Published in final edited form as:

Clin Nutr. 2008 December ; 27(6): 832–841. doi:10.1016/j.clnu.2008.06.007.

Multifrequency bioelectrical impedance analysis and bioimpedance spectroscopy for monitoring fluid and body cell mass changes after gastric bypass surgery☆

Jennifer R. Mager^{a,d}, Shalamar D. Sibley^{b,e}, Tiffany R. Beckman^{b,f}, Todd A. Kellogg^{c,g}, and Carrie P. Earthman^{a,*}

Jennifer R. Mager: dobra011@umn.edu; Shalamar D. Sibley: sible004@umn.edu; Tiffany R. Beckman: beckm004@umn.edu; Todd A. Kellogg: kell0018@umn.edu; Carrie P. Earthman: cearthma@umn.edu

^aDepartment of Food Science and Nutrition, University of Minnesota, 1334 Eckles Avenue, St. Paul, MN 55108-6099, USA

^bDepartment of Medicine, Endocrine Division, University of Minnesota, St. Paul, MN 55108-6099, USA

^cDepartment of Surgery, University of Minnesota, St. Paul, MN 55108-6099, USA

Summary

Background & aims—There is a growing need for clinically applicable body composition assessment tools for extremely obese individuals. The objective of this research was to evaluate several bio impedance techniques for monitoring changes in fluid, particularly intracellular water (reflecting body cell mass) after bariatric surgery.

Design—Fifteen extremely obese women (body mass index: $48.9 \pm 7.0 \text{ kg/m}^2$; age: 48 ± 9 years) were assessed before (baseline; T1), and approximately 6 weeks after gastric bypass surgery (T2) by several multifrequency bioelectrical impedance analysis approaches (MFBIA; QuadScan 4000), a bioimpedance spectroscopy device (BIS; Hydra 4200), and multiple dilution.

Results—BIS provided intracellular water estimates that were comparable to criterion, based on mean comparisons, at both time points (T1: criterion: $24.2 \pm 3.1 \text{ L}$, BIS: $24.0 \pm 3.7 \text{ L}$; T2: criterion: $20.6 \pm 3.7 \text{ L}$, BIS: $19.7 \pm 3.2 \text{ L}$). MFBIA (with Deurenberg equations) provided comparable measures to criterion only at T2 (criterion: $20.3 \pm 3.7 \text{ L}$, MFBIA: $20.6 \pm 2.7 \text{ L}$). Both MFBIA (with QuadScan proprietary equations) and BIS produced estimates of intracellular water change that were comparable to dilution. There was substantial variability in individual volume measures.

☆Conference poster presentation: Food and Nutrition Conference & Expo, Philadelphia, PA, September 29–October 2, 2007.

© 2008 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

*Corresponding author. Tel.: +1 612 624 9278; fax: +1 612 625 5272.

^dTel.: +1 612 626 5888.

^eTel.: +1 612 624 8460.

^fTel.: +1 612 626 1960.

^gTel.: +1 612 625 8425.

Conflict of interest statement: None of the authors have a financial conflict of interest in this research.

Conclusions—Although MFBIA and BIS hold promise as convenient techniques for assessing fluid changes, individual variability in measurements makes them impractical for assessment of extremely obese patients in the clinical setting.

Keywords

Bioimpedance; Multiple frequency; Obesity; Intracellular water

Introduction

Body composition assessment in extremely obese individuals is often problematic because of logistical difficulties related to patient size, equipment design, and nature of the testing protocol. Nonetheless, assessment and monitoring of body composition are important in this population, particularly as a way to evaluate the efficacy and clinical impact of weight loss interventions. Bioimpedance technologies offer clinicians the possibility of using a convenient tool to assess body composition and fluid compartments.

Multiple frequency bioelectrical impedance analysis (MFBIA) differs from the more commonly utilized single frequency bioelectrical impedance analysis in that bioimpedance data is obtained at several different frequencies, allowing for quantification of extracellular water (ECW) at low frequencies (e.g. 1 or 5 kHz), and total body water (TBW) at higher frequencies (e.g. 100, 200, or 500 kHz).¹ Intracellular water can be assessed by subtraction of the two measured water compartments: $TBW - ECW = ICW$. BIS is a different multifrequency approach that consists of bioimpedance measurements across a range of frequencies (5–1000 kHz). With the software accompanying the BIS devices manufactured by Xitron Technologies, San Diego, CA (e.g. the 4000B and the newer Hydra 4200), data undergo nonlinear curve fitting based on the Cole—Cole model.² Cole model terms can then be applied to equations derived from Hanai mixture theory^{3,4} for calculation of ECW and ICW, and by summation, TBW.

The ability of these techniques to quantify ICW would be particularly advantageous to clinicians, because ICW provides a close approximation to body cell mass (BCM), which is the lean tissue compartment representing the metabolically active and energy-consuming tissue.⁵ The focused assessment of the ICW compartment is thus ideal when the objective is to monitor and limit lean tissue loss, as it would be in extremely obese individuals undergoing rapid weight loss after gastric bypass surgery. In addition, obese individuals have abnormal fluid distribution that may remain after weight loss.^{6–10} The ability to monitor changes in both ECW and ICW (and BCM) would be advantageous for patient care. Thus, the purpose of this study was to compare MFBIA and BIS with multiple dilution for the measurement of fluid volumes and BCM in extremely obese women over a period of rapid weight loss.

Materials and methods

Women were recruited from the Weight Management Center at the University of Minnesota Medical Center — Fairview; study participants were extremely obese, and planned to undergo the laparoscopic Roux-en-Y gastric bypass procedure. This longitudinal evaluation

was part of a larger clinical study, and involved inpatient testing at the General Clinical Research Center (GCRC): baseline, before surgery (T1), and ~6 weeks post-operatively (T2). Exclusion criteria included: use of corticosteroids, testosterone, or anabolic agents; liver, renal, or heart failure; pulmonary hypertension; thyroid disease (included if treated and within normal limits); neoplastic disease; or Type 1 or uncontrolled Type 2 diabetes mellitus. The study protocol was reviewed and approved by the Institutional Review Board and the GCRC at the University of Minnesota, and subjects provided written, informed consent before participating in the study.

Participants were instructed the day before admission to the GCRC to avoid caffeine, alcohol and vigorous exercise for 24 h before testing. Participants received 1600 ml of IV hydration at a rate of 200 ml/h during the afternoon of Day 1 of their admission. They were provided a dinner meal at the GCRC, and were fasted after 8 pm with the exception of water.

Multiple dilution

TBW and ECW were measured by deuterium and bromide dilution, respectively. A fasted, baseline blood and urine sample was taken at 7 am. A 3% (weight/volume) sodium bromide solution (NaBr; Sigma Chemical, St. Louis, MO) was infused by IV at a rate of 300 ml/h to provide a dose of 1 ml 3% NaBr solution/kg body weight. Approximately 10 min before completion of the NaBr infusion, a weighed dose of deuterium oxide (99.9 atom %; Isotec, Miamisburg, OH) providing 0.1 g/kg body weight was IV pushed over a 5-min period. Completion of the NaBr infusion marked the start of a 4-h equilibration period during which subjects did not eat or drink anything. Hourly urine samples were collected, as well as a final blood and urine sample at 4-h post-infusion.

All serum and urine samples were tightly sealed, packed on dry ice, and stored at -70°C . Serum samples (for ECW assessment) were shipped to Pennington Biomedical Research Center (Baton Rouge, LA) for analysis; bromide enrichment was measured by high performance liquid chromatography.¹¹ The coefficient of variation (CV) for bromide measurements by this technique is ~5%.¹¹ ECW volume was corrected by 10% for nonextracellular distribution and 5% for the Donnan equilibration.¹² Baseline, and 3- and 4-h post-dose urine samples were shipped to Dr. Michael Jensen's laboratory at the Mayo Clinic (Rochester, MN) for analysis; deuterium enrichment was measured by isotope ratio mass spectrometry (model Thermo Delta V Advantage; Thermo Fisher Scientific, Waltham, MA). The intra-assay CV for samples injected into the Delta V instrument was found to be ~1%. The inter-assay CV for two quality control (QC) samples run over a 1-year period ($n = 47$) was 4.73% for the low QC sample (90 delta per mil) and 6% for the high QC sample (600 delta per mil). TBW was calculated from the average deuterium enrichment of the 3- and 4-h urine samples, following the method of Halliday and Miller,^{13,14} and then reduced by 4% to correct for exchange with the nonaqueous compartment.¹⁴

Bioimpedance measurements

Subjects were instructed to remove all metal from their clothing and body before measurements. Electrodes were placed in a standard, tetrapolar arrangement,¹⁵ assuring that

the distance between hand and foot electrodes was recorded at baseline and repeated at all subsequent measurements. Subjects were encouraged to walk around for 3 min after electrodes were placed before assuming a still, supine position. Arms and legs were abducted from the body, and in order to completely separate leg and arm tissue, a rolled blanket was placed snugly between the legs and between the arms and trunk. Measurements were taken at 10-min after assuming a supine position, in accordance with recommendations by Ellis et al.¹⁶

The MFBIA device, QuadScan 4000 (Bodystat Ltd, Isle of Man, British Isles), measured bioimpedance at 5, 50, 100, and 200 kHz. Impedance (Z) values at 5 kHz were utilized for assessment of ECW, and 100 or 200 kHz for TBW, depending on the prediction equation, as shown in Table 1. Upon reviewing the published literature, prediction equations were chosen for validation in the current study based on several criteria: (1) if an equation was regressed from a population of overweight or obese individuals, and found to be most accurate in a study, and (2) if an equation was regressed from a population of non-obese individuals, and was found to be most accurate in a subsequent validation study that included overweight or obese individuals. Bioimpedance data needed for entry into the chosen prediction equations were obtained from the QuadScan device. Only those equations that utilized variables measured by the QuadScan device were included for validation (e.g. Z at 5 kHz). In addition, the QuadScan device is programmed with proprietary equations; the water volume values obtained directly from the software accompanying the device were also evaluated in our analyses. As variables in the prediction equations, height was measured using a stadiometer (model S100, Ayrtton Corporation, Prior Lake, MN), and weight by a digital scale (model 5002, Scale-Tronix, White Plains, NY). Also, the GCRC dietitians measured hip circumference of the study participants following the method described in the Anthropometric Standardization Manual.¹⁷ The average value of two hip circumference measurements was used in the prediction equations. Finally, the Hydra 4200 (Xitron Technologies, San Diego, CA) BIS device was also evaluated in this study. The Hydra 4200 was used to estimate ECW, ICW and TBW through the device software, which subjects the bioimpedance data to Cole—Cole modeling with subsequent application of modeled terms to equations developed from Hanai mixture theory.^{3,4} The same-day interobserver mean absolute differences (MAD) and technical errors (TE) for the MFBIA method (Xitron 4000B device) were reported to be ~1% (or 4—9 ohms) for resistance up to 1 MHz and for reactance up to 200 kHz, with greater errors (up to ~28 ohms) above 200kHz.¹⁸ The MAD, TE, and CV for ECW and ICW measurements by BIS (Xitron Hydra 4200 device) have also been evaluated previously. The interday, interobserver TE and MAD with electrode repositioning were 0.072L and 0.022L for ECW, respectively and 0.110 L and 0.066L for ICW, respectively. CVs for ECW and ICW measurements with electrode repositioning were reported to be 1.28% (0.013 L) and 1.72% (0.017 L), respectively.¹⁹

Statistical analyses

TBW, ECW and ICW absolute volume measurements by the multiple dilution (i.e. criterion) method were compared to measurements by each MFBIA method and BIS by paired t -tests and correlation analyses (r). Volume changes from T1 to T2 were calculated; paired t -tests were performed to compare volume changes by the criterion method with each

bioimpedance method. Bland—Altman (B—A) plots²⁰ were created for ICW, our primary clinical outcome measure, in terms of absolute volumes and volume changes, to allow for a visual inspection of the individual data, and evaluation of agreement between methods. A significance (α) of 0.10 was used for comparison between multiple dilution and MFBIA methods, in order to minimize the possibility of making a Type 2 error (falsely accepting the null hypothesis of no differences between methods), given our relatively small sample size. The software SPSS version 12.0 (SPSS, Chicago, IL) was utilized for statistical analyses.

Results

A detailed description of subject characteristics has been provided in Table 2. TBW and ICW, as determined by criterion methods, decreased after surgery (T1—T2); there was no difference between the decrease in TBW compared to the decrease in ICW from T1 to T2 (3.6 ± 3.3 vs. 3.8 ± 3.5 L, respectively; $P = 0.657$). ECW did not change (T1—T2). The calculated TBW/weight ratio remained stable from T1 to T2. On the contrary, the ECW/weight ratio increased post-operatively (T1—T2). The ECW/TBW and ECW/ICW ratios also increased post-operatively (T1—T2).

Absolute volumes

Table 3 provides a summary of the mean comparisons between the criterion method and each bioimpedance method for absolute volumes. At T1, the Hydra BIS device provided absolute volume measurements of TBW, ECW, and ICW that were not different from those measured by multiple dilution; no other methods consistently produced volume measurements that were comparable to the criterion. However, TBW, ECW, and ICW measured by all the bio-impedance methods were correlated to criterion measures.

At T2, all methods yielded measures of TBW, ECW, and ICW that were correlated with those by the criterion method. The QuadScan device with proprietary equation (QP) was the only method that provided ECW measures that were not different from criterion; measures of TBW and ICW by the QP method were different from criterion. Both the QuadScan with Deurenberg equations (QD) method and BIS yielded estimates of ICW that were not different from the criterion.

Volume changes

Table 4 provides a summary of the comparisons between the criterion method and each bioimpedance method for the change in TBW, ECW and ICW from T1 to T2. Criterion-measured ECW did not significantly change between time points, and for all methods, the calculated ECW change values were associated with relatively large standard deviation values. Therefore, the errors in ECW change measures were larger than the actual criterion-measured ECW change, making it difficult to draw meaningful conclusions from comparisons between criterion-measured and bioimpedance-estimated changes in ECW from T1 to T2. From baseline to T2, only the QP and BIS methods yielded measures of TBW and ICW change that were not significantly different from criterion-measured changes.

Bland–Altman and analyses of error

Although it appears that several methods were able to produce measures of body water volumes, as well as volume changes that were not different from criterion on the basis of group mean comparisons, there may be significant variability between individuals. In order to provide a visual inspection of our primary clinical outcome measure, B–A plots were constructed comparing each bioimpedance method with criterion at T1 for ICW volumes and ICW volume changes. The B–A plots for ICW absolute volumes are presented in Fig. 1. For all methods, the limits of agreement were wide at all time points, with data points spread evenly around the mean of the difference between methods. One data point consistently fell outside the limits of agreement at T2.

The B–A plots for ICW volume change (Fig. 2) also indicate variability on the individual level. For all methods, the magnitude of error is often more than 100% of the criterion-measured change in ICW. Considering that the average mean change in ICW measured by criterion from T1 to T2 was 3.8 L, the magnitude of potential error in any individual measure of change makes all of these techniques unreliable on an individual basis.

Discussion

The rise in obesity in the United States presents a challenge to clinicians who are in the position of caring for the ever-increasing numbers of obese and extremely obese patients. Body composition assessment in obese patients undergoing treatment has not been a routine component of clinical care, given the methodological limitations of commonly available methods such as anthropometry. Monitoring changes in ICW in particular, would allow for both quantitative and qualitative evaluation of an obese person's response to weight loss treatments. Our primary goal was to validate MFBIA and BIS against multiple dilution as clinical tools for evaluating fluid status and lean tissue changes in extremely obese individuals after bariatric surgery. This kind of evaluation has been recognized as important in the ESPEN guidelines,^{21,22} and can contribute to improvements in clinical practice.

In our hands, on the basis of *t*-test comparisons, BIS appeared to agree best with multiple dilution for the estimation of absolute volumes and change of TBW and ICW in our extremely obese subjects. The QP method also produced TBW and ICW change measures that were not different from criterion; however, for the most part, it yielded measures of absolute volumes that differed from criterion. Interestingly, the QD method yielded less consistent results, only sometimes providing absolute volume and volume change estimates that did not differ from criterion. On the basis of B–A plots, it appears that all MFBIA and BIS techniques are problematic on the individual level.

There are a limited number of published cross-sectional studies that have investigated the accuracy of MFBIA in overweight and obese individuals,^{8,23–26} although to our knowledge, none have focused solely on the extremely obese population. Two of the studies were notably different from the others, in that one was in obese children,⁸ and one used an eight-polar electrode placement, rather than the standard tetrapolar arrangement.²⁶ The study by Sartorio et al.²⁶ was also the only one to specify a clear delineation of an extremely obese subgroup. The rest of the studies reported mean BMI values in the 30–35 kg/m² range.

Nevertheless, it is useful to compare the results from these studies with those from the current study.

The majority of reviewed studies reported reasonable agreement between the MFBIA technology and the multiple dilution. Several investigators found that several MFBIA equations were able to accurately predict mean absolute volumes of TBW and ECW in overweight and obese individuals; although none of these reported ICW volumes.^{8,23–26} When inaccuracies were reported in the studies we reviewed, the errors were primarily in the direction of overestimation. For example, two out of the five MFBIA equations investigated by Bedogni et al.,⁸ and three out of the five MFBIA equations studied by Steijaert et al.²³ significantly overestimated TBW. Steijaert et al.²³ also found that two out of the three MFBIA equations tested for ECW volumes yielded significant overestimations.

These are not entirely different from our findings. We found that the QP method overestimated TBW at both time points. Interestingly, the TBW equations derived from obese individuals (De Lorenzo et al.^{24,25}) also produced significant overestimation errors of TBW. These equations included the variable of squared hip circumference, which could potentially skew the TBW estimates upward if an obese individual presented with substantial abdominal adiposity. Because these equations were developed in an obese, but not extremely obese population, it is likely that they would be less accurate in our study population. Moreover, it is possible that additional error could have been introduced due to the difficulties in obtaining accurate hip circumference measurements in extremely obese individuals, who frequently have multiple abdominal adipose folds. Our results differed from those reported by Steijaert et al.²³ with regard to the accuracy of the Deurenberg equations,²⁷ which were developed in a relatively lean population. Although they reported that the equations produced measures of both TBW and ECW that were not different from criterion,²³ we found that they underestimated TBW and ECW at all time points.

The BIS technology has also been evaluated in obese individuals. In a cross-sectional study, Cox-Reijven et al.²⁸ found that a Xitron 4000B BIS device using software programmed with the Hanai mixture theory-based equations yielded TBW volumes that were not different from the criterion, but produced ECW estimates that were different. However, BIS measures of both TBW and ECW were correlated to the criterion measures.

There are important issues that should be considered when evaluating the results of absolute volume, cross-sectional data comparisons. The sole reliance on cross-sectional data for the validation of a method is limited, and may be misleading. Cross-sectional comparisons between methods may yield differences when absolute volumes are compared by paired *t*-tests, despite high correlations between methods.¹⁹ This can occur as a result of scaling differences between the current criterion method and the bioimpedance method that may have been calibrated to a different criterion method in its development; therefore, absolute volume data should not be used alone to validate a method. Perhaps a more potent test of the validity of a particular body composition assessment method is its accuracy to measure *changes* in TBW, ECW, and ICW volumes during periods of overall body water and composition change. Evaluation of a method based upon the measurement of volume changes can minimize the impact of scaling differences between methods, and provide

useful information regarding the validity of a method. In the current study, we aimed to evaluate the bioimpedance techniques for their ability to measure *longitudinal changes* in water volume.

One other group of investigators has evaluated the accuracy of BIS to measure volume changes in an extremely obese population.²⁹ In a 1-year longitudinal study of patients undergoing vertical banded gastroplasty, Cox-Reijven et al.²⁹ reported change in TBW and ECW compared to criterion from baseline (before surgery) to 2 weeks, 3 months, and 1 year after surgery. They did not report ICW volumes or changes. A thorough critique of this study can be found elsewhere.³⁰ The Xitron 4000B BIS device yielded estimates of ECW change from baseline to 2 weeks, 3 months, and 1 year after surgery that were not different from criterion. By 1 year after surgery, TBW loss was overestimated by the BIS device, with a mean overestimation of 5 L. However, BIS was found to underestimate TBW change from baseline to 2 weeks after surgery, but yielded estimates of TBW change from baseline to 3 months after surgery that were not different from criterion. In the current study, we found BIS to yield estimates of TBW change that were not different from criterion-measured TBW change from before surgery to approximately 6 weeks post-operatively, based on mean data comparisons.

There are several considerations to be made in light of the current research. First, the fact that the equations programmed into the QuadScan device remain proprietary warrants some concern. Although the device provided reasonable estimates of TBW and ICW changes in the current study, these results should be interpreted with caution. It is possible that the manufacturer could make future changes in the programmed equations in the device, thus invalidating our results. Second, the potential influence of methodological error was considered. Error can theoretically be introduced at the level of the criterion method, as well as the bioimpedance techniques. In terms of the criterion method, errors due to dosing and sampling were minimized as much as possible by strict adherence to a carefully designed IV dilution protocol. Generally speaking, errors may be introduced to bioimpedance methods by failing to adhere to standard guidelines for testing, such as appropriate placement of electrodes, maintenance of moderate ambient temperatures, and assurance of a subject's euhydrated status. In our study, we maintained strict adherence to standard guidelines, e.g. having the subject abstain from caffeine and vigorous exercise 24-h before testing, providing standardized hydration the evening before each testing session, and ensuring that the testing room was maintained at a comfortable ambient temperature.

Specific to the extremely obese population, the accuracy of MFBIA and BIS may be affected by several methodological concerns. For example, the standard protocol for performing bioimpedance measurements is to abduct the limbs from the body in order to obtain a clear path for the bioelectrical current. In the extremely obese individual, it is quite difficult to accomplish complete limb separation. We attempted to minimize this problem by placing rolled cotton blankets between the legs, and between each arm and the trunk. In addition, certain assumptions regarding the translation of the bioimpedance technology to the calculation of body are violated in extremely obese individuals. First, bioimpedance methods assume that the body is made of a homogeneous conducting material, and consistent cross-sectional width.¹ The underlying bioimpedance principle, $V = \rho L^2 / R$ (V :

volume of conducting material, R : resistance in ohms, L : length of conductor in cm, ρ : specific resistivity in $\text{cm} \times \text{ohms}$)³¹ may be violated, particularly in obese individuals because of the lack of homogeneity across body tissues (e.g. variability in specific resistivity), and the variability in the cross-sectional width of the body. Because of the nature of the equation, the resistance measured in the legs and arms contributes substantially to the overall body resistance; the limbs have the greatest length and the smallest cross-sectional area, and the resistance is inversely proportional to the cross-sectional area.¹ Those individuals who carry excessive abdominal fat are likely to violate this assumption to a greater extent than those with more evenly distributed body fat. Second, a concern relevant to any bioimpedance approach (MFBIA and BIS) that has been suggested by others^{29,32,33} is that adiposity, both in degree and distribution, can affect resistance and yield variable responses across the extremely obese population, particularly when a prediction equation derived from one population is applied to a different population. The BIS approach requires the use of specified resistivity constants; it has been suggested that obesity-specific resistivity constants may enhance the accuracy of BIS in the extremely obese population.²⁹ Lastly, for the MFBIA approaches, such as the Deurenberg equation²⁷ and the De Lorenzo equations (1995²⁵ and 1999²⁴), the accuracy of the approach depends on the regression equation. Specifically, the population that the equation was derived from, as well as the variables included in the equation, can vary and influence the accuracy when applied to a different group of individuals. Further, the above equations utilize a set upper frequency of 100 kHz is utilized for the calculation of TBW. The upper frequency required for the complete quantification of TBW has been shown to vary in studies utilizing the BIS approach, based on differences in fluid distribution and cell membrane integrity. For example, individuals on dialysis have been observed to require frequencies upwards of 200 kHz to obtain complete quantification of the TBW compartment.⁴ Only the BIS approach offers the flexibility of measuring bioimpedance over the entire spectrum of frequencies, thus allowing for a more individualized approach to the measurement of water volumes. In conclusion, although we found that both the Hydra 4200 BIS device and the QuadScan MFBIA device (with proprietary equations) produced measures of TBW and ICW change that were not different from our criterion on the basis of mean level comparisons, the individual variability in measurements make these techniques impractical for the assessment of extremely obese women in the clinical setting. Given the underlying theoretical basis and convenience of these technologies, the MFBIA and BIS approaches continue to hold promise as tools for monitoring fluid and body cell mass changes in extremely obese individuals. Additional research is warranted to investigate the factors that affect bioimpedance measurements in extreme obesity, in order to minimize error.

Acknowledgments

Grants/funding: Funding for this study was provided by the Rhoads Research Foundation of the American Society for Parenteral and Enteral Nutrition, by U.S. Public Health Service grant DK50456 which provides support for Dr. Michael Jensen's Metabolic Studies Core at the Mayo Clinic; Grant MO1-RR00400 from the National Center for Research Resources, the National Institutes of Health, which supports the General Clinical Research Center at the University of Minnesota; the Minnesota Agricultural Experiment Station; and the Midwest Dairy Association. None of the study sponsors had involvement in any aspect of the study design, data collection or analyses, or writing of this manuscript.

Other contributors: We thank the study participants for their commitment to our study, and the team at the Fairview Obesity Surgery Center and the GCRC at the University of Minnesota for their ongoing support of this study. We thank Dr. Michael Jensen, Charles Ford, and Jaime Gransee at the Mayo Clinic for their assistance with the deuterium analyses. We also thank Dr. Dale Schoeller for his input on the total body water method.

Statement of authorship: JM served as the study coordinator, participated in the recruitment of subjects, was involved in the collection, management, and analysis of data, and drafted the manuscript. SS participated in the collection of data, served as a study physician, and provided significant advice/consultation in study planning. TB participated in the collection of data, and served as a study physician. TK assisted with recruitment of subjects as the bariatric surgeons overseeing obesity surgery patients at the Weight Management Center. CE was the PI of the project and senior author of the manuscript, and was primarily responsible for the study design, and providing oversight of all aspects of the study. All authors read, provided feedback, and approved the final manuscript.

References

1. Buchholz AC, Bartok C, Schoeller DA. The validity of bioelectrical impedance models in clinical populations. *Nutr Clin Pract*. 2004; 19:433–46. [PubMed: 16215137]
2. Cole KS. Permeability and impermeability of cell membranes for ions. *Cold Spring Harbor Symp Quant Biol*. 1940; 8:110–22.
3. Hanai, T. Electrical properties of emulsions. In: Sherman, PH., editor. *Emulsion science*. London: Academic Press; 1968. p. 354–477.
4. De Lorenzo A, Andreoli A, Matthie J, Withers P. Predicting body cell mass with bioimpedance by using theoretical methods: A technological review. *J Appl Physiol*. 1997; 82:1542–58. [PubMed: 9134904]
5. Moore FD, Boyden CM. Body cell mass and limits of hydration of the fat-free body: Their relation to estimated skeletal weight. *Ann N Y Acad Sci*. 1963; 110:62–71. [PubMed: 14062407]
6. Marken Lichtenbelt WD, Fogelholm M. Increased extracellular water compartment, relative to intracellular water compartment, after weight reduction. *J Appl Physiol*. 1999; 87:294–8. [PubMed: 10409587]
7. Battistini N, Virgili F, Severi S, et al. Relative expansion of extracellular water in obese vs. normal children. *J Appl Physiol*. 1995; 79:94–6. [PubMed: 7559253]
8. Bedogni G, Bollea MR, Severi S, Trunfio O, Manzieri AM, Battistini N. The prediction of total body water and extracellular water from bioelectric impedance in obese children. *Eur J Clin Nutr*. 1997; 51:129–33. [PubMed: 9076401]
9. Mazariegos M, Kral JG, Wang J, et al. Body composition and surgical treatment of obesity. Effects of weight loss on fluid distribution. *Ann Surg*. 1992; 216:69–73. [PubMed: 1632704]
10. Waki M, Kral JG, Mazariegos M, Wang J, Pierson RN Jr, Heymsfield SB. Relative expansion of extracellular fluid in obese vs. nonobese women. *Am J Physiol*. 1991; 261:E199–203. [PubMed: 1872382]
11. Miller ME, Cappon CJ. Anion-exchange chromatographic determination of bromide in serum. *Clin Chem*. 1984; 30:781–3. [PubMed: 6713640]
12. Miller ME, Cosgriff JM, Forbes GB. Bromide space determination using anion-exchange chromatography for measurement of bromide. *Am J Clin Nutr*. 1989; 50:168–71. [PubMed: 2750689]
13. Halliday D, Miller AG. Precise measurement of total body water using trace quantities of deuterium oxide. *Biomed Mass Spectrom*. 1977; 4:82–7. [PubMed: 884210]
14. Schoeller, DA. Hydrometry. In: Roche, AF.; Heymsfield, SB.; Lohman, TG., editors. *Human body composition*. Champaign, IL: Human Kinetics; 1996. p. 25–43.
15. Lukaski HC, Bolonchuk WW, Hall CB, Siders WA. Validation of tetrapolar bioelectrical impedance method to assess human body composition. *J Appl Physiol*. 1986; 60:1327–32. [PubMed: 3700310]
16. Ellis KJ, Bell SJ, Chertow GM, et al. Bioelectrical impedance methods in clinical research: a follow-up to the NIH technology assessment conference. *Nutrition*. 1999; 15:874–80. [PubMed: 10575664]
17. Lohman, TG.; Roche, AF.; Martorell, R. *Anthropometric standardization reference manual*. Champaign, IL: Human Kinetics Books; 1991.

18. Chumlea WC, Guo SS, Bellisari A, Baumgartner RN, Siervogel RM. Reliability for multiple frequency bioelectrical impedance. *Am J Human Biol.* 1994; 6:195–202.
19. Earthman CP, Matthie JR, Reid PM, Harper IT, Ravussin E, Howell WH. A comparison of bioimpedance methods for detection of body cell mass change in HIV infection. *J Appl Physiol.* 2000; 88:944–56. [PubMed: 10710390]
20. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986; 1:307–10. [PubMed: 2868172]
21. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis – part I: review of principles and methods. *Clin Nutr.* 2004; 23:1226–43. [PubMed: 15380917]
22. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. *Clin Nutr.* 2004; 23:1430–53. [PubMed: 15556267]
23. Steijaert M, Deurenberg P, Van Gaal L, De Leeuw I. The use of multi-frequency impedance to determine total body water and extracellular water in obese and lean female individuals. *Int J Obes Relat Metab Disord.* 1997; 21:930–4. [PubMed: 9347412]
24. De Lorenzo A, Sorge RP, Candeloro N, Di Campi C, Sesti G, Lauro R. New insights into body composition assessment in obese women. *Can J Physiol Pharmacol.* 1999; 77:17–21. [PubMed: 10535661]
25. De Lorenzo A, Sasso GF, Andreoli A, Sorge R, Candeloro N, Cairella M. Improved prediction formula for total body water assessment in obese women. *Int J Obes Relat Metab Disord.* 1995; 19:535–8. [PubMed: 7489022]
26. Sartorio A, Malavolti M, Agosti F, et al. Body water distribution in severe obesity and its assessment from eight-polar bioelectrical impedance analysis. *Eur J Clin Nutr.* 2005; 59:155–60. [PubMed: 15340370]
27. Deurenberg P, Tagliabue A, Schouten FJ. Multi-frequency impedance for the prediction of extracellular water and total body water. *Br J Nutr.* 1995; 73:349–58. [PubMed: 7766559]
28. Cox-Reijven PL, Soeters PB. Validation of bioimpedance spectroscopy: effects of degree of obesity and ways of calculating volumes from measured resistance values. *Int J Obes Relat Metab Disord.* 2000; 24:271–80. [PubMed: 10757619]
29. Cox-Reijven PL, van Kreel B, Soeters PB. Accuracy of bioelectrical impedance spectroscopy in measuring changes in body composition during severe weight loss JPEN. *J Parenter Enteral Nutr.* 2002; 26:120–7.
30. Chertow GM. With bioimpedance spectroscopy, the errors get fat when the patients get slim JPEN. *J Parenter Enteral Nutr.* 2002; 26:128–9.
31. Hoffer EC, Meador CK, Simpson DC. Correlation of whole-body impedance with total body water volume. *J Appl Physiol.* 1969; 27:531–4. [PubMed: 4898406]
32. Coppini LZ, Waitzberg DL, Campos AC. Limitations and validation of bioelectrical impedance analysis in morbidly obese patients. *Curr Opin Clin Nutr Metab Care.* 2005; 8:329–32. [PubMed: 15809537]
33. Deurenberg P. Limitations of the bioelectrical impedance method for the assessment of body fat in severe obesity. *Am J Clin Nutr.* 1996; 64:449S–52S. [PubMed: 8780361]

