific aim 1: Reproducibility (ankle and plate electrodes)

**Timeframe**

<table>
<thead>
<tr>
<th></th>
<th>t = 0</th>
<th>t = 15 min.</th>
<th>t = 30 min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeframe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of measurement</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>Plate or ankle electrodes</td>
<td>Plate or ankle electrodes</td>
<td>Plate or ankle electrodes</td>
<td></td>
</tr>
</tbody>
</table>

To measure the reproducibility of the GAIA 359 PLUS 10 subsequent measurements were done in 4 of the study subjects using both ankle and plate electrodes, within a timeframe of 30 minutes. The order in which plate and ankle electrodes were used was switched between subjects to exclude variance due to order of measurement.

2.4 Data analysis

**Statistical analysis**

All analyses were carried out using the statistical program Graphpad PRISM (version 5.02 for Windows). Results are expressed as mean ± SD.

For comparison of whole-body FFM between the three methods repeated measures one-way ANOVA was used, with post hoc Bonferroni test. The paired t test was used for pairwise comparisons of multiple body composition parameters, of postabsorptive versus prandial state and of ankle versus plate electrodes. Linear regression analysis was performed to determine the relative agreement between estimates of whole-body FFM and appendicular and trunk SLM for 2 methods and to describe the correlation between intermethod differences and age, for both men and women. The unpaired t test was used for pairwise comparisons between men and women. Values for body composition assessed by GAIA between 90 and 110% of values found by DXA were considered an accurate measurement, values <90% were considered an underestimation by GAIA and values >110% were considered an overestimation by GAIA. To define accuracy on group level the mean percentage difference (bias) for body composition values between GAIA and DXA were
calculated. The root mean squared prediction error (RMSE) was used to indicate how well GAIA assessed body composition, as compared to DXA (51, 52). The RMSE is calculated by the root square of the mean of differences between 2 methods, when each individual difference is first squared. The limits of absolute agreement between the different methods were calculated as the mean intermethod difference ± 2 SD according to the method described by Bland and Altman (53). Significance of difference was set at the 0.05 probability level. Operational characteristics of the GAIA 359 PLUS were examined by evaluating the within- and between-day coefficient of variation [100*(SD/mean)].
3. Results

In 21 healthy volunteers (10 men and 11 women) body composition was measured by GAIA, DXA and BIS. Due to some difficulties in the recruitment process and the limited time available, it was not possible to study any COPD patients. Subject characteristics of the 21 healthy volunteers are shown in Table 4. Weight, height, BMI and TBW were significantly higher in the men than in the women.

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>Total group (n = 21)</th>
<th>Range</th>
<th>Men (n = 10)</th>
<th>Women (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>37.6 ± 10.7</td>
<td>21 – 57</td>
<td>40.6 ± 11.6</td>
<td>34.8 ± 9.5</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.75 ± 0.09</td>
<td>1.59 – 1.90</td>
<td>1.79 ± 0.07</td>
<td>1.71 ± 0.08*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.2 ± 16.0</td>
<td>61.1 – 113.0</td>
<td>88.1 ± 17.5</td>
<td>69.3 ± 7.4**</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>25.5 ± 3.9</td>
<td>20.5 – 32.8</td>
<td>27.4 ± 4.5</td>
<td>23.9 ± 2.5*</td>
</tr>
<tr>
<td>TBW(_{GAIA}) (L)</td>
<td>41.0 ± 8.3</td>
<td>29.8 – 57.2</td>
<td>47.8 ± 6.6</td>
<td>34.9 ± 3.3***</td>
</tr>
<tr>
<td>FM(_{DXA}) (kg)</td>
<td>6.8 ± 2.4</td>
<td>2.3 – 10.6</td>
<td>6.0 ± 2.9</td>
<td>7.5 ± 1.8</td>
</tr>
<tr>
<td>FFM(_{DXA}) (kg/m(^2))</td>
<td>18.2 ± 2.8</td>
<td>14.6 – 23.0</td>
<td>18.8 ± 5.1</td>
<td>17.8 ± 3.1</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD. BMI: body mass index; TBW: total body water; FMI: fat mass index; FFMI: fat-free mass index; GAIA: bioelectrical impedance analysis by the GAIA 359 PLUS; DXA: dual-energy X-ray absorptiometry. *, **, ***: Significantly different from men (unpaired sample t test): *P < 0.05, **P < 0.01, ***P < 0.001.

### 3.1 Body composition data obtained by GAIA, DXA and BIS in the total healthy volunteer group and after stratification by gender

The total healthy volunteer group had a mean whole-body FFM between 54.1 kg to 57.0 kg (Table 5). The mean whole-body FM was between 20.6 kg and 21.3 kg. The studied men had significantly higher values for whole-body FFM than the women, as assessed by all 3 methods. The highest mean whole-body FFM difference between men and women was found using BIS (mean difference: 23.5 ± 2.6 kg; P < 0.001). On whole-body level, there was no significant difference in FM between the men and the women by both GAIA and DXA. DXA, unlike GAIA did measure a significantly higher FM in the total of limbs for the women, as compared to the men (mean difference: 2.3 ± 1.5 kg; P < 0.05). Both GAIA and DXA measured significantly higher values for trunk SLM for the men, than for the women (both ~ 8.0 ± 1.5 kg; P < 0.001). Also appendicular SLM was significantly higher for the men by both GAIA and DXA, as compared to the women (mean difference: 8.9 ± 1.4 kg and 10.5 ± 1.1 kg; P < 0.001).

### Table 5

<table>
<thead>
<tr>
<th></th>
<th>Total group (n = 21)</th>
<th>Men (n = 10)</th>
<th>Women (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Whole body</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFM(_{DXA}) (kg)</td>
<td>55.9 ± 11.7</td>
<td>66.2 ± 2.6</td>
<td>46.5 ± 2.8***</td>
</tr>
<tr>
<td>FFM(_{GAIA}) (kg)</td>
<td>57.0 ± 11.6</td>
<td>66.5 ± 9.3</td>
<td>48.5 ± 4.6***</td>
</tr>
<tr>
<td>FFM(_{BIS}) (kg)</td>
<td>54.1 ± 13.4</td>
<td>66.4 ± 8.3</td>
<td>42.9 ± 2.4***</td>
</tr>
<tr>
<td>FM(_{DXA}) (kg)</td>
<td>20.6 ± 7.7</td>
<td>19.4 ± 9.9</td>
<td>21.7 ± 5.2</td>
</tr>
<tr>
<td>FM(_{GAIA}) (kg)</td>
<td>21.3 ± 7.6</td>
<td>21.7 ± 10.0</td>
<td>20.9 ± 5.0</td>
</tr>
<tr>
<td><strong>Appendicular</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLM(_{DXA}) (kg)</td>
<td>23.6 ± 5.9</td>
<td>29.1 ± 3.4</td>
<td>18.6 ± 1.2***</td>
</tr>
</tbody>
</table>
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

Results are expressed as mean ± SD. TBW: total body water; FFM: fat-free mass; FM: fat mass; SLM: soft lean mass; DXA: dual-energy X-ray absorptiometry; GAIA: bioelectrical impedance analysis by the GAIA 359 PLUS; BIS: bioelectrical impedance spectroscopy. **: Significantly different from men (unpaired sample t test): *P < 0.05, ***P < 0.001.

3.2 Comparison of body composition data obtained by GAIA, DXA and BIS in the healthy volunteer group

There was no significant intermethod difference in whole-body FFM between GAIA and DXA and DXA and BIS (mean difference: 1.2 kg and 1.8 kg, respectively, ns) (Figure 6). Although data not shown, RMSE for whole-body FFM of GAIA, as compared to DXA for the total healthy volunteer group was 3.3 kg, and the percentage bias 2.3%. Bias was much higher for the women than for the men (4.2% and 0.4% respectively). The maximum negative error for the total group was -7.4% and the maximum positive error was 11.5%. For the total healthy volunteer group GAIA provided 95% accurate results for whole-body FFM. %FFM\textsubscript{GAIA}, as compared to %FFM\textsubscript{DXA} showed a mean difference of -0.04% ± 3.9% (data not shown).

There was a significant intermethod difference in whole-body FFM between GAIA and BIS (mean difference: 3.0 kg, P < 0.01) (Figure 6).

![FIGURE 6. Intermethod difference in fat-free mass (FFM), fat mass (FM) and body weight in 21 healthy volunteers. Mean ± SE. Significantly different (repeated measures one-way ANOVA and paired sample t test): *P < 0.05, ***P < 0.005.](image)

Although data not shown, RMSE for whole-body FFM of GAIA, as compared to BIS for the total healthy volunteer group was 5.9 kg, and the percentage bias 7.0%. Bias was much higher for the women than for the men (13.3% and 0.2%, respectively). The maximum negative error for the total group was -9.9% and the maximum positive error was 39.4%. For the total healthy volunteer group GAIA provided 57% accurate results for whole-body FFM.

There was no significant intermethod difference in whole-body FM between GAIA and DXA (mean difference: 0.7 kg, ns) (Figure 6). Although data not shown, RMSE for whole-body FM of GAIA, as compared to DXA for the total healthy volunteer group was 3.3 kg, and the percentage bias 5.6%. Bias was much higher for the men than for the women (mean percentage deviation: 15.5% and 3.4%, respectively). The maximum negative error for the total group was -34% and the maximum positive error was 46%. For the total healthy
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

volunteer group GAIA provided 43% accurate results, \%FM_{GAIA}, as compared to \%FM_{DXA} showed a mean difference of 0.3% ± 4.0% (data not shown).

There was a significant intermethod difference in body weight between GAIA and DXA. On average, GAIA gave higher values for body weight than DXA (mean difference: 1.9 kg; \( P < 0.001 \)) (Figure 6).

Correlation and agreement for whole-body FFM data obtained by GAIA and DXA in the healthy volunteer group

There was a significant correlation between mean whole-body FFM_{DXA} and FFM_{GAIA} in the healthy volunteer group (\( r = 0.96, P < 0.001 \)) (Figure 7).

A Bland-Altman plot of the intermethod difference in whole-body FFM against mean value of FFM by DXA and GAIA (FFM_{DXA-GAIA} versus FFM_{DXA-GAIA}/2) showed wide limits of agreement (-5.0 to 7.3 kg) and a substantial bias between individuals (Figure 7). Mean FFM_{GAIA} was not significantly different from mean FFM_{DXA} (mean difference: 1.2 kg, ns).

Correlation and agreement for FFM data obtained by GAIA and BIS in the healthy volunteer group

There was a significant correlation between mean FFM_{BIS} and FFM_{GAIA} in the healthy volunteer group (\( r = 0.92, P < 0.001 \)) (Figure 8).
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

A Bland-Altman plot of the intermethod difference in FFM against mean value of FFM by DXA and GAIA (FFM_{DXA-GAIA} versus FFM_{DXA-GAIA}/2) showed wide limits of agreement (-7.2 to 13.1 kg) and a substantial bias between individuals (Figure 8). On average, GAIA resulted in significantly higher FFM values than BIS (mean difference: 3.1 kg; P < 0.05). This higher whole-body FFM was particularly found for the women.

Correlation and agreement for appendicular SLM data obtained by GAIA and DXA in the healthy volunteer group
There was a significant correlation between mean appendicular SLM_{DXA} and appendicular SLM_{GAIA} in the healthy volunteer group (r = 0.95, P < 0.001) (Figure 9).

A Bland-Altman plot of the intermethod difference in appendicular SLM against mean value of appendicular SLM by DXA and GAIA (Appendicular SLM_{DXA-GAIA} versus appendicular SLM_{DXA-GAIA}/2) showed wide limits of agreement (-0.8 to 6.2 kg) and a substantial bias between individuals (Figure 9). On average, GAIA resulted in systematically higher appendicular SLM values than DXA (2.7 kg; P < 0.001). This higher appendicular SLM was particularly found for the women.

Correlation and agreement for trunk SLM data obtained by GAIA and DXA in the healthy volunteer group
There was a significant correlation and agreement between GAIA and DXA for measuring trunk SLM (r = 0.93, P < 0.001) (Figure 10).
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

FIGURE 10. a. Estimates of trunk soft lean mass (SLM) by bioelectrical impedance analysis by GAIA and dual-energy X-ray absorptiometry (DXA) in 10 male healthy volunteers (●) and 11 female healthy volunteers (○). \( r = 0.93 \) (P< 0.001); trunk SLM\(_{\text{DXA}}\) = (0.98 x trunk SLM\(_{\text{GAIA}}\)) + 0.6; Line of identity is included. b. Difference in trunk SLM between GAIA and DXA for the 21 healthy volunteers versus the mean in trunk SLM between the 2 methods. The intermethod difference in trunk SLM (dotted line) is 0.01 kg; the limits of agreement (dashed lines) are -3.8 to 3.8 kg. \( R^2 = 0.02 \).

A Bland-Altman plot of the intermethod difference in trunk SLM against mean value of trunk SLM by DXA and GAIA (trunk SLM\(_{\text{DXA-GAIA}}\) versus trunk SLM\(_{\text{DXA-GAIA/2}}\)) showed a considerably good absolute agreement for the total group (Figure 10). On average, GAIA gave similar values for trunk SLM as DXA (mean difference: 0.01 kg, ns). The mean intermethod difference in trunk SLM values ranged from -3.8 and 3.8 kg.

Comparison of appendicular and trunk FM by the GAIA 359 PLUS versus DXA in the healthy volunteer group

On average, appendicular FM measured by GAIA and DXA resulted in comparable values, (mean difference: 0.3 kg, ns). However, on average, GAIA did give 1.3 kg higher values for trunk FM than DXA, and this intermethod difference was significant (P < 0.01) (Figure 11).

FIGURE 11. Intermethod difference in appendicular and trunk fat mass (FM) in 21 healthy volunteers. Mean ± SE. Significantly different (paired sample t-test): **P < 0.01.

Intermethod difference in body composition data by the GAIA 359 PLUS versus DXA in the healthy volunteer group after stratification by age and gender

The intermethod differences for whole-body FFM and appendicular and trunk SLM were not related to age for both men and women.

FIGURE 12. Intermethod differences by Bland-Altman for whole-body fat-free mass (FFM), appendicular and trunk soft lean mass (SLM) in 10 male healthy volunteers (●) and 11 female healthy volunteers (○).
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

3.3 Comparison of body composition data obtained by the GAIA 359 PLUS and DXA in COPD patients

No data have been obtained.

3.4 Between-day variation of the GAIA 359 PLUS

The between-day variation of the GAIA 359 PLUS was determined by measuring body composition three times a day for five consecutive days on one of the study subjects, using plate electrodes. This resulted into 15 individual measurements. The between-day coefficient of variation (CV) \[100\% \times \text{SD/mean}\] for different body composition parameters calculated from these measurements are given in Table 7. The between-day CV varied between 0.9 and 2.4%.

| TABLE 7 | Between-day variation of the GAIA 359 PLUS. Values are coefficients of variation expressed as percentage, calculated from three measurements performed \(3 - 4\) h from each other for five consecutive days (n = 1) |
|---|---|---|---|---|---|---|---|
| Whole-body FFM | Appendicular SLM | Trunk SLM | Whole-body FM | Appendicular FM | Trunk FM | %FM |
| 1.0 | 1.5 | 0.9 | 2.3 | 2.3 | 2.3 | 2.4 |

FFM: fat-free mass; SLM: soft lean mass; FM: fat mass; %FM: percentage body fat

3.5 Reproducibility of the GAIA 359 PLUS (ankle and plate electrodes)

The reproducibility of the GAIA 359 PLUS was determined by measuring four subjects a total of 10 times with ankle and plate electrodes, both within a 15 minute time period. The within-day CV for different body composition parameters calculated from these 10 measurements are given in Table 8. Data shown are the lowest and highest variation coefficients calculated in these four subjects.

| TABLE 8 | Reproducibility of the GAIA 359 PLUS. Values are coefficients of variation expressed as percentage, calculated from 10 measurements performed within a 15 min. time period (n = 4) |
|---|---|---|---|---|---|---|---|
| Whole-body FFM | App.SLM | Trunk SLM | Whole-body FM | App. FM | Trunk FM | %FM |
| Plate | 0.16 – 0.21 | 0.24 – 0.35 | 0.19 – 0.55 | 0.35 – 0.58 | 0.45 – 0.59 | 0.30 – 0.59 | 0.40 – 0.65 |
| Ankle | 0.08 – 0.28 | 0.18 – 0.53 | 0.13 – 0.51 | 0.47 – 1.00 | 0.37 – 1.06 | 0.58 – 0.95 | 0.39 – 0.85 |

FFM: fat-free mass; App. SLM: appendicular soft lean mass; App. FM: appendicular fat mass; %FM: percentage body fat

In general, plate electrodes gave variation coefficients between 0.16 and 0.65% and ankle electrodes gave variation coefficients between 0.08 and 1.06%. No significant differences were found between ankle and plate electrodes for impedance, whole-body FM and SLM (Table 9). Also no significant differences were found for appendicular and trunk SLM, and appendicular and trunk FM (data not shown).

| TABLE 9 | Impedance, whole-body fat mass (FM) and soft lean mass (SLM) in 4 healthy volunteers, calculated from 10 measurements performed within a 15 min. time period. |
|---|---|---|---|---|
| Impedance\(_{GAIA}\) (Ω) | 467.5 ± 83.0 | 469.4 ± 74.8 | ns | 0.99 |
| Whole-body FM (kg) | 22.9 ± 4.3 | 22.6 ± 4.8 | ns | 0.98 |
| Whole-body SLM (kg) | 53.3 ± 14.3 | 53.6 ± 13.3 | ns | 1.00 |

Results are expressed as mean ± SD. FM, fat mass; SLM, soft lean mass

3.6 The GAIA 359 PLUS postabsorptive versus prandial state
Body weight and whole-body FM in prandial state were significantly higher, as compared to these parameters in the postabsorptive state (mean difference: 0.2 ± 0.5 kg and 0.4 ± 0.8 kg, respectively; \( P < 0.05 \)) (Table 10). For the other parameters in table 10 there were no significant differences found.

