8-1-2011

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Technical Note

Evaluation of Adipose Tissue Volume Quantification With IDEAL Fat–Water Separation

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Purpose: To validate iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) for adipose tissue volume quantification. IDEAL allows MRI images to be produced only from adipose-containing tissues; hence, quantifying adipose tissue should be simpler and more accurate than with current methods.

Materials and Methods: Ten healthy controls were imaged with 1.5 Tesla (T) Spin Echo (SE), 3.0T T1-weighted spoiled gradient echo (SPGR), and 3.0T IDEAL-SPGR. Images were acquired from the abdomen, pelvis, mid-thigh, and mid-calf. Mean subcutaneous and visceral adipose tissue volumes were compared between the three acquisitions for each subject.

Results: There were no significant differences ($P > 0.05$) between the three acquisitions for subcutaneous adipose tissue volumes. However, there was a significant difference ($P = 0.0002$) for visceral adipose tissue volumes in the abdomen. Post hoc analysis showed significantly lower visceral adipose tissue volumes measured by IDEAL versus 1.5T ($P < 0.0001$) and 3.0T SPGR ($P < 0.002$). The lower volumes given by IDEAL are due to its ability to differentiate true visceral adipose tissue from other bright structures like blood vessels and bowel content that are mistaken for adipose tissue in non-fat suppressed images.

Conclusion: IDEAL measurements of adipose tissue are equivalent to established 1.5T measurement techniques for subcutaneous depots and have improved accuracy for visceral depots, which are more metabolically relevant.

KNOWLEDGE OF THE distribution of adipose tissue is of great clinical and research importance as visceral adipose tissue and hepatic lipid content are associated with the long-term development of type 2 diabetes and cardiovascular disease (1,2). Specifically, it is the visceral component of the abdominal adipose tissue that is more metabolically relevant and most intimately associated with metabolic disease and adverse outcomes (1,2). However, while the knowledge of the volume and distribution of adipose tissue is important, it is difficult to quantify adipose tissue volume using most imaging acquisitions. For instance, computed tomography (CT) scans use ionizing radiation, which brings into question the safety of such methods and limits their use. In addition, ultrasound technology is not useful for adipose tissue volume quantification as ultrasonic waves have difficulty penetrating through significant superficial adipose tissue.

MRI using T1-weighted image acquisition at 1.5 Tesla (T) has been shown to be a sensitive, replicable, noninvasive, and safe method to determine the distribution of adipose tissue (3). Nonetheless, existing MRI methods for evaluating adipose tissue volume are generally based on non-fat suppressed imaging and require manual differentiation between adipose tissue and other non-adipose structures that have similar signal intensity on the image such as blood vessels and bowel content. This is time consuming and potentially prone to errors.

Therefore, we set out to validate and use an investigational version of the iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) technique, which allows MR images to be produced only from adipose-containing tissues, allowing in turn for better adipose tissue volume quantification (4–6). Because IDEAL images show only adipose tissue, quantifying adipose tissue volume should be simpler, quicker, and more accurate than current methods. Our aim was to validate IDEAL for adipose tissue volume measurements. We

compared measurements of adipose tissue volume from IDEAL images acquired on a 3.0T MRI system to similar measurements derived from T1-weighted MRI acquisitions made at both 3.0T and 1.5T.

MATERIALS AND METHODS

Study Subjects

Ten healthy controls (mean age, 34 years; 5 males and 5 females) were recruited. For the male subjects, average height was 179 cm (standard deviation [SD] ± 7 cm), average weight 77 kg (SD ± 11 kg), and average BMI 24 (SD ± 2.3). For the female subjects, average height was 168 cm (SD ± 5 cm), average weight 65 kg (SD ± 4.9 kg), and average BMI 23 (SD ± 2.1). All subjects provided informed consent to participate and human ethics approval was obtained from the University of Western Ontario Institutional Review Board (protocol #10854E and 7481).