Non-standard abbreviations

B–A	Bland–Altman
BCM	body cell mass
BIS	bioimpedance spectroscopy
D₂O	deuterium oxide
ECW	extracellular water
GCRC	General Clinical Research Center

ICW	intracellular water
MFIA	multiple frequency bioelectrical impedance analysis
NaBr	sodium bromide
T1	Time 1, or the baseline, before surgery time point
T2	Time 2, or ~6 weeks after surgery
QD	QuadScan device with the Deurenberg equation(s)
QP	QuadScan device with the proprietary equation(s)

Figure 1.

(A) Agreement between hydra bioimpedance device and multiple dilution method for intracellular water (ICW) at time. (B) Agreement between QuadScan device with proprietary equations and multiple dilution for measuring intracellular water (ICW) at Time 1. (C) Agreement between QuadScan device with equations and multiple dilution method for intracellular water (ICW) at Time 1.

Figure 2.

(A) Agreement between hydra bioimpedance device and multiple dilution method for intracellular water (ICW) changes from Time 1 to Time 2. (B) Agreement between QuadScan device with proprietary equations and multiple dilution method for intracellular water (ICW) changes from Time 1 to Time 2. (C) Agreement between QuadScan device with equations and multiple dilution method for intracellular water (ICW) changes from Time 1 to Time 2.

Table 1
Equations for calculation of total body water, extracellular water, and intracellular water from bioimpedance data

Method	Label	Equation calculation	Subject population	Criterion method
<i>Total body water</i>				
De Lorenzo et al. ²⁵	A. TBW _{100Z}	$0.069 * [ht * C^2 / (4\pi * Z_{100})] + 19.671$	Overweight to obese F	² H ₂ O dilution
De Lorenzo et al. ²⁴	B. TBW _{5Z&100Z}	$0.0242 * (V/Z_5) + 0.3048 \{V[(Z_5 * Z_{100}) / (Z_5 - Z_{100})] + 22.0319, \text{ where } V (\text{body volume, cm}^3) = (\text{hip } C^2) * (Ht/4\pi)\}$	Overweight to obese F	² H ₂ O dilution
Deurenberg et al. ²⁷	C. TBW _{100Z}	$0.51303 * (Ht^2/Z_{100}) + 6.29$	Relatively lean (M and F)	² H ₂ O dilution
QuadScan MFBIA device	D. TBW _{200Z}	Unpublished equation/proprietary	NA	NA
Hydra BIS device	E. TBW _∞	Cole-Cole modeling/Hanai mixture theory-derived equations	NA	NA
<i>Extracellular water</i>				
Deurenberg et al. ²⁷	A. ECW _{5Z}	$0.23413 * (Ht^2/Z_5) + 4.2$	Relatively Lean (M and F)	Br dilution
QuadScan MFBIA device	B. ECW _{5Z}	Unpublished equation/proprietary	NA	NA
Hydra BIS device	C. ECW ₀	Cole-Cole, Hanai Mixture Theory	NA	NA
<i>Intracellular water</i>				
Deurenberg et al. ²⁷	A. TBW _{100Z} - ECW _{5Z}	$\{0.51303 * (Ht^2/Z_{100}) + 6.29\} - \{0.23413 * (Ht^2/Z_5) + 4.2\}$	Relatively lean (M and F)	NA
QuadScan MFBIA device	B. ICW _{BS}	Unpublished equation/proprietary	NA	NA
Hydra BIS device	C. ICW _{∞-0}	Cole-Cole modeling/Hanai mixture theory-derived equations	NA	NA

Abbreviations: C, Hip circumference; ECW, extracellular water; F, Female; Ht, Height; ICW, Intracellular water; M, Male; R, Reactance; TBW, Total body water; Wt, Weight; and Z, Impedance.

Table 2
Description of study participants

	Time 1	Time 2
Age (years)	48.4 ±9.2	
Weight (kg)	133.9±22.7	120.0 ±21.3 *
Height (cm)	165.3 ±4.7	
BMI (kg/m ²)	48.9 ±7.0	43.8 ±6.7 *
Hip circumference (cm)	149.5± 13.8	
TBW, L	44.7±6.1	41.1 ±5.6 *
ECW, L	20.6 ±3.9	20.9 ±3.4
ICW, L	24.1 ±3.0	20.3 ±3.7 *
TBW (kg)/weight (kg)	0.334 ±0.034	0.344 ±0.035
ECW (kg)/weight (kg)	0.153 ±0.009	0.174 ±0.019 *
ECW (L)/TBW (L)	0.459 ±0.036	0.507 ±0.048 *
ECW (L)/ICW (L)	0.857 ±0.120	1.044 ±0.188 *

Abbreviations: BMI, body mass index; ECW, extracellular water; ICW: intracellular water; L, liters; and TBW, total body water. Data provided as mean ± standard deviation.

TBW, ECW, and ICW are criterion measures of body water (TBW, by deuterium dilution, ECW by bromide dilution, and ICW by, subtraction, or TBW – ECW = ICW).

* Statistically significant change from T1 to T2 ($P < 0.01$).

