Introduction

The prevalence of obesity in the United States has steadily risen over the past decade, and continues to be a growing epidemic in adolescents and adults. It is a tremendous burden to health care, with an annual cost that exceeds billions of dollars. The 2007 statistics from the Center for Disease Control report more than 16% of children are overweight or obese according to the body-mass-index (BMI) (FIG. 1).

Obesity is linked to multiple cardiovascular, digestive, and organ diseases, collectively referred to as the metabolic syndrome. During childhood, obesity increases the risks of developing physical impairment and certain cancers later in life. Clinical evidence has linked obesity-related health risks to the human body’s accumulation of subcutaneous (underneath skin), visceral (intra-abdominal), and ectopic (organ, muscle) fat, with visceral and ectopic fat deposition carrying the greatest risks.

Magnetic resonance imaging (MRI) is the only modality that can comprehensively assess subcutaneous, visceral, and ectopic fat in a single body composition examination. Furthermore, MRI is non-invasive, utilizes no ionizing radiation, and generates intrinsic 3D volumetric data. It can also be safely and repeatedly applied to children.

Approach

Our laboratory is in the process of developing and improving MRI-based tools for fat quantification and body composition assessment in obesity research. MRI is well suited for fat detection because it can differentiate fat and lean tissues based on frequency and phase shifts in the acquired signals. In other words, the resonant frequencies of hydrogen nuclei in lipids (fat) and water molecules are different and detectable, a phenomenon which is exploited by fat-water separation methods.

Fat imaging has been researched over the past 25 years, and recent advances have led to the development of a 3D technique called IDEAL (Iterative Decomposition with Echo Asymmetry and Least squares). The IDEAL signal model is summarized in FIG. 2. By measuring multiple MRI signals at several time points s, the individual contributions of water W, fat F, and bone marrow can be scalar solved on a voxel-by-voxel basis across the imaging volume. Furthermore, the resultant signal ratio F / (F+W), referred to as the fat fraction, can then be used to quantify the degree of ectopic fat infiltration in muscle and organs.

\[
s(t) = (W + F)e^{j2\pi ft}e^{-j2\pi ft/\beta} + \text{fat phase shift term} + \text{magnet non-uniformity and signal relaxation term}
\]

We work closely with investigators from the USC Childhood Obesity Research Center (CORC, www.childhoodobesitycenter.org) to study the causes and consequences of childhood and adolescent obesity. CORC researchers are interested (1) in the ways which fat is regulated and deposited throughout the body, and (2) in understanding the mechanisms linking fat accumulation to the risks of diabetes, cardiovascular, fatty liver diseases, and cancer. One area of emphasis is the study of differences in fat regulation and deposition across ethnicity, particularly in Hispanics and African Americans adolescents. CORC also designs interventions that attempt to reverse fat accumulation in visceral and ectopic depots.

Our group provides state-of-the-art imaging protocols that allow CORC researchers to accurately assess the distribution of abdominal fat with MRI. FIG. 3 illustrates a 3D visualization of fat depots across the whole-abdomen with 2 mm spatial resolution. The data was acquired using IDEAL-MRI in approximately 2 minutes, using six 20-second breath-holds. All areas in white denote fat depots. To date, more than 100 CORC participants in several studies have been imaged with IDEAL-MRI.

I. RAPID 3D IMAGING

One of our research goals is rapid fat imaging with high spatial resolution that can accurately resolve distributions of fat within organs. MRI is inherently slow, requiring multiple repetitions to adequately sample the spatial Fourier domain (called k-space). For abdominal applications, respiratory motion can cause image artifacts. It is thus necessary for subjects to perform breath-holds during data acquisition. In obese populations, the duration of stable breath-holds is limited (<15 seconds).

We are currently pursuing approaