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Assessment of EchoMRI-AH™ vs. Dual-energy X-ray Absorptiometry (DXA) to Measure Human Body Composition

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Abstract

Background—The sensitivity to detect small changes in body composition (fat mass and fat-free mass) largely depends on the instrument's precision. We compared EchoMRI-AH™ and DXA (Hologic QDR-4500A) for estimating fat mass in 301 volunteers.

Methods—Body composition was evaluated in 136 males and 165 females with a large range of body mass index (19–49 kg/m²) and age (19–91 y old) using DXA and EchoMRI-AH™. In a subsample of 13 lean (BMI=19–25 kg/m²) and 21 overweight/obese (BMI>25 kg/m²) individuals, within-subject precision was evaluated from repeated measurements taken within one hour ($n=3$) and one-week apart (mean of three measurements taken on each day).

Results—Using Bland-Altman analysis, we compared the mean of the fat mass measurements vs. the difference in fat mass measured by both instruments. We found that EchoMRI-AH™ quantified larger amount of fat vs. DXA in non-obese (BMI<30 kg/m²; [1.1, CI₉₅:-3.7 – 6.0 kg]) and obese (BMI ≥ 30 kg/m²; [4.2, CI₉₅:-1.4 – 9.8 kg]) participants. Within-subject precision (coefficient of variation %) in fat mass measured within one hour was remarkably better when measured by EchoMRI-AH™ than DXA (<0.5% vs. <1.5%, respectively; $p<0.001$). However, one-week apart within-subject variability showed similar values for both instruments (<2.2%; $p=0.15$).

Conclusions—EchoMRI-AH™ yielded greater fat mass values when compared with DXA (Hologic QDR-4500A), particularly in fatter subjects. EchoMRI-AH™ and DXA showed similar one-week apart precision when fat mass was measured both in lean and overweight/obese individuals.

Keywords

Obesity; Nuclear magnetic resonance; Fat mass; Lean mass; Body mass index

Introduction

Excess body fat is associated with many health impairments and contributes to excess morbidity and mortality (1). Behavioral and pharmacological treatments are available to

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reduce excess fat mass and therefore improve health (2–3). Assessment of the efficacy of these interventions requires instruments capable to measure small changes in fat mass. Recently, a quantitative nuclear magnetic resonance instrument to measure whole-body composition was introduced (EchoMRI-AH™). EchoMRI-AH™ is a non-imaging method that uses a low strength magnetic field to count hydrogen atoms and therefore measure water and fat mass with remarkable precision in small animals (4). By detecting differences in the spin characteristics between hydrogen atoms in lipid and water, EchoMRI-AH™ quantifies the mass of fat, water, and lean tissue within a subject. Importantly, EchoMRI-AH™ does not rely on ionizing radiation as does DXA. Furthermore, while the precision and accuracy of DXA can be significantly compromised by subject movements, the EchoMRI-AH™ technology is not affected by these variables.

Fat mass can be accurately measured by a 4-compartment model, which is considered the gold-standard for estimating fat mass in humans. This model includes measurements of body density, total body water, total bone mineral mass, and body weight. In humans, EchoMRI-AH™ underestimated the amount of fat mass when compared with a 4-compartment model (5). This difference was accentuated as the amount of fat mass increased (5). A similar result was observed when EchoMRI-AH™ was compared against DXA (5). Since a small number of subjects was included in that study ($n = 30$), we compared whole-body composition measured by DXA and EchoMRI-AH™ in a larger sample ($n = 301$). Additionally, we determined the within-subject body composition precision from repeated measurements taken within one hour and one-week apart.

Methods

Subjects

Three hundred and one participants (136 males and 165 females) covering a large range of age and body mass were recruited by advertising (Table 1). Distribution by sex, age and body mass index is shown in Table 2. Participants had body weight changes less than 2 kg for at least 3 months before enrollment in the study. Pregnant/lactating females or attempting to become pregnant were excluded from the study. Volunteers enrolled in pharmacological and/or lifestyle clinical trials for obesity or diabetes were excluded. Additionally, we excluded individuals with ferromagnetic materials, pacemakers or defibrillators or weighing more than 150 kg.

A sub-sample of 34 participants was recruited to assess the within-subject body composition variability using EchoMRI-AH™ and DXA. The protocol was approved by the Pennington Biomedical Research Center Institutional Review Board and all subjects provided written informed consent prior to study participation.