**TABLE 10**
Total body water (TBW), whole-body fat-free mass (FFM) and fat mass (FM), appendicular and trunk soft lean mass (SLM) and FM of the healthy volunteer group in postabsorptive and prandial state (n = 21)

<table>
<thead>
<tr>
<th></th>
<th>Fasted state</th>
<th>Fed state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>78.3 ± 16.2</td>
<td>78.5 ± 16.0*</td>
</tr>
<tr>
<td>TBW (L)</td>
<td>41.0 ± 8.3</td>
<td>40.9 ± 8.2</td>
</tr>
<tr>
<td>Whole body</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>57.0 ± 11.5</td>
<td>56.8 ± 11.4</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>21.3 ± 7.6</td>
<td>21.7 ± 7.3*</td>
</tr>
<tr>
<td>Appendicular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLM (kg)</td>
<td>26.3 ± 5.6</td>
<td>26.2 ± 5.5</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>10.3 ± 3.7</td>
<td>10.5 ± 3.7</td>
</tr>
<tr>
<td>Trunk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLM (kg)</td>
<td>26.2 ± 5.1</td>
<td>26.2 ± 5.2</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>11.0 ± 3.9</td>
<td>11.1 ± 3.9</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD. TBW: total body water; FFM: fat-free mass; FM: fat mass; SLM: soft lean mass. * ** Significantly different from postabsorptive state (paired t-test): * \( P < 0.05 \).  

Body weight measured by DXA gave also significantly higher values in prandial state, as compared to postabsorptive state (mean difference: 0.3 ± 0.4 kg; \( P < 0.05 \)). Furthermore, trunk SLM differed between postabsorptive and prandial state, with slightly higher values for prandial state (mean difference: 0.4 ± 0.7 kg; \( P < 0.05 \)).
4. Discussion

The present study was conducted to examine the validity, reproducibility and applicability of a new device, recently brought on the market, the GAIA 359 PLUS (Jawon Medical). This device is non-invasive, easy to use and results are rapidly obtained, therefore the question rises if it is a useful tool for assessing body composition, and especially for (early) detection of skeletal muscle loss in patients with a chronic wasting disease.

The general purpose of the present study was to examine whether the GAIA 359 PLUS provides valid and reproducible data for body composition in healthy subjects, and in patients with COPD, characterized by muscle wasting. Therefore the emphasis of this study was on whole-body FFM and (appendicular) skeletal muscle mass. For this study, measurements were done only in healthy volunteers. Unfortunately no COPD patients were enrolled, partly due to the limited time available. Although several patients were screened, they appeared not to be eligible as they did not fulfill all the in- and exclusion criteria. Still, research has to be done in this patient population to examine the validity and applicability of the GAIA 359 PLUS in chronic wasting diseases.

Whole-body composition

Results of this study showed a high level of relative agreement between GAIA and DXA, and GAIA and BIS in the estimation of whole-body FFM. Highly significant correlation coefficients were found when comparing whole-body $\text{FFM}_{\text{GAIA}}$ to whole-body $\text{FFM}_{\text{DXA}}$ and to whole-body $\text{FFM}_{\text{BIS}}$. These estimates for GAIA, as compared to DXA are slightly better than those reported for other BIA formulas and systems, a comparable BIA system of Jawon Medical included (54, 55, 56). On average, whole-body FFM measured by GAIA was not significantly different from whole-body FFM measured by DXA (mean difference: 1.2 kg, ns). Intermethod differences in whole-body FFM were randomly distributed in relation to the mean of the two estimates according to Bland-Altman analysis.

Systematically and significantly higher values for whole-body FFM were given by GAIA, as compared to BIS (mean difference: 3.1 kg), particularly in women. To exclude interindividual variability by BIS measurements, all subjects were measured at the same side of the body (left side). The difference in prediction equation for FFM by GAIA and BIS and the assumption made for several factors in the equation (ie. $K_6$ in BIS: factor correcting for whole-body measurement between wrist and ankle) could also contribute to the explanation of the higher values for whole-body FFM as assessed by GAIA. Although relative agreement was also high for GAIA, as compared to BIS again absolute agreement needs to be discussed due to the large bias and wide limits of agreement.

Although data were not presented in the results section, estimates for whole-body FFM obtained by measurements with GAIA, as compared to whole-body FFM calculated by a previously published prediction equation by Deurenberg et al. (1991) (40) gave comparable results (mean difference: 0.44 kg ± 1.7 kg; ns, r = 0.99). Therefore for in this small group of healthy volunteers, GAIA and the predictive by Deurenberg et al. seem to be interchangeable for calculating whole-body FFM.

Results of this study also showed a highly significant correlation for whole-body $\text{FM}_{\text{GAIA}}$, as compared to whole-body $\text{FM}_{\text{DXA}}$ ($r = 0.92; P < 0.001$). This estimation for whole-body FM is as good as that reported by other research done with the Zeus 9.9, from Jawon Medical. Comparison of whole-body FM between GAIA and BIS was irrelevant, due to the fact that BIS used body weight as assessed by GAIA in its predictive equation to calculate FFM and consequently FM (body weight – FM).

The high bias on individual level and the wide limits of agreement diminish the accuracy considerably for the studied methods. However, the good reproducibility and the low between-day variance of the GAIA indicate that this method is a good method to follow individuals during weight losing and weight gaining periods. The large difference in bias on
whole-body level between men and women most likely is related to the amount of FFM in the body.

Furthermore, GAIA provides values for body weight that are significantly higher than DXA in the total healthy volunteer group (mean difference: 1.9 kg). Two reasons for this difference should be considered. DXA is a well validated method for measuring bone density, however for body composition it is known to show inconsistencies (57). DXA defines body weight by measuring the amount of soft tissue and bone, while the GAIA measures the actual body weight. The difference in body weight between GAIA and DXA influences all related parameters. When calculating the FFM and FM on the basis of % body weight, the differences were < 1%. Also, during this study period GAIA did not subtract any weight for clothing, which also can partly explain the higher values measured for body weight, as compared to DXA. For classifying a patient as underweight or overweight based on BMI criteria this probably is not a key factor determining an appropriate (dietary) treatment.

Segmental body composition
As muscle wasting is a common complication in COPD patients, negatively influencing their prognosis (58), accurate results for appendicular skeletal muscle mass by GAIA 359 PLUS is of special importance.

The present study showed a high relative agreement between GAIA and DXA in the estimation of appendicular and trunk SLM. Highly significant correlations were found when appendicular and trunk SLM\(_{\text{GAIA}}\) were compared to appendicular and trunk SLM\(_{\text{DXA}}\) and these estimates were as good as those reported for another widely used BIA system (59).

Systematically and significantly higher values for appendicular SLM were given by GAIA, as compared to DXA (mean difference: 2.7 kg), especially in women. The higher body weight estimation of GAIA could play a role in this difference. Intermethod differences in appendicular and trunk SLM in the healthy volunteers were randomly distributed in relation to the means of the two estimates for appendicular and trunk SLM, according to Bland-Altman-type analysis. A possible reason for the lower appendicular SLM values by DXA might also be related to the fact that DXA and GAIA have a different starting-point for measuring FFM and a different way to divide the body into five cylinders (manually by DXA, automatically by GAIA). Drawing the lines during analysis of appendicular SLM in DXA slightly different at each subject can increase the variability. In addition, for especially the arms, DXA can have difficulty in completely measuring the arms due to the limited area of the scan table. Especially in larger (muscular) men and women at least one of the arms would fall partly outside the measurement range of the table, even when the subject was instructed to place their hands vertically with the fifth finger on the table pad.

The prediction equation by Janssen et al. (2000) (44) for whole-body skeletal muscle mass (SMM) compared to estimates of SSM by GAIA gave significantly higher values for whole-body SMM\(_{\text{Janssen}}\), as compared to SMM\(_{\text{GAIA}}\) (mean difference: 5.7 kg ± 3.5 kg; \(P < 0.01, r = 0.95\)). Therefore this prediction equation is not valid for this cohort.

Trunk FM\(_{\text{GAIA}}\), as compared to FM\(_{\text{DXA}}\), was significantly higher for the GAIA than for DXA. DXA however excludes the pelvis when defining segmental regions. It is therefore acceptable to assume that the GAIA defines a larger area for the trunk than DXA. Correlation analysis is therefore more appropriate.

In the clinical assessment of both whole-body and segmental body composition it should be evaluated if a systematically higher or lower value for GAIA, as compared to an other technique is of relevance. When GAIA is used to evaluate time related changes it is valuable method as the between-day and repeatability variance is very low.

Evaluation of operational characteristics
The precision of the GAIA 359 PLUS is good, because the between-day variation for whole-body values and values separately for trunk and the total of limbs was low (CV ≤ 2.4%). In particular, low CV values were found for appendicular and trunk SLM, which is of special
importance, because of future plans to use this device in the (early) detection of muscle loss in chronic wasting diseases. This between-day variation is comparable to values found for another widely used BIA system, the Tanita BC-418 (SF-BIA) (59). It has to be emphasized that the between-day variation was measured in only one subject. Between-day variation is influenced by factors like vigorous exercise throughout the day, alcohol and caffeine use (37). In the studied subject all these factors were absent which might contribute to the low CV by the GAIA.

The GAIA 359 PLUS appears to be a reproducible method for body composition analysis. The within-day variation (10 subsequent measurements in 15 minutes) is low for both ankle and plate electrodes (CV ≤ 1.1%). This within-day variation is in line with values found for the Tanita BC-418 (CV ≤ 1.4%) (59).

In conclusion, the within- and between-day CVs of the GAIA 359 PLUS on whole-body level and for segmental values are not influences by the type of electrodes used (ankle or plate).

In clinical practice, for measuring body composition, it can be useful if patients do not have to be fasted for an appointment later in the morning. Comparison between postabsorptive and prandial state for the GAIA 359 PLUS did not show significant differences for all parameters measured, except for body weight and whole-body FM. The significantly higher values for body weight and whole-body FM were only 0.2 and 0.4 kg, respectively. In clinical practice these small elevations will not change any additional therapy. Therefore there appear to be no concerns around using this device on patients after breakfast, later in the morning.

**Study limitations**

This study examined a relatively small cohort (n = 21). Especially for comparisons between men and women a bigger population would improve the power of this study.

In order to compare the validity and applicability of the GAIA in healthy subjects, men and women were included regardless of age. However to be able to evaluate the validity and applicability of the GAIA in elderly with a chronic wasting disease, a healthy elderly control group above 50 years of age should have been studied for comparison. Because IRB approval is needed for including research subjects into a study it was only possible to measure subjects from our own team and therefore is was difficult to add more elderly subjects to the healthy study group.

Neither one of the devices used in this study is a gold standard. Although DXA shows a reasonable agreement in several studies, a considerable interindividual variation exists (57). Therefore relative errors of GAIA against DXA can not be interpreted as an inaccuracy of only GAIA. This has to be considered when comments are made about validity.

An important reason that all three methods are not gold standards is the common assumption of uniform hydration of the FFM (TBW = ∼ 0.73 × FFM). Extensive interindividual variation exists (67-78%) (60), although changes in FFM due to fluid changes are expected to be relevantly minor according to research by Pietrobelli et al (61). This factor however will not influence the FFM data in our study as healthy subjects without fluid shifts were studied.

**Insecurities study design**

In the process of performing this study certain insecurities regarding the study design emerged, that should be considered for alteration in future studies.

First of all self reported height should be replaced by a measured height to obtain more accurate results. Body weight was measured using the scale function of the GAIA 359 PLUS and then used by BIS for calculation of whole-body FFM, therefore a comparison with BIS for whole-body FM (body weight – whole-body FFM) was not possible. Measurements of body weight with a different scale can prevent this problem.

The daily quality-assurance tests performed by DXA were done for whole-body bone mineral, but not for the attenuation characteristics of lean and fat mass. A whole-body phantom (available by Hologic) can improve the accuracy of DXA.
Furthermore interindividual variability was influenced, because certain conditions were not or partly not standardized, due to circumstances (ie. breakfast, wearing metal parts/jewelry, voiding bladder).

Due to inexperience of the performer, the lines drawn on the DXA-scan to define the subregions of the body were not always exactly placed the same way.

**Recommendations and considerations for clinical practice**

The GAIA 359 PLUS is a device that is easy applicable, fast and gives reproducible results. Therefore, it could be considered a good alternative method for the evaluation of body composition in clinical practice, although more research has to be done on the validity and applicability in specific populations at high risk for muscle wasting (1). After working with this device during this study, several factors are considered important for clinical practice.

When performing a measurement, a subject has to be instructed about the measurement procedure on beforehand. This instruction should include an explanation on how to stand properly on the plate electrodes or lean against the ankle electrodes and how to hold the electrode handles. Especially in elderly it is recommended to use the ankle electrodes instead of the plate electrodes, as corn under the feet may interfere with the accuracy of a measurement. The measurement of body weight is quickly taken by the GAIA 359 PLUS. For accurate results it is therefore important that a subject diminishes movement as much as possible.

The print-out of the GAIA 359 PLUS gives a considerable amount of information. This form is attractive for patients, because patients often favor something tangible to take back home. The print-out, however, provides absolute values for body composition parameters and a classification of body type and an optimal range for certain values. Classifying a person into a certain body type is based on BMI and percentage body fat (PBF), defined by the manufacturer’s own cut-off points. FFMI is not included in this classification and therefore muscular subjects will easily be classified as obese. For the treating physician or dietician it is therefore important to look at absolute values. The optimal range provided on the form for weight, BMI, %FM and SLM varies greatly for age and between healthy individuals and patients with a chronic wasting disease. This should be explained properly to the patient, rectified by the right values. Another limitation is the large number of abbreviations used on the form. Patients might have a hard time understanding the meaning of certain values. Therefore an explanation should always be provided by the treating physician or dietitian.

To conclude, it is important that a well trained and educated person performs the measurement, and that repeated measurements in one subject are always done under the same conditions. In order to use the GAIA 359 PLUS as a clinically applicable method for assessing body composition, this device should be validated in more disease specific populations, and in disease conditions characterized by changes in water balance (ie. cardiac insufficiency, liver and renal failure). As research at the Donald W. Reynolds Institute on Aging is done in elderly and children with multiple chronic wasting diseases such as Chronic Renal Failure, Heart Failure, Cancer, Cystic Fibrosis, applicability and validity of the GAIA 359 PLUS in these populations is of great interest. Whether this device is suitable method for assessing body composition in the above mentioned elderly and pediatric populations remains to be studied.

**General conclusion**

In the present study, the validity and reproducibility of the GAIA 359 PLUS was examined in healthy subjects. Highly significant correlations in the estimation of whole-body FFM, appendicular and trunk SLM were found between GAIA, DXA and BIS. Between-day variability was low and reproducibility high. Although relative agreement was high for all body composition parameters, absolute values showed a substantial bias and wide limits of agreement. When expressing values as a % of body weight, differences, bias and limits of
agreement strongly diminished. Because neither one of the methods used in this study is a
gold standard for body composition analysis, it is not clear which device is responsible for the
bias.
It can be said that the GAIA 359 PLUS is an easy applicable, reproducible, relatively cheap
and fast method for the assessment of body composition. Therefore this device can be a
good alternative method to DXA to follow individuals during weight losing and weight gaining
periods. However its accuracy, with the emphasis on muscle mass needs to be further
examined, also to show its utility in any individual. Also more research must show its validity
and applicability in disease specific populations and conditions.
5. References

54. Pateyjohns IR, Brinkworth GD, Buckley JD, Noakes M, Clifton PM. Comparison of three bioelectrical impedance methods with DXA in overweight and obese men. Obesity (Silver Spring) 2006;14:2064-70.

Appendixes
Appendix I

SOP GAIA 359 PLUS

Introduction
GAIA 359 PLUS measures the impedance through BIA method and personal data (height, age, gender, weight) and then performs various analysis about body composition such as mass of body fat, lean body mass, soft lean mass, total body water, protein mass, mineral mass, BMI, percent body fat, BMR, W.H.R., age matched of body, segmental soft lean mass and mass of body fat etc.

GAIA 359 PLUS measures the impedance via tetra-polar electrode method, with 8 touch electrodes. Touch electrodes measure impedance with light touch namely by grasping soft handle electrodes and by standing on plate electrodes.

The results of this device require expert’s analysis. As a patient it is advised to consult with a doctor. Consumers cannot use this for dose or cure on his judgment.

Exclusion criteria for measurement
This device should not be used in the following conditions:
- If a subject has implants made of metallic materials like a pacemaker, defibrillator, stent, and/or metal suture in the heart and great vessel etc;
- If a subject is equipped with devices that inject electrical current, such as an artificial heart and heart lung machine;
- If a subject is connected to a liquid-filled catheter and/or other electronic products of good conductivity.

Using the GAIA 359 PLUS in the following conditions can cause danger to the subject or produce invalid results due to disturbance of the electric signal:
- If a subject uses an electronic stimulator (for various purposes);
- If a subject is connected to a device that injects electrical current: ECG, EMG, and EEG;
- If a subject is diagnosed by the doctor to be influenced even by imperceptible micro-current.

A doctor should be consulted before using this device in the following conditions:
- Any woman with contraceptive devices.
- Any woman in pregnancy.
- Anyone who can be damaged physically by even a small amount of electric stimulation.
- In case of using conductivity by electronic devices.

Safety precautions
- This device must be operated only by a qualified person or a manufacturer who is trained and completely understands the device. Therefore users must not touch or handle the inner side of the system at anytime. It may cause an electric shock and a flame out.
- This device has been factory-adjusted for optimum performance. Please do not attempt to modify or adjust any preset controls or switches except those specified for operation. If any modification is desired, ask the authorized dealer for service.
- If there occurs any trouble with the unit, switch off immediately and contact the authorized dealer for assistance.
- Avoid the following environments during storage and installation:
  1. Where the ambient temperature falls below -20°C or exceeds 60°C for storage;
2. Where the ambient temperature falls below 10°C or exceeds 40°C for use;
3. Where the atmospheric pressure falls below 70kPa (700mbar) or exceeds 106kPa (1060mbar);
4. Where the humidity is under 30% and over 75% for use;
5. Where the humidity is over 95% for storage;
6. Where the unit exposed to dust;
7. Where the unit is exposed to water stream or splashing water;
8. Where the unit is exposed to high-density oil vapor;
9. Where the unit is exposed to salty atmosphere;
10. Where the unit is exposed to explosive gas;
11. Where the unit is exposed to excessive shock or vibration;
12. Where the floor is inclined over 10 degree of an angle;
13. Where the unit is exposed to direct sunlight.

- The device should be used only under grounded conditions. (Avoid touching earth with gas or water pipe, lighting rod, telephone line or other things which may cause electric problems.);
- Power should be supplied through 3 prong plug and accessories approved by International Standard;
- Turn off power before pulling out the plug;
- Turn off power of main unit when connecting it to optional devices.
- Use only the fuses provided by manufacturer, or they may cause a flame out.
- Don’t manipulate the device with wet hands.
- Using this device, especially in subjects who have an implant or who are in connection with a liquid filled catheter are exposed to unavoidable shock by leakage of the current or because of a potential difference between two surfaces of conductive materials, if any electrical appliance is placed near this device. To protect a person from those risks, please connect equipment surface on rear panel of the appliance to earth wire in chamber;
- Exposing the device to foreign materials and exceptional environments should be checked before using.
- When re-using the device after a long period absence, please check the device carefully before usage, even if the unit and other options are in good condition.
- Please remember to always take other general cautions against electric device usage.

Calibration

To calibrate follow steps below:

1. Press → 4 → 3 → 2 → 1 → on key-pad
2. Select < Scale cal.> from set up view
3. Adjust the weight accordingly
4. Press ‘SET’ button to fix it and return to main ‘SYSTEM SET UP’ view with ‘CLOSE’ button

Plate or ankle electrode

There is the option to measure impedance using the plate or the ankle electrodes. Which electrode is used depends on which one is selected in the menu. For selecting an electrode follow these steps:

1. Press → 1 → 2 → 3 → 4 → on the key-pad
2. Select < PLATE / ANKLE > from main system set up view
3. Select ‘Plate’ or ‘Ankle’ by pressing the touch panel or using the ‘ ’, ‘ ’ buttons or key-pad ‘ ’, ‘ ’ buttons.
4. Press ‘SET’ button to fix it and return to main ‘SYSTEM SET UP’ view with ‘CLOSE’ button.
Measurement precautions

Standardize conditions:
- It is recommended to measure in fasted state (at least 4~6 hours) and no use of alcohol or caffeine is recommended for at least 24 hours;
- Subject must drink 2 cups of water 2 hours before measurement;
- Measure before or 3-4 hours after respiratory actions (like exercise, sauna or bath);
- Subject should wear clothes lightly as possible;
- Measure subject always after at least 5 minutes in standing position;
- Clean both measurement site and electrodes and make sure nothing is in between;
- Measurement should be done in normal body temperature in room;
- Void bladder before measurement;
- Keep correct position and posture to measure;
- Clean both measurement site and electrodes and remove sweat or foreign material between measuring site and electrode;
- Repeated measurements should always be done at the same time under similar conditions to get a more accurate picture of the measurements over time;
- To prevent inaccurately low body fat percentage measurements and other measurement errors, always hold both arms straight down when taking measurements.
- Ensure that the subject arms are not touching their side and that the inner thighs are not touching each other during measurements; if necessary, place a dry towel between your arm and side and/or between the thighs.
- Do not take measurements while using transmitters, such as mobile phones, which may affect readings.

Position of subject
- After taking position on the electrode scale, grip handles electrodes, then put down both arms comfortably and abduct from the body about 30 degrees
- Do not move, speak or bend during measurement
- Measuring sites should touch electrodes continuously

When using pedal plate, the subject must take off shoes and socks or stockings and then stand on plate electrodes fairly in order so that hill and toe touch electrodes impartially. When using the ankle electrodes, pull down socks of subject to bear skin to touch electrodes. Stand close to touch all 4 ankle electrodes (light pressure is acquired when touching the electrodes).

![Figure 1. How to stand on the electrode scale](image-url)
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

How to touch the electrode handle (figure 2):
- Remove sweat or foreign material between electrode and hands;
- Grip handle electrodes with fingers and palms, the two 2 electrodes on each handle should be touched impartially;
- Press start button with a thumb;
- When the subject has too small hands or feet to cover all electrodes sufficiently for measurement, make sure the subject touches all electrodes equally;
- During the measurement the subject should not be touched by other person or conductive materials;
- If the 8 electrodes are not perfectly touched during the measurement, the measurement is stopped or the data is not reliable.

FIGURE 2. How to touch the electrode handle

Entering personal data
For entering personal data on the computer the software program “Bodypass Plus” is used. To enter data for measurement start up this program and follow the steps below:
- Enter member’s information
- After putting in the member’s basic information press the registration button (= ‘Insert’).
- To change any information delete current data and then press the modification button (= ‘Modify’)
- To transmit the data to the device press the button ‘Member’ on the right top of the screen. If data is transmitted this will appear in blinking read letters left of the ‘Member’ button.

After entering and transmitting the personal data the subject step on the plate electrode scale. When stepping on the plate electrode scale, the view turns to ‘Measuring’ with a chime bell and weight measurement starts. Subject should not move or speak until measurement is finished. A voice message states “Don’t move or speak please”. If the measuring is completed, the result is displayed on LCD (possible range is 10~250kg).

After measuring weight a figure explaining the next measurement will appear on the LCD screen with the voice message “Grasp holder and press start button on the holder”. Subject should then grip the electrode holders and hold them according to the right procedure and then press the start button with both thumbs. Then the LCD turns to ‘Measuring’ view and the voice warns to the subject with this voice message: “Starting measurement, don’t move or speak.”
Appendix II

Note to participating subjects.

Procedure measurements body composition (GAIA, BIS and DXA)

Dear .....,

Please take care of the following things:

- Be in a fasting state (after 10 pm the day before) and no use of alcohol or caffeine is recommended for at least 12 hours
- Wear clothes lightly as possible
- No exercise less than 3 or 4 hours before measurements
- Void bladder before measurements
- Don’t wear anything with metal or silver. For example: jewelry, clothing with zipper, buttons etc. It is preferable to wear sweat pants or a jogging suit
- Do not move or speak during the measurements

The measurement with the GAIA, BIS and DEXA will be performed twice. Once in fasting state and once after a meal (breakfast). It is important to make sure your breakfast contains enough energy. You should aim for a total of 300-400 kcal. For example: 2 slices of bread with something on them and a cup of milk/ juice. Try to finish your meal within 10 – 15 minutes.