Magnetic Resonance Imaging

All subjects were imaged with standard MRI (London Health Sciences Centre, London, Ontario); scanning was performed on a 1.5T MRI (CV/I, GE Healthcare, Waukesha, WI) and images were acquired using a T1-weighted Spin Echo (SE) pulse sequence in an image acquisition protocol previously validated for adipose tissue volume measurement (7). Images were acquired from the abdomen, pelvis, mid-thigh, and mid-calf. Data acquisition was performed during an end-expiratory breath hold during abdominal imaging.

This imaging was repeated with the same subjects on the same day on a 3.0T MRI (MR Discovery 750, GE Healthcare, Waukesha, WI) at a second site (Robarts Research Institute, London, Ontario). The 1.5T protocol was repeated at 3.0T with minor modifications for imaging the pelvis, thigh and calf. In the abdomen, it was not possible to use a SE pulse sequence due to constraints on specific absorption rate (SAR), so a T1-weighted spoiled gradient echo (SPGR) pulse sequence was used instead. To evaluate fat–water separated imaging for adipose tissue volume quantification, an investigational version of the 3D IDEAL-SPGR chemical shift imaging sequence was used to acquire images from all four anatomical locations. A T2* corrected IDEAL reconstruction that incorporates accurate spectral modeling of fat signal (8) was used to create "fat-only" and "in-phase" (water plus fat) images from the data collected with the IDEAL-SPGR pulse sequence. See Table 1 for image acquisition parameters.

Adipose Tissue Quantification Method

A previously validated adipose tissue quantification protocol was used for the standard 1.5T spin echo MR images, the 3.0T T1-weighted SPGR images and the 3.0T IDEAL-SPGR fat images (7). For each MRI data set acquired, the subcutaneous adipose tissue volume was quantified using ImageJ image analysis software (version 1.34 n), specifically using the Connected Threshold Grower and Voxel Counter tools. Subcutaneous

Table 1
Image Acquisition Parameters

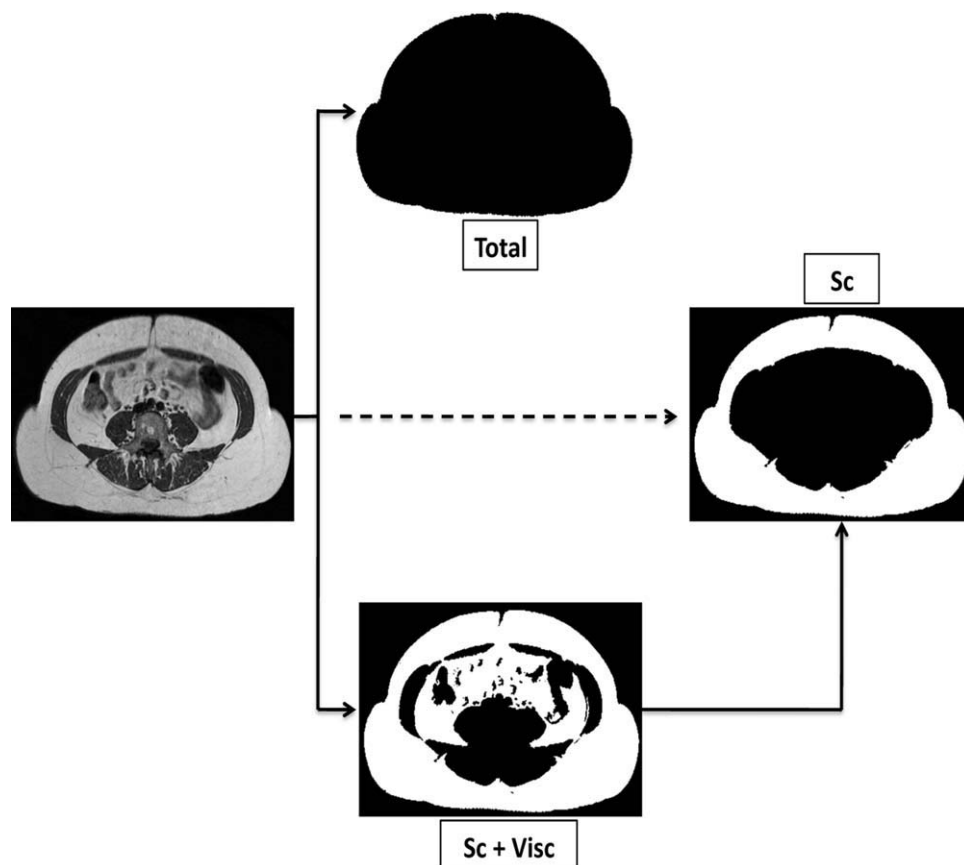|	Region	Sequence	TR (ms)	TE (ms)	Matrix (pixels)	Slices	FOV (mm)	Slice thickness (mm)	Flip angle (°)	Bandwidth (kHz)	Number of averages	Acquisition time (s)	Receiver coil
1.5T	Abdomen	SE	600.0	14.0	256 × 256	1	480	3.0	90	15.63	2	80	Body
	Gluteal	SE	150.0	14.0	256 × 256	1	480	10.0	90	15.63	2	80	Body
	Mid-thigh												
	Mid-calf												
3T	Abdominal	SPGR	4.1	2.1	256 × 256	32	480	3.0	15	62.5	1	18	8 element torso
	Gluteal	SE	200.0	13.0	256 × 256	1	480	10.0	90	20.83	2	80	Body
	Mid-thigh												
	Mid-calf												
IDEAL	Abdominal	SPGR	11.4	6 echoes 1.0–9.0 ms	224 × 160	32	480	6.0	5	142.86	1	21	8 element torso
	Gluteal	SPGR	11.4	6 echoes 1.0–9.0 ms	224 × 224	32	480	6.0	5	142.86	1	61	Body
	Mid-thigh												
	Mid-calf												

Figure 1. Quantification of % adipose tissue in abdominal region. For a given axial MR image, both the total volume and the subcutaneous (sc) and connected visceral (sc + visc) adipose tissue volumes were selected using the Connected Threshold Grower tool. The sc adipose tissue cannot be obtained directly due to software limitations, and is selected for by manually eliminating visceral signals present in (sc + visc) images. Their corresponding volumes were determined using the Voxel Counter tool. The % sc adipose tissue was calculated by dividing the voxel count determined for the sc adipose tissue by the total voxels for the slice. The %visc adipose tissue was calculated by subtracting the sc adipose tissue voxel count from that of sc + visc and then dividing the value obtained by the total voxels for the slice. Solid lines in the figure represent direct automated attainment of threshold image by means of ImageJ. Dotted lines represent indirect attainment of threshold image, requiring manual modification (9).

adipose tissue was defined as the adipose tissue that circulated the circumference of the anatomical region of interest, adjacent to the skin. Visceral adipose tissue volume, defined as adipose tissue adjacent to the viscera, was quantified for the abdominal region using a similar approach. Each voxel was classified as either fat or water following the method of Al-Attar et al (7).

Abdominal (at the level of the L4 vertebra), gluteal (at the level of the femoral heads), mid-thigh (at the mid-point of the femur), and mid-calf (at the mid-point of the tibia) adipose tissue volumes were calculated for all imaging measurements for a single slice in each anatomic region.

For a given axial MR image, the total volume, the subcutaneous adipose tissue volume, and the total connected subcutaneous and visceral) adipose tissue volumes were selected. Quantification of subcutaneous adipose tissue was done indirectly by manually eliminating visceral signals present in the total connected subcutaneous and visceral adipose tissue volumes and dividing by the total threshold signal (Fig. 1) (9). Quantification of visceral adipose tissue in the abdominal region was then calculated by subtracting

the subcutaneous adipose tissue signal from total connected subcutaneous and visceral signals and dividing by the total threshold signal (Fig. 1) (9). Marrow tissue and intramuscular adipose tissue were excluded from all our calculations. Adipose tissue volume measurements from 1.5T SE, 3.0T SPGR, and 3.0T IDEAL were compared for volume variability.

Statistical Analysis

Subcutaneous and visceral adipose tissue volumes for all 3 acquisitions were statistically analyzed using VassarStats (Web Site for Statistical Computation, Vassar College, Poughkeepsie, NY) and Microsoft Excel version 12.2.0 (Microsoft Corporation). Mean subcutaneous and visceral adipose tissue volume measures were compared between the three acquisitions (1.5T SE, 3.0T SPGR, and 3.0T IDEAL) for each subject with one-way repeated measures analysis of variance (ANOVA) using VassarStats. A post hoc paired sample two-tailed t-test was then used to compare abdominal visceral adipose tissue volume measurements between the three acquisitions using
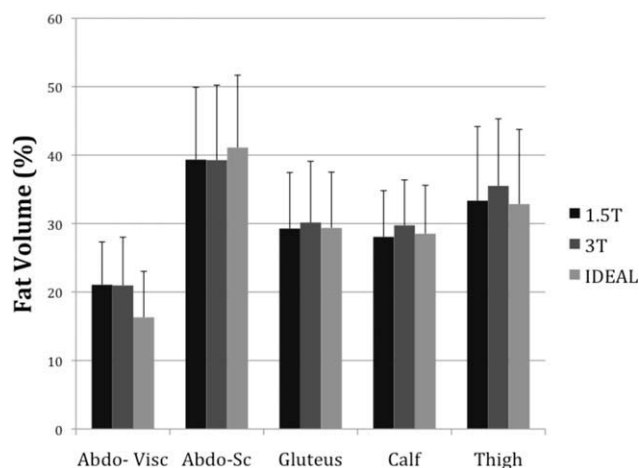
Figure 2. Mean adipose tissue volume measurements for all subjects as a percent of total volume in the slice analyzed for the following regions: Abdominal Visceral (Abdo-Visc), Abdominal Subcutaneous (Abdo-Sc), Gluteus, Calf, and Thigh. Mean volumes are being compared between the three acquisitions (1.5T, 3T, and IDEAL). The error bars indicate one standard deviation.

Microsoft Excel. A nominal *P*-value < 0.05 was chosen as the threshold for significance for all statistical comparisons.

RESULTS

The standard MRI acquisitions with T1-weighted SE or SPGR sequences provided a bright, high-threshold adipose tissue signal in raw image data, relative to other tissues and background. Other tissues, such as muscle and connective tissue, appeared as dark regions with low threshold values in MR images. IDEAL provided images with bright regions that corresponded to adipose tissue only, with no signal from lipid free tissues.

Mean adipose tissue volumes as a percent of total volume in the slice analyzed are shown in Figure 2. One-way repeated measures ANOVA showed no significant differences (*P* > 0.05) between the three acquisitions for subcutaneous adipose tissue volume measurements in the abdominal, gluteal, mid-thigh, and mid-calf regions. However, when the three acquisitions were compared for visceral adipose tissue volume measurements in the abdominal region the null hypothesis of no difference was rejected with *P* = 0.0002. This led us to perform post hoc paired sample two-tailed t-test between the three possible pairs of 1.5T SE, 3.0T SPGR, and 3.0T IDEAL-SPGR. We found that there was a significant difference (*P* < 0.0001) between 1.5T SE and 3.0T IDEAL; there was also a significant difference (*P* < 0.002) between 3.0T SPGR and 3.0T IDEAL. At the same time there was no significant difference (*P* > 0.05) between 1.5T SE and 3.0T SPGR measurements.

IDEAL measurements of adipose tissue volume were not statistically significantly different from standard 1.5T SE measurements, except for visceral abdominal adipose tissue measurements. In Figure 3A,B, the lower values of visceral adipose tissue volume given by IDEAL (9.9% versus 14.8% and 10.4% versus 16.7%) reflect an improved ability to differentiate between true visceral adipose tissue and bright structures like blood vessels and bowel content that could be mistaken for adipose tissue in the non-fat suppressed T1-weighted images as shown (Fig. 3A,B). In general, in all the subjects studied, when the IDEAL volume estimates were lower than those from the 1.5T SE and 3.0T SPGR, the difference was due to the erroneous inclusion of bright structures such as blood vessels and bowel contents in the visceral adipose tissue volume.

DISCUSSION

Thus far, thorough descriptions of adipose tissue distribution have taken advantage of both clinical assessment and, more recently, noninvasive imaging methods, such as MRI (7). Because quantification of adipose tissue volume on MRI could (i) enhance the description of these rare disorders, (ii) allow for statistical comparisons, and (iii) yield new quantitative traits to follow serially, it is important to develop robust and replicable tools and methods to quantify adipose tissue (10,11).

We have demonstrated the use of IDEAL as a reliable and noninvasive option for adipose tissue volume quantification. Because IDEAL images show only adipose tissues, quantifying adipose tissue volume is simpler and more accurate than current methods. We have determined that IDEAL correlates strongly with our reference standard (1.5T imaging) except for visceral adipose tissue measurements. The lower value of visceral adipose tissue volume given by IDEAL reflects an improved ability to differentiate between true visceral adipose tissue and bright structures like blood vessels or bowel contents that could be mistaken for adipose tissue in the non-fat suppressed T1-weighted images. In fact, while it may be possible to eliminate some instances of mistaking bowel content or blood vessels for adipose tissue on standard MRI by more conservatively segmenting the fat in the images, the additional vigilance in segmentation will significantly lengthen the volume measurement process. With IDEAL fat only images, there is no water signal that could be confused with fat, so the segmentation process is greatly simplified and data analysis is much faster.

We chose to a T1 independent, T2* corrected version of IDEAL for our analysis because it has already been validated for measuring hepatic lipid content (8,12–14). Hence, IDEAL MRI should allow simultaneous quantification of adipose tissue volumes (subcutaneous adipose tissue and visceral adipose tissue) as well as hepatic lipid content.

IDEAL is one of the most recent versions of a large family of fat–water separation methods dating back over 20 years (4,15–19). The method for determining the adipose tissue volumes we used could be applied to fat-only images produced by any of the wide variety of fat–water separation methods that have been developed in recent years (14,20–22).
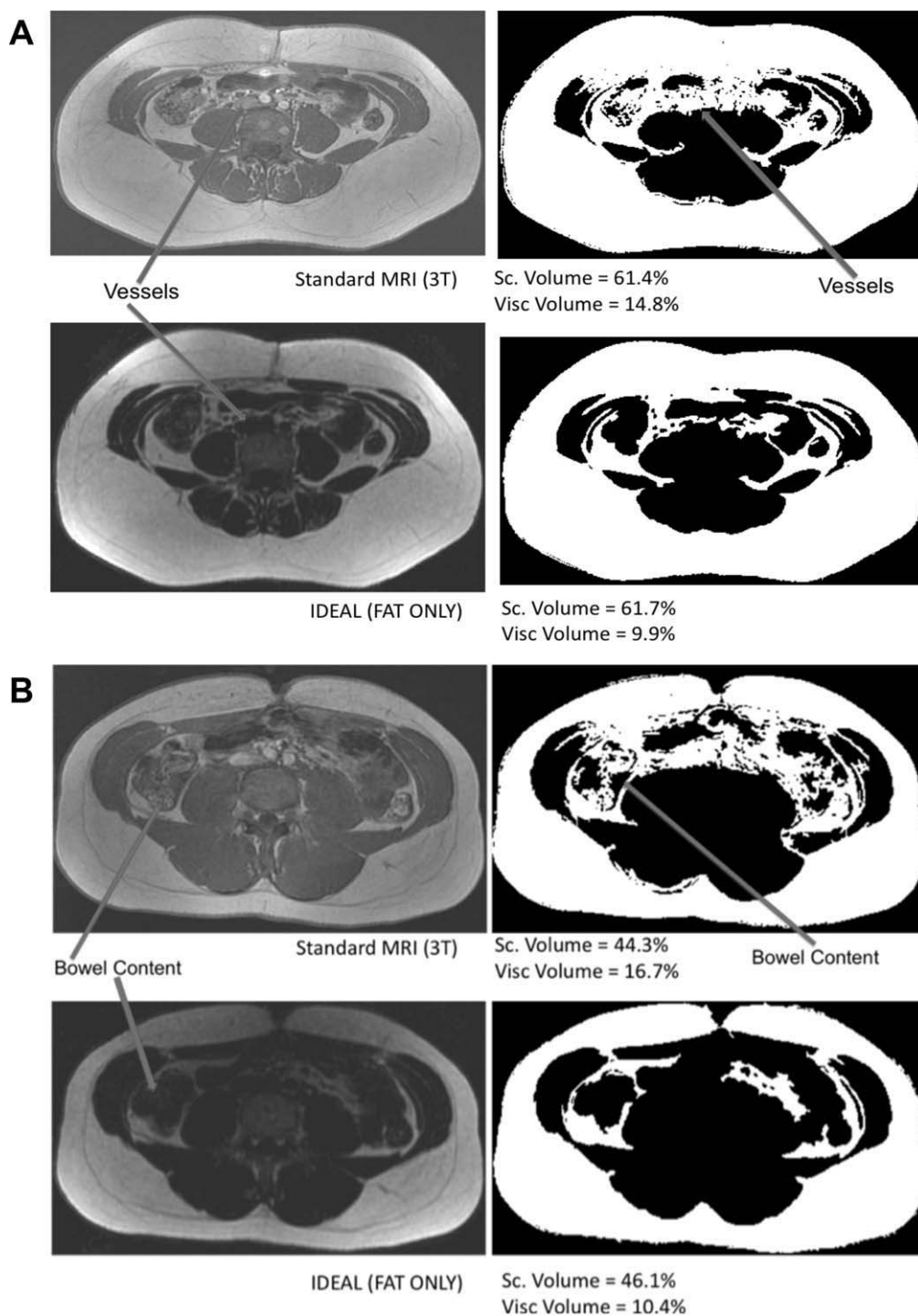
Figure 3. A: The lower value of visceral adipose tissue volume given by IDEAL relative to 3.0T SPGR imaging (9.9% versus 14.8%) reflects an improved ability to differentiate between true visceral adipose tissue and bright structures like blood vessels that could be mistaken for adipose tissue in the non-fat suppressed T1-weighted images as shown. B: The lower value of visceral adipose tissue volume given by IDEAL relative to 3T SPGR imaging (10.4% versus 16.7%) reflects an improved ability to differentiate between true visceral adipose tissue and bright structures like bowel content that could be mistaken for adipose tissue in the non-fat suppressed T1-weighted images as shown.

We found that the IDEAL fat–water separation was very reliable with no instances of fat and water being mis-identified by IDEAL in this study. In general the IDEAL technique is very reliable in separating water and fat correctly. Yu et al (23), reported a fat–water separation failure rate of 1.8% for IDEAL, which is consistent with our experience. We note that recently there has been considerable research regarding more reliable methods of B_0 field mapping for fat–water separation (24,25) and implementation of some of these newer methods will reduce the failure rate even further.

As part of our protocol, we analyzed a single slice for each anatomical body section (abdomen, gluteus, thigh, and calf). This adipose tissue quantification protocol was previously validated for 1.5T spin echo MR images (7). With this approach there maybe some vulnerability to mis-registration errors, because we imaged each anatomic section three separate times. However, using our technique, possible mis-registrations errors are only likely to occur based on variation in the breathholding pattern by the subject. Anatomic mis-registration would be minimized because we used specific anatomic locations for each region of interest: Abdomen (at the level of the L4 vertebra), gluteus (at the level of the femoral heads), mid-thigh (at the mid-point of the femur) and mid-calf (at the mid-point of the tibia).

We are using 1.5T T1-weighted spin echo images as our standard of reference, because they have been previously validated against an anatomical reference standard with high intraobserver and interobserver correlation. This is a limitation of our technique, as we are not comparing our results to the "gold standard" anatomical reference. An additional limitation of our method is that IDEAL reconstruction can become unreliable around implanted metal; however, the presence of metal would in general cause artifacts on all three types of images analyzed in this study so that is a limitation of MRI in general and not specific to IDEAL.

In conclusion, IDEAL is a reliable and noninvasive method for the determination of quantitative differences in adipose tissue distribution among normal controls. IDEAL imaging will provide a reliable and noninvasive method that will allow for the determination of quantitative differences in the distribution of adipose tissue across metabolically relevant depots that have implications for a broader range of conditions, such as type 2 diabetes, metabolic syndrome, human immunodeficiency virus-associated lipoatrophy, and hereditary syndromes of lipodystrophy.

ACKNOWLEDGMENTS

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