Experimental Design

Participants were instructed to avoid intense physical activity for the 2 days preceding body composition testing. After an overnight fast, body weight was measured while subjects wore a gown and after emptying their bladder. Then, body composition was measured using DXA and EchoMRI-AH™ in a random order. Both instruments are located in the same

temperature-controlled room (24.6 ± 0.5 °C [SD]) and both measurements were completed within 20 minutes.

In a sub-sample of 34 individuals (18 males and 16 females) and following the same protocol described above, three measurements of body composition using both instruments were performed alternately within one hour on Day 1. The exact sequence of measurements was repeated one week later (day 8). Participants were instructed to maintain their usual food intake and physical activity pattern in between those sets of measurements.

Assessment of human body composition by EchoMRI-AH™ instrument

The EchoMRI-AH™ (with proprietary software) is 3.66 m long, 1.45 m wide and 1.52 m high. The subject is introduced on a rolling sled-mounted bed into an internal 0.74 m square bore extending the length of the instrument. The bore is surrounded by a resistive electro-magnet, which generates a static low-intensity field of 0.0065 Tesla. Hydrogen nuclei are stimulated by radio frequency pulses in the magnetic field. Their subsequent relaxation generates electro-magnetic signals characteristic of the chemical environment in which the protons are incorporated. These are detected by an aerial antenna surrounding the bore and processed to derive total fat, lean, and free water masses (4). Calibration with known standards allows the expression of the numbers in kilograms. At the start of each day the instrument was calibrated according to manufacturers' instructions using 45 kg Canola rapeseed oil at room temperature. Each EchoMRI-AH™ measurement lasted less than 5 min. The instrument generates values for whole-body fat and lean (bone mass not included) masses.

Assessment of human body composition by Dual Energy X-ray Absorptiometer instrument

Whole-body composition was measured on a Hologic Dual Energy X-ray Absorptiometer (DXA) in the fan beam mode (QDR-4500A; Hologic, Waltham, MA) using the software provided by the manufacturer (QDR for Windows Version 11.1.2). The instrument generates values for whole-body fat mass, fat-free mass and bone mass. The difference between whole-body fat-free mass and bone mass was calculated and this value was compared against lean mass estimated by EchoMRI-AH™.

Statistical analysis

All analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA). Within each sex, Pearson and Bland-Altman analyses were used to compare fat and lean mass measurements obtained by EchoMRI-AH™ and DXA (6). Regression analysis was used to calculate the slope and intercept values between the differences in fat/lean mass estimated by both instruments vs. the mean in fat/lean mass. Analysis of covariance was performed to assess fat mass and lean mass differences between instruments (DXA and EchoMRI-AH™), time (days 1 and 8) and their interaction. Within-subject variability was estimated on a single day and one-week apart as the coefficient of variation (%) using one-way ANOVA to calculate the between-subject variance (S^2_b) and within-subject variance (S^2_w). Single-day within-subject variability was calculated from the 3 repeated measurements of fat and lean masses. Within-subject variability was also estimated one week apart using the average of the 3 repeated measurements taken on each week. F-tests

were used to compare variances between instruments. The 95% confidence intervals were calculated as standard deviation times 1.96. $P < 0.05$ was considered statistically significant.

Results

Agreement in body composition between EchoMRI-AH™ and DXA

Fat mass measured by EchoMRI-AH™ and DXA were highly correlated both in males and females (Figure 1). The agreement in fat mass between instruments is shown in the Bland-Altman plots in Figure 2. Males and females showed a similar pattern characterized by a direct relationship between the difference in fat mass measured by both instruments and the mean of the measurements (males: $r=0.74$; $p<0.0001$; females: $r=0.75$; $p<0.0001$). In most of the individuals and particularly those with larger fat mass, EchoMRI-AH™ determined a greater amount of fat compared to DXA with a mean difference for non-obese ($<30 \text{ kg/m}^2$) and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) individuals of 1.1 ($\text{CI}_{95}:-3.7 - 6.0$) kg and 4.2 ($\text{CI}_{95}:-1.4 - 9.8$) kg, respectively (Figure 2). In relative terms, the mean difference corresponded to 3.6 ($\text{CI}_{95}:-27 - 34$)% and 10.5 ($\text{CI}_{95}:-5 - 26$)% in non-obese and obese subjects, respectively. The slopes calculated in males and females were $0.21 \pm 0.02 \text{ kg/kg fat mass}$ ($p<0.0001$) and $0.15 \pm 0.01 \text{ kg/kg fat mass}$ ($p<0.0001$), respectively. Consistently, the difference in fat mass measured by both methods against body mass index showed a positive slope in males ($0.32 \pm 0.04 \text{ kg/unit BMI}$; $p < 0.0001$) and females (0.26 ± 0.02 ; kg/unit BMI ; $p < 0.0001$).