Table 3

Absolute volumes of criterion-measured and bioimpedance-estimated total body water, extracellular water, and intracellular water

Label	Time 1 (n=15)				Time 2 (n=15)			
	Volume (L)	P-value ^d	r	P-value ^b	Volume (L)	P-value ^d	r	P-value ^b
<i>Total body water</i>								
Criterion								
² H ₂ O dilution	44.7 ± 6.1				41.1 ± 5.6 [*]			
De Lorenzo et al. ²⁵	A. TBW _{100Z}	<0.001	0.85	<0.001	59.4 ± 13.2 [*]	<0.001	0.84	<0.001
De Lorenzo et al. ²⁴	B. TBW _{5Z&100Z}	<0.001	0.79	<0.001	58.3 ± 10.7 [*]	<0.001	0.78	0.001
Deurenberg et al. ²⁷	C. TBW _{100Z}	<0.001	0.93	<0.001	36.7 ± 4.7 [*]	<0.001	0.85	<0.001
QuadScan proprietary equation	D. TBW _{200Z}	<0.001	0.90	<0.001	47.2 ± 6.7 [*]	<0.001	0.88	<0.001
BIS	E. TBW _∞	0.889	0.81	<0.001	39.6 ± 6.1 (n = 14) [*]	0.05	0.86	<0.001
<i>Extracellular water</i>								
Criterion								
NaBr dilution	20.6 ± 3.9				20.8 ± 3.4			
Deurenberg et al. ²⁷	A. ECW _{5Z}	<0.001	0.93	<0.001	16.1 ± 1.9	<0.001	0.89	<0.001
QuadScan proprietary equation	B. ECW _{5Z}	<0.001	0.96	<0.001	20.9 ± 2.8 [*]	0.699	0.88	<0.001
BIS	C. ECW ₀	0.802	0.93	<0.001	20.0 ± 3.4 (n = 14) [*]	0.043	0.89	<0.001
<i>Intracellular Water</i>								
Criterion								
² H ₂ O–NaBr dilution	24.1 ± 3.0				20.3 ± 3.7 [*]			
Deurenberg et al. ²⁷	A. TBW _{100Z} – ECW _{5Z}	0.002	0.76	0.001	20.6 ± 2.7 [*]	0.789	0.54	0.037
QuadScan proprietary equation	B. ICW _{BS}	<0.001	0.60	0.019	26.3 ± 3.9 [*]	<0.001	0.59	0.020
BIS	C. ICW _{∞-0}	0.960	0.55	0.041	19.7 ± 3.2 (n = 14) [*]	0.323	0.57	0.035

Abbreviations: BIS, bioimpedance spectroscopy; ECF, extracellular fluid; ICF, intracellular fluid; L, liters; and TBF, total body fluid. Data provided as mean ± standard deviation. Impedance data from the QuadScan device were utilized for the De Lorenzo et al.,²⁵ De Lorenzo et al.,²⁴ and Deurenberg et al.²⁷ equations.

The N listed at the top of the column pertains to the number of subjects at each visit. One data point was missing for the BIS method at both Time 1 and 2 (n = 14); the missing BIS data at each Time are different subjects.

^{*} Statistically significant change from T1 to T2 (P < 0.05).

^d P-value provided t-test for t-test comparisons between criterion and each bioimpedance method within the same time point (T1 and T2).

^bCorrelation analyses performed between criterion and each bioimpedance method within same time point (T1 and T2).

Table 4
Change in criterion-measured versus. bioimpedance-estimated total body water, extracellular water, and intracellular water volumes

Method	Label	Baseline to Time 2 (<i>n</i> = 15)	
		Mean ± SD	<i>P</i> -value ^a
<i>Total body water</i>			
Criterion	² H O dilution	3.6± 3.3	
De Lorenzo et al. ²⁵	A. TBW _{100Z}	7.8 ±4.2	0.005
De Lorenzo et al. ²⁴	B. TBW _{5Z&100Z}	11.7±4.1	<0.001
Deurenberg et al. ²⁷	C. TBW _{100Z}	1.8± 1.8	0.078
QuadScan proprietary equation	D. TBW _{200Z}	4.0 ± 1.2	0.633
BIS	E. TBW _∞	5.3±2.5 (<i>n</i> = 13)	0.180
<i>Extracellular water</i>			
Criterion	NaBr dilution	−0.2 ± 1.7	
Deurenberg et al. ²⁷	A. ECW _{5Z}	0.3 ±0.8	0.179
QuadScan proprietary equation	B. ECW _{5Z}	1.3±0.6	0.002
BIS	C. ECW ₀	0.9± 1.1 (<i>n</i> = 13)	0.057
<i>Intracellular water</i>			
Criterion	² H ₂ O–NaBr dilution	3.8±3.5	
Deurenberg et al. ²⁷	A. TBW _{100Z} −ECW _{5Z}	1.4± 1.1	0.030
QuadScan proprietary equation	B. ICW	2.7±0.6	0.286
BIS	C. ICW _{∞−0}	4.5± 1.8 (<i>n</i> = 13)	0.508

Abbreviations: BIS, bioimpedance spectroscopy; ECF, extracellular fluid; ICF, intracellular fluid; L, liters; and TBF, total body fluid. Data provided as mean ± standard deviation.

Impedance data from the QuadScan device were utilized for the De Lorenzo et al.,²⁵ De Lorenzo et al.,²⁴ and Deurenberg et al.²⁷ equations.

The *N* listed at the top of the column pertains to the number of subjects at each visit. One data point was missing for the BIS method at both Time 1 and 2, and the missing BIS data at each Time are different subjects; thus, *n* = 13 for Hydra measures of change.

^a*P*-value provided for comparison of criterion to each bioimpedance method within the same time (T1 and T2).