Proton magnetic resonance spectroscopy for assessment of human body composition[1,2]

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ABSTRACT

Background: The usefulness of magnetic resonance spectroscopy (MRS)–based techniques for assessment of human body composition has not been established.

Objective: We compared a proton MRS-based technique with the total body water (TBW) method to determine the usefulness of the former technique for assessment of human body composition.

Design: Proton magnetic resonance spectra of the chest to abdomen, abdomen to pelvis, and pelvis to thigh regions were obtained from 16 volunteers by using single, free induction decay measurement with a clinical magnetic resonance system operating at 1.5 T. The MRS-derived metabolite ratio was determined as the ratio of fat methyl and methylene proton resonance to water proton resonance. The peak areas for the chest to abdomen and the pelvis to thigh regions were normalized to an external reference (≈2200 g benzene) and a weighted average of the MRS-derived metabolite ratios for the 2 positions was calculated. TBW for each subject was determined by the deuterium oxide dilution technique.

Results: The MRS-derived metabolite ratios were significantly correlated with the ratio of body fat to lean body mass estimated by TBW. The MRS-derived metabolite ratio for the abdomen to pelvis region correlated best with the ratio of body fat to lean body mass on simple regression analyses ($r = 0.918$). The MRS-derived metabolite ratio for the abdomen to pelvis region and that for the pelvis to thigh region were selected for a multivariate regression model ($R = 0.947$, adjusted $R^2 = 0.881$).

Conclusion: This MRS-based technique is sufficiently accurate for assessment of human body composition. *Am J Clin Nutr* 2001;73:172–6.

KEY WORDS Men, body composition, deuterium oxide, fat, nuclear magnetic resonance, water, women

INTRODUCTION

Although estimates of human body composition are made with a wide variety of techniques (1, 2), no one technique is optimal for all clinical circumstances. There is a need for a body-composition-measurement technique that is rapid, safe, sufficiently accurate, and feasible for clinical practice. We proposed a proton magnetic resonance spectroscopy (MRS)–based technique for measurement of human body composition (3). Proton MRS resolves resonances of various metabolites, including water and fat methyl and methylene groups. The ratio of fat methyl and methylene proton resonance to water proton resonance indicates the fat content relative to that of visible water that can be measured by MRS. Results of our preliminary study showed good linear relations between the MRS-derived metabolite ratio and the ratio of oil weight to water weight for an experimental phantom and the ratio of fat to lean body mass for the human body estimated by bioelectrical impedance analysis (3). In the present study, we compared our MRS-based technique with the total body water technique to determine the accuracy and usefulness of the former method for assessment of human body composition.

SUBJECTS AND METHODS

Sixteen volunteers (7 men and 9 women) were enrolled as participants. Their mean (±SD) age was 43.2 ± 13.7 y. The body mass index (in kg/m^2) of the participants ranged from 20.2 to 37.6 (27.7 ± 4.2). Individuals with metallic implants other than dental work and those with medical conditions contraindicating either MRS examination or deuterium oxide administration (eg, pregnancy, lactation, severe claustrophobia, and a poor general condition) were excluded from the study. After the subjects were given a complete description of the study, written, informed consent was obtained. This study was approved by the Ethics Committee of Tottori University.

MRS was performed with a Magnetom Vision (Siemens, Erlangen, Germany) operating at 1.5 T with an embedded body coil. We used liquid fluorocarbon pads (Sat Pad; Alliance Pharmaceutical, San Diego) and a multiangle projection shim (4) to improve static magnetic field homogeneity. Nonlocalized proton MR spectra were acquired from the human body by using single, free induction decay (FID) with a flip angle of 90° and 512 data points at a spectral width of 1 kHz. Five FIDs were obtained at 1-min intervals. The result of our previous study showed that an observed MR signal originates within 25 cm of the magnet isocenter in Z direction (3). Because of the active volume of the embedded body coil, MR spectra were obtained at 3 different positions: the chest to

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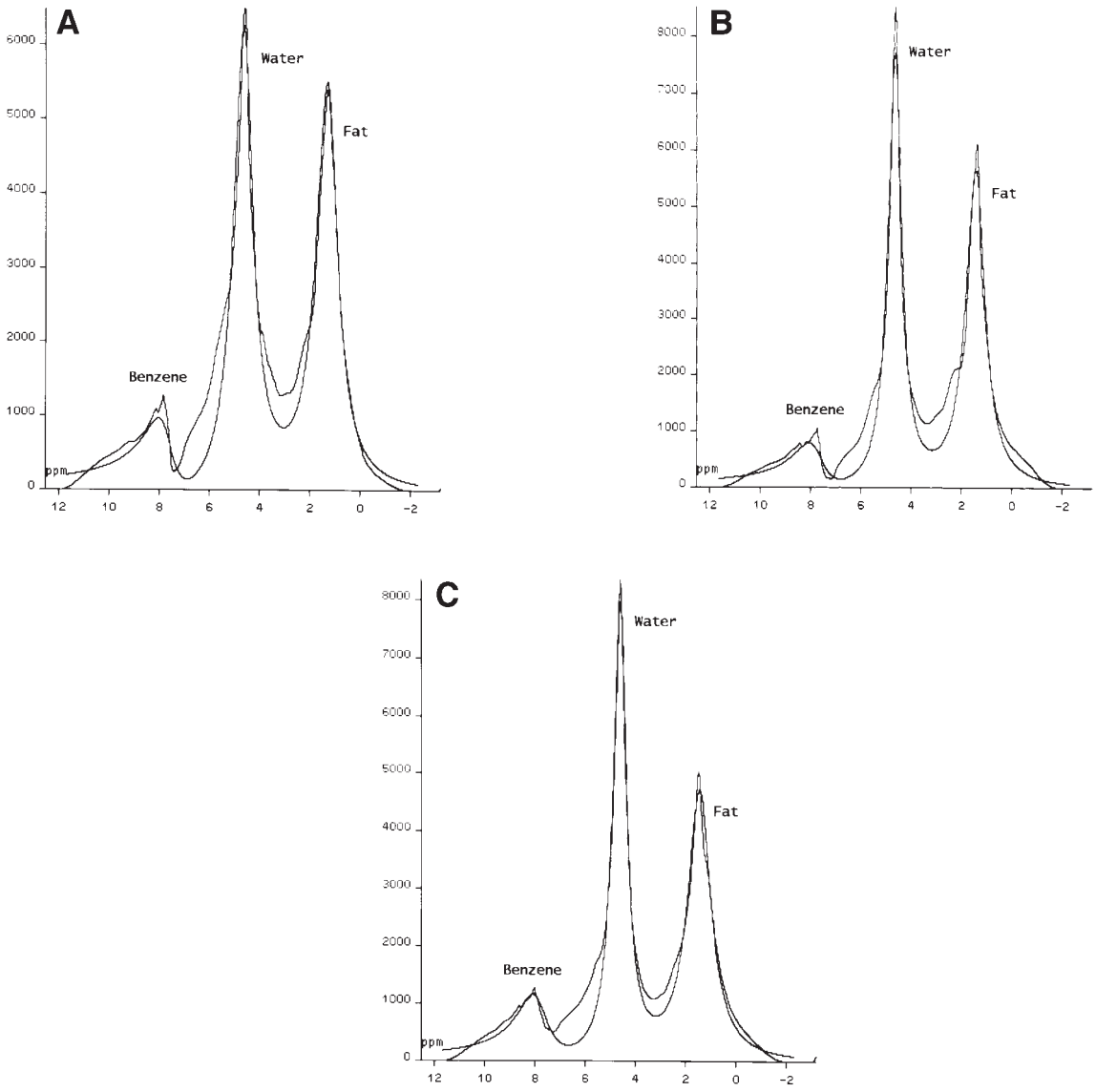

FIGURE 1. Representative magnetic resonance spectra for a 52-y-old woman for the chest to abdomen (A), abdomen to pelvis (B), and pelvis to thigh (C) regions, including fitted lines. Resonances of protons of fat methyl and methylene, water, and benzene are resolved.

abdomen, the abdomen to pelvis, and the pelvis to thigh regions. The xiphoid process, umbilicus, and midpoint between the superior anterior iliac process and the top of the patella were used as anatomical landmarks. We placed a bottle of benzene (≈2200 g) at the level of the magnet isocenter under the subject and used it as an external reference. This procedure required ≈50 min.

Acquired FIDs were processed by using Luise software (Siemens). The raw data with 512 points were converted to data with 1024 data points by filling the latter half of the 1024 points with zeros. No apodization was applied. After fast Fourier transformation, spectral data were obtained through manual phase and baseline correction. Peak areas and resonance line widths (full width at half maximum) for water protons, methyl and methylene protons, and benzene protons were calculated by fitting the spectrum to a sum of Lorenzian curves. The positions of the water peak and the methyl and methylene peak were restricted to 0.5 ppm of the starting values. Restrictions on the position, width, and phase of the benzene peak and an upper limit for the width of the water peak were determined to minimize the effects of resonance from the protons of HC = CH (5.5 ppm), a shoulder of the water peak, on the fitting model. The MRS-derived metabolite ratio was defined as the ratio of fat methyl and methylene proton resonance to water proton resonance. The MRS-derived metabolite ratio and resonance line widths for each position were determined by averaging results from the 5 measured FIDs. The peak areas for the chest to abdomen and the pelvis to thigh regions were normalized to the benzene proton resonance, and a weighted average of the MRS-derived metabolite ratios for the 2 positions was calculated from the 5 FIDs for each position.