Lean mass measured by EchoMRI-AH™ and DXA were highly correlated both in males and females (Figure 3). Lean mass estimated by both instruments showed a better agreement in males with a slope not different from zero ($-0.048 \pm 0.034 \text{ kg/kg lean mass}$; $p=0.16$), an intercept of $-4.71 \pm 2.14 \text{ kg}$ ($p=0.03$) and a mean difference between instruments of -7.7 ($\text{CI}_{95}:-15 - -1$) kg equivalent to -11.7 ($\text{CI}_{95}:-22 - -2$)% (Figure 2). Females showed an inverse relationship between the difference in lean mass measured by both instruments and the mean of the measurements ($r=-0.44$; $p<0.0001$; slope = $-0.20 \pm 0.03 \text{ kg/kg lean mass}$; $p<0.0001$) with a mean difference between instruments of -7.5 ($\text{CI}_{95}:-14 - -2$) kg, equivalent to -15.2 ($\text{CI}_{95}:-26 - -5$)% (Figure 2). The relationship between the differences in lean mass measured by both methods with body mass index showed negative slopes in males ($-0.38 \pm 0.04 \text{ kg/unit BMI}$; $p<0.0001$) and females ($-0.32 \pm 0.03 \text{ kg/unit BMI}$; $p<0.0001$; data not shown).

Comparison of the precision

The characteristics of the subset of subjects participating in the precision study are shown in Table 3. Body weight did not change significantly after one week in lean ($0.09 \pm 0.77 \text{ kg}$; $p=0.50$; $\text{BMI}=19-25 \text{ kg/m}^2$) and overweight/obese ($-0.15 \pm 0.98 \text{ kg}$; $p=0.67$; $\text{BMI} \geq 25 \text{ kg/m}^2$) individuals. The within-subject body weight SD and coefficient of variation (CV%) were 0.53 kg and 0.8% and 0.69 kg and 0.7% in lean and overweight/obese subjects, respectively. Fat mass showed similar values between instruments ($p=0.65$) and days ($p=0.97$; Table 4). Lean mass showed similar values between days ($p=0.99$); however, DXA measured a greater amount of lean mass when compared with EchoMRI-AH™ ($p=0.03$; Table 4).

Within-subject variability in fat mass calculated from 3 repeated measurements taken within one hour was virtually identical on days 1 and 8 using both DXA or EchoMRI-AH™ ($p=0.99$; Table 4 and Figure 4; only data on day 1). Within-subject SD in fat mass measured by EchoMRI-AH™ was lower than 120 g in lean and overweight/obese individuals. This value was at least 3 times lower when compared with DXA ($p<0.001$; Table 4). In relative terms, fat mass showed a within-subject CV% lower than 0.5% for EchoMRI-AH™ and 1.5% for DXA when calculated over one hour (Figure 4). Within-subject variability in lean mass measured from 3 repeated measurements showed similar results when EchoMRI-AH™ and DXA were compared ($p=0.18$; Table 4). The within-subject CV% in lean mass measured by both instruments was around 0.45% and 0.80% in lean and overweight/obese subjects, respectively.

Within-subject variability was also calculated for fat and lean masses from mean values obtained on days 1 and 8 (Table 4 and Figure 4). When fat mass was estimated one-week apart by EchoMRI-AH™, within-subject variability was >2-fold higher than within-subject variability calculated over one hour both in lean and overweight/obese individuals ($p<0.0001$; Table 4 and Figure 4). However, DXA showed similar within-subject variability calculated over one hour or one week in both groups ($p=0.09$; Table 4 and Figure 4). In summary, one-week apart within-subject CV% for fat mass was lower than 2.2% for both instruments (Figure 4). One-week apart within-subject variability in lean mass showed a CV % lower than 1.5% in lean and overweight/obese individuals for both instruments.

The change in body weight after one week (day 8 – day 1) was compared with the change in fat and lean masses over the same period measured by DXA and EchoMRI-AH™. Mean change in fat mass for DXA was -0.13 (CI₉₅: $-1.2 - 0.9$) kg and for EchoMRI-AH™ was -0.06 (CI₉₅: $-0.88 - 0.75$) kg. The changes in body weight did not relate to the changes in fat mass measured by DXA ($r=-0.09$; $p=0.60$), whereas a significant positive association was found using EchoMRI-AH™ ($r=0.66$; $p<0.001$; Figure 5). We also found similar SD values for the change in fat mass in lean (DXA: 0.47 kg and EchoMRI-AH™: 0.36 kg; $p=0.17$) and overweight/obese (DXA: 0.54 kg and EchoMRI-AH™: 0.45 kg; $p=0.22$) individuals.

Regarding to the change in lean mass over one week, a direct association with the change in body weight was observed when DXA ($r=0.87$; $p<0.001$) and EchoMRI-AH™ ($p=0.65$; $p<0.001$) were used (data not shown).

Discussion

This study showed that EchoMRI-AH™ yielded higher fat mass values when compared with DXA (QDR 4500A). This observation is in contrast to a previous report showing that EchoMRI-AH™ yielded lesser amount of fat mass when compared with DXA (Lunar Prodigy) or a 4-compartment model (5). Methodological differences between studies might explain our divergent results. First, we did not include a 4-compartment model that would allow better comparison of measurements. Second, the measurement of fat mass depends on the hardware (DXA machine) and software (algorithms) used, which is different between

manufacturers (7–8). Finally, our study included a large sample size with large ranges of body mass index and body fat.

The underestimation of fat mass by DXA relative to EchoMRI-AH™, particularly in obese individuals, may have a physical explanation. For the DXA methodology, photons passing through tissues are absorbed or scattered (i.e., attenuation). The attenuation is a function of the length of the absorber (i.e., human body tissues) and the substance's linear attenuation coefficient (i.e., tissue chemical composition) (9). Basically, X-ray penetration decreases as tissue thickness and depth increase leading to an underestimate of the amount of fat when compared with direct analysis (10). In contrast, the measurement of fat mass by nuclear magnetic resonance should not be influenced by tissue thickness, depth or even the shape of the object to analyze. Therefore, EchoMRI-AH™ might provide a more accurate measure of fat mass in obese individuals when compared with DXA. Alternatively, QDR 4500A (DXA instrument) has repeatedly shown to underestimate fat mass when compared with criterion methods such as total body water, densitometry or a 4-compartment model. Such underestimation is around 10% when compared with a 4-compartment model (11).

EchoMRI-AH™ showed a remarkable better precision than DXA to estimate fat mass when evaluated from 3 repeated measurements performed within one hour. Since negligible changes in fat mass are expected to occur in such a short period of time, the observed errors become a surrogate for the analytical precision. In that case, an “analytical error” lower than 0.5% for EchoMRI-AH™ and 1.5% for DXA (Hologic QDR-4500A) were observed both in lean and overweight/obese individuals. However, within-subject variability calculated over one week showed similar values for both instruments, being close to 2% and 1% in lean and overweight/obese subjects, respectively.

In the present study, one-week apart precision (SD: 0.2–0.3 kg) in fat mass measured by EchoMRI-AH™ was close to calculated precision from repeated measurements taken over a day (two in the morning and two in the afternoon; SD: 0.2–0.4 kg) by Napolitano et al (5). Since Napolitano et al. (5) made some of their measurements after a meal, they speculated that the thermic effect of food and increased core temperature might increase the signal from central fat and then the total amount of fat detected. In our study, changes in core temperature are presumably lower because our measurements were always performed after an overnight fast.

As expected, body weight did not significantly change after one week. Within-subject variability was lower than 1% and similar to previously reported over a consecutive 12-day period (12). We related the change in body weight over one week with the change in fat and lean mass over the same period of time. The fluctuation in body weight was related to the change in fat mass measured by EchoMRI-AH™ but not by DXA, whereas the change in lean mass measured by DXA or EchoMRI-AH™ were both associated with the change in body weight. Assuming that most of the change in body weight is accounted for by body water gain or loss, with minimal changes in body fat, then changes in total mass and fat mass should not be related, whereas a positive association with the change in lean mass should be noted. Such prediction fits with our DXA-derived results. On the contrary, if a change in body weight was accompanied by a parallel change in fat mass, then, this is better

picked if fat mass is measured by EchoMRI-AH™. The lack of a reference method to measure body composition is impeding efforts to better measure the accuracy of DXA and EchoMRI-AH™ and therefore the ability to detect changes in body composition.

In conclusion, EchoMRI-AH™ yielded greater fat mass values when compared with DXA (Hologic QDR-4500A), particularly in fatter subjects. Since DXA has physical limitations in its ability to measure body composition from obese subjects (not the case for nuclear magnetic resonance), EchoMRI-AH™ has probably a better reliability in determining fat mass in fatter individuals. Further assessments of accuracy, specificity and sensitivity of EchoMRI-AH™ will be needed to confirm such prediction. When precision was calculated from repeated measurements taken over a short period of time (minutes), EchoMRI-AH™ showed a remarkably better precision than DXA (<0.5 vs. <1.5%, respectively). However, when precision was calculated over one week, similar values were found for both instruments (<2.2%).

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Figure 1. Relationship between fat mass measured by DXA and EchoMRI-AH™ in females (A) and males (B)

Fig. 1A: females ($n = 165$); Fig. 1B: males ($n = 136$)

Figure 2. Bland and Altman analysis for fat and lean mass measured by EchoMRI-AH™ and DXA (Hologic QDR-4500A) in females (A, C) and males (B, D)

Fig. 2A,C: females ($n = 165$); Fig. 2B,D: males ($n = 136$). Solid lines correspond to mean change and dotted lines to ± 2 SD.

Figure 3. Relationship between lean mass measured by DXA and EchoMRI-AH™ in females (A) and males (B)

Fig. 3A: females ($n = 165$); Fig. 3B: males ($n = 136$)

Figure 4. Within-subject coefficient of variation (%) in fat mass determined from repeated measurements on a single day and one-week apart

Day: From 3 repeated measurements taken within one hour (day 1).

Week: From average of 3 repeated measurements (day) taken one-week apart.

Figure 5. Association between the change in body weight and fat mass measured by DXA and EchoMRI-AH™ in lean and overweight/obese individuals

Lean ($n=13$) and overweight/obese ($n=21$) individuals represented by open and closed symbols, respectively. Solid lines correspond to mean change and dotted lines to ± 2 SD.

Table 1

Characteristics of the subjects

	Male (n=136)		Female (n=165)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Age (y)	49.2 $\pm$ 16.6	19.1 – 80.3	51.4 $\pm$ 15.2	18.7 – 90.5
Weight (kg)	95.2 $\pm$ 18.4	51.9 – 134.9	84.3 $\pm$ 18.7	44.6 – 132.6
Height (m)	176 $\pm$ 7	153 – 195	162 $\pm$ 6	144 – 178
BMI (kg/m²)	30.6 $\pm$ 5.7	19.8 – 45.0	32.0 $\pm$ 6.8	18.7 – 49.0

Table 2

Sample size distribution by sex, age and body mass index.

Age (y)	BMI (kg/m ²)			
	18.5 – 24.9	25 – 29.9	30	Total
Males				
18 – 34	14	13	9	36
35 – 44	2	7	4	13
45 – 54	3	4	18	25
55	7	14	41	62
Total	26	38	72	136
Females				
18 – 34	10	10	5	25
35 – 44	7	6	15	28
45 – 54	3	9	30	42
55	9	14	47	70
Total	29	39	97	165

Table 3

Characteristics of the subjects studied to estimate within-subject variability

	Lean	Overweight/Obese
Male / Female	5/8	11/10
Age (y)	36 ± 15	41 ± 13
Weight (kg)	65.0 ± 12.4	93.8 ± 16.9
Height (cm)	170 ± 10	170 ± 11
Body mass index (kg/m ²)	22.4 ± 2.5	32.7 ± 6.2

Mean ± SD.

Table 4

Mean, between- and within-subject variability for fat and lean masses measured by EchoMRI-AH™ and DXA (Hologic QDR-4500A).

	EchoMRI-AH™				DXA Hologic QDR-4500A			
	Mean	SD _b	SD _{w,h}	SD _{w,w}	Mean	SD _b	SD _{w,h}	SD _{w,w}
Fat mass (kg)								
Lean	15.1	7.9	0.065	0.241	15.0	6.7	0.217*	0.323
OW/Obese	33.0	23.9	0.116	0.322	31.2	20.1	0.426*	0.409
Lean mass (kg)								
Lean	44.2	13.9	0.182	0.574	48.2 [†]	15.5	0.238	0.597
OW/Obese	54.2	21.2	0.489	0.580	60.3 [†]	19.8	0.432	0.869*

OW: overweight. SD_b: between-subject variability; SD_{w,h}: within-subject variability measured within one hour (day 1); SD_{w,w}: within-subject variability measured one-week apart.

* Different from respective SD measured by EchoMRI-AH™ ($p < 0.001$). Values compared using F-test.

[†] Different from respective mean measured by EchoMRI-AH™ ($p < 0.001$). Values compared using covariance analysis.