Take in account that you will have to take off your shoes and socks for the measurements.

Thank you for participating.
Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

Appendix III

Print-Out GAIA 359 PLUS.

<table>
<thead>
<tr>
<th>Name / ID</th>
<th>Renate Jonker / 000000001</th>
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<tr>
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<tr>
<td>Height</td>
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**Body Composition**

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<th>Body Fat Over</th>
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**Assessment of Weight Control**

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<th>Over</th>
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<th>S.L.M.</th>
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<td>120</td>
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<tr>
<td>B.M.I.</td>
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<tr>
<td>P.B.F.</td>
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<td>S.L.M.</td>
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</table>

**Energy Expenditure**

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<th>Over</th>
<th>A.M.G.</th>
<th>W.H.R.</th>
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<tr>
<td>W.H.R.</td>
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<td></td>
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<td>0.76</td>
</tr>
<tr>
<td>B.M.R.</td>
<td>1299 kcal</td>
<td>T.E.E.</td>
<td>2000 kcal</td>
<td>Impedance</td>
<td>591 Q</td>
</tr>
</tbody>
</table>

**Synthetic Analysis**

Your body weight and Percent Body Fat are optimal on a basis of BMI. In case of 20s and 30s, it is encouraged to keep Percent Body Fat lower than 20%. If Percent Body Fat is close to 30%, it is recommended to decrease body fat and increase taking of protein. Most case of young women, they have optimal PBF or somewhat over and heavily lack of muscle mass. However, as getting older Percent Body Fat is increased generally, while muscle mass is decreased. Although same body weight, the women having more muscle look more slender and springy than the others having less muscle. So, please try anaerobic exercise steadiness since today.

<table>
<thead>
<tr>
<th>[Target to Control]</th>
<th>[Kcal]</th>
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<tbody>
<tr>
<td>Body Fat</td>
<td>28.9</td>
</tr>
<tr>
<td>S.L.M.</td>
<td>100.1</td>
</tr>
<tr>
<td>WEIGHT</td>
<td>144.6</td>
</tr>
</tbody>
</table>

| [Practical Body Composition] | Weight | 139.3 |

Renate Jonker

6/15/2009 Project# 2009243
Appendix IV

Validity and reproducibility of the GAIA 359 PLUS and applicability in chronic wasting diseases

Renate Jonker

Patient ID: Patient ID
DOB: December 21, 1983
Sex: Female
Ethnicity: White
Height: 68.0 in
Weight: 134.7 lb
Age: 25

Scan Information:
Scan Date: March 25, 2009
ID: A03250905
Scan Type: Whole Body
Analysis: March 25, 2009 11:02 Version 11.2
Whole Body
Operator:
Model: Delphi W (S/N 70696)
Comment:

DXA Results Summary:

<table>
<thead>
<tr>
<th>Region</th>
<th>Area (cm²)</th>
<th>BMC (g)</th>
<th>BMD (g/cm²)</th>
<th>T-Score</th>
<th>Z-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Arm</td>
<td>188.03</td>
<td>132.93</td>
<td>0.707</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R Arm</td>
<td>195.33</td>
<td>138.73</td>
<td>0.710</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L Ribs</td>
<td>79.59</td>
<td>51.21</td>
<td>0.643</td>
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<td></td>
</tr>
<tr>
<td>R Ribs</td>
<td>91.13</td>
<td>57.73</td>
<td>0.634</td>
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</tr>
<tr>
<td>T Spine</td>
<td>79.98</td>
<td>71.11</td>
<td>0.889</td>
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</tr>
<tr>
<td>L Spine</td>
<td>81.52</td>
<td>88.27</td>
<td>1.083</td>
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<tr>
<td>Pelvis</td>
<td>268.01</td>
<td>288.17</td>
<td>1.075</td>
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<tr>
<td>L Leg</td>
<td>353.75</td>
<td>380.75</td>
<td>1.076</td>
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<tr>
<td>R Leg</td>
<td>347.60</td>
<td>387.95</td>
<td>1.116</td>
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<tr>
<td>Subtotal</td>
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<td>1596.85</td>
<td>0.948</td>
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<td></td>
</tr>
<tr>
<td>Head</td>
<td>237.25</td>
<td>511.00</td>
<td>2.154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1922.19</td>
<td>2107.85</td>
<td>1.097</td>
<td>-0.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Total BMD CV 1.0%

Physician’s Comment:

Image not for diagnostic use
318 x 150

Reference curve and scores matched to White Female

Source: Hologic

6/15/2009 Project# 2009243
Renate Jonker
Scan Information:
Scan Date: March 25, 2009
Scan Type: a Whole Body
Analysis: March 25, 2009 11:02 Version 11.2
Whole Body
Operator: 
Model: Delphi W (S/N 70696)
Comment: 

DXA Results Summary:

<table>
<thead>
<tr>
<th>Section</th>
<th>BMC (g)</th>
<th>Fat (g)</th>
<th>Lean (g)</th>
<th>Lean+BMC (g)</th>
<th>Total Mass (g)</th>
<th>% Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Arm</td>
<td>132.93</td>
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<td>2020.1</td>
<td>2153.0</td>
<td>3135.6</td>
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<tr>
<td>R Arm</td>
<td>138.73</td>
<td>1002.9</td>
<td>2173.2</td>
<td>2312.0</td>
<td>3314.9</td>
<td>30.3</td>
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<tr>
<td>Trunk</td>
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<td>5600.6</td>
<td>20430.8</td>
<td>20987.3</td>
<td>26587.9</td>
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<tr>
<td>L Leg</td>
<td>380.75</td>
<td>3992.5</td>
<td>7233.9</td>
<td>7614.6</td>
<td>11607.1</td>
<td>34.4</td>
</tr>
<tr>
<td>R Leg</td>
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<td>4087.4</td>
<td>7124.3</td>
<td>7512.3</td>
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<tr>
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<td>38982.2</td>
<td>40579.1</td>
<td>56245.2</td>
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</tr>
<tr>
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<td>861.4</td>
<td>3353.1</td>
<td>3864.1</td>
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<tr>
<td>Total</td>
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<td>16527.5</td>
<td>42335.3</td>
<td>44443.1</td>
<td>60970.6</td>
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</table>

TBAR2311