Total body water was determined by the deuterium oxide dilution method (2, 5, 6). The subjects were given ≈1 g D_2O (99.9 atom% D; Isotec, Miamisburg, OH)/kg body wt orally diluted in a quantity of drinking fluid to ensure a concentration of ≤20% D_2O. No further

food or drink was consumed after administration of deuterium oxide. The subjects rested in bed to avoid sweating. Urine samples were collected before and 1, 2, and 3 h after administration of deuterium oxide. The urine samples were distilled and the concentrations of deuterium oxide were determined by infrared spectrophotometry. Absorption at 2510 cm^{-1} was measured by using an FT/IR-5300 infrared spectrophotometer with a calcium fluoride cell with a thickness of 0.1 mm (JASCO, Tokyo). Total body water was estimated by using the amount of deuterium oxide administered and the equilibrium urine deuterium oxide concentration. Body fat was calculated under the assumption that 73.2% of lean body mass is water (2, 7).

Each participant came to the Tottori University Hospital (Yonago City, Japan) at 0800 after fasting for ≥10 h. The MRS measurements were performed first. The total body water measurement was made after height and body weight were measured. These procedures required ≈4.5 h.

Linear regression analysis was used to assess relations between the MRS-derived metabolite ratios and the ratio of body fat to lean body mass. Analysis of covariance was used to test for homogeneity of regression lines. Explanatory variables for a multivariate regression model were selected by using a stepwise method. One-way analysis of variance was used to compare mean line widths of resonances of water protons and fat methyl and methylene protons for spectra from the 3 positions. Tukey's honestly significant difference test was used post hoc. The level of statistical significance was set at $P < 0.05$. SPSS for WINDOWS (SPSS Japan, Tokyo) was used for the statistical analyses. The results are expressed as means ± SDs.

RESULTS

Representative spectra from the human body are shown in **Figure 1**. Resonances of protons of water, fat methyl and methylene, and benzene were resolved. There were significant linear relations between the ratio of fat to lean body mass estimated by total body water and the MRS-derived metabolite ratios for the 3 positions and the weighted average of the MRS-derived metabolite ratios for the chest to abdomen and the pelvis to thigh regions (**Figure 2**). The homogeneity of slopes and means was not rejected by analysis of covariance ($P = 0.867$ and 0.319, respectively). However, homogeneity of residual variances was rejected ($P = 0.002$).

Two models were selected for predicting the ratio of body fat to lean body mass by multivariate regression analyses. The regression equations were as follows:

$$\text{Fat:lean body mass} = 1.508\ (95\%\ \text{CI: } 1.088, 1.929) \times \text{MRS}_{\text{abdomen to pelvis}} - 0.444\ (95\%\ \text{CI: } -0.813, -0.074) \times \text{MRS}_{\text{pelvis to thighs}} - 0.110\ (95\%\ \text{CI: } -0.295, 0.074) \quad (1)$$

where $R = 0.947$, $R^2 = 0.897$, and adjusted $R^2 = 0.881$ ($P = 3.83 \times 10^{-7}$), respectively.

$$\text{Fat:lean body mass} = 1.083\ (95\%\ \text{CI: } 0.816, 1.350) \times \text{MRS}_{\text{abdomen to pelvis}} - 0.101\ (95\%\ \text{CI: } -0.319, 0.116) \quad (2)$$

where $R = 0.918$, $R^2 = 0.844$, and adjusted $R^2 = 0.832$ ($P = 5.16 \times 10^{-7}$), respectively, and where $\text{MRS}_{\text{abdomen to pelvis}}$ is the MRS-derived metabolite ratio for the abdomen to pelvis region and $\text{MRS}_{\text{pelvis to thighs}}$ is the MRS-derived metabolite ratio for the pelvis to thigh region.

Resonance line widths of water protons for the chest to abdomen, abdomen to pelvis, and pelvis to thigh regions were 74.3 ± 16.1, 58.4 ± 9.6, and 53.4 ± 10.2 Hz, respectively. There was a significant intergroup difference in the resonance line width of water protons ($P < 0.001$). The resonance line width for the chest to abdomen region was significantly broader than those for the abdomen to pelvis and pelvis to thigh regions ($P = 0.002$ and $P < 0.001$, respectively). Resonance line widths of fat methyl and methylene protons for the chest to abdomen, abdomen to pelvis, and pelvis to thigh regions were 89.3 ± 24.5, 67.9 ± 13.3, and 74.0 ± 14.5 Hz, respectively. There was a significant intergroup difference in the resonance width of fat methyl and methylene protons ($P = 0.005$). The resonance line width for the chest to abdomen region was significantly broader than that for the abdomen to pelvis region ($P = 0.005$).

DISCUSSION

MRS enables assessment of resonances from fatty acid chains and has been used to evaluate the regional fat content of various locations of the human body, including the liver and muscle (8–10). Although there are a few reports on use of MRS-based techniques to assess the relative fat content of small animals at high magnetic fields (11, 12), the applicability of this method to assessment of human body composition has not been established. Our MRS-based technique resolved resonances of protons of water, fat methyl and methylene, and benzene, and enabled assessment of the fat content relative to that of water. There was a linear relation between the ratio of the fat methyl and methylene proton resonance to the water proton resonance and the ratio of body fat to lean body mass estimated by the total body water method. Thus, we conclude that this MRS-derived metabolite ratio can be used as an indicator of human body composition.

Assessment of the relative fat content by the MRS-derived metabolite ratio is based on the assumption that the concentration of MRS visible water in lean body mass is constant in healthy adult subjects. Therefore, our MRS-based technique cannot be used for subjects with an abnormal water content or distribution, including subjects with edema and ascites. Our MRS-based technique is similar to the total body water method in this regard. Our technique, however, enables assessment of body water and fat independently.

Our MRS-based technique is relatively rapid, requiring ≈15 min at each position, including 5 successive measurements (3). Postprocessing of our MRS-based technique is easier than that for magnetic resonance imaging (MRI)-based techniques, which require image analyses of multiple sections for segmentation of adipose tissue, correction of image artifacts, and volume calculation (13–15). Unlike MRI-based techniques, our MRS-based technique, which does not have spatial resolution, cannot distinguish fat in organs and bone marrow from that in adipose tissue. MRI studies for assessment of adipose tissue distribution can be performed consecutively. The relative fat content and adipose tissue distribution can be rapidly assessed by combined use of our MRS-based technique and MRI. Our MRS-based technique is noninvasive, usable with a clinical magnetic resonance system, and probably useful in clinical practice.

The MRS-derived metabolite ratio for the abdomen to pelvis region correlated best with the ratio of body fat to lean body mass on simple regression analyses. Resonances of water protons and fat methyl and methylene protons were clearly sepa-

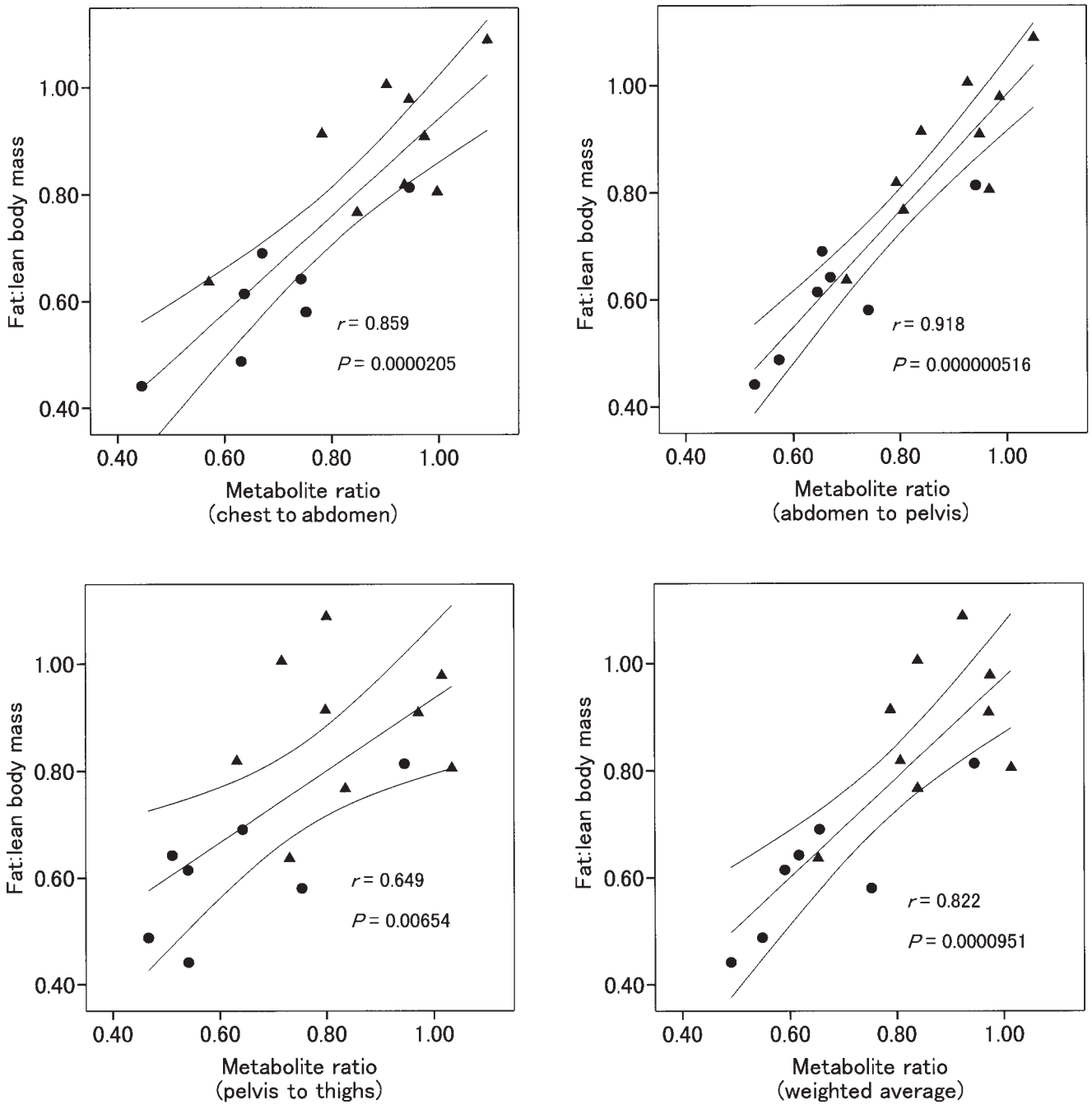

FIGURE 2. Relations in men (●) and women (▲) between the ratio of body fat to lean body mass estimated by total body water and the magnetic resonance spectroscopy (MRS)–derived metabolite ratios for the chest to abdomen, abdomen to pelvis, and pelvis to thigh regions, and the weighted average of the MRS-derived metabolite ratios for the chest to abdomen and pelvis to thigh regions. Lines are means and 95% CIs for the estimates.

rated from each other in spectra from this region, enabling precise area calculation. Results of previous studies of adipose tissue measurement with computed tomography and MRI showed that cross-sectional adipose tissue area obtained in the abdominal region was highly predictive of total body fat (13, 16–19). Our findings appear compatible with these results.

Significant resonance line broadening was found in spectra for the chest to abdomen region. Magnetic susceptibility effects due to irregular body shape and air in the lungs produced resonance line broadening and probably led to errors in determination of the MRS-derived metabolite ratio for this region. This explanation does not hold true for considerable errors in the regression model for the pelvis to thigh region. Another explanation for errors in the regression model for the pelvis to thigh region is regional differences in relative fat content. Cross-sectional adipose tissue areas of the legs were less correlated with total body fat than were those of the chest and abdomen (16). A negative correlation was found between the fractional amount of

adipose tissue in the legs and that in the trunk (18). Compared with obese women, lean women had more adipose tissue in the thighs than in the abdomen (13). These previous findings and our own findings agree that the fat content of the thighs is not suitable for predicting total body fat. The weighted average of the MRS-derived metabolite ratios for the chest to abdomen and pelvis to thigh regions did not cancel out errors in estimates for the ratio of body fat to lean body mass.

The best prediction of the ratio of body fat to lean body mass was obtained by combined use of the MRS-derived metabolite ratio for the abdomen to pelvis region and that for the pelvis to thigh region (Equation *1*). A negative correlation between the MRS-derived metabolite ratios for these 2 positions in this equation appears compatible with the previous findings of adipose tissue distribution (13, 18). The best single predictor of the ratio of body fat to lean body mass was the MRS-derived metabolite ratio for the abdomen to pelvis region (Equation *2*). Removal of the MRS-derived metabolite ratio for the pelvis to thigh region from the regression model led to a slight deterioration in the accuracy of predicting the ratio of body fat to lean body mass. These findings suggest that the MRS-derived metabolite ratio for the abdomen to pelvis region is the most useful and a sufficiently accurate predictor of total body composition.

Our MRS-based technique enabled assessment of body fat in combination with water. The technique is relatively rapid, safe, accurate, and feasible for use in clinical practice. Improvements in technical aspects, including automatic postprocessing, are needed to increase the ease of use and efficiency of this method. Further investigation is needed to determine the characteristics that will enable the most efficient use of this method for the assessment of human body composition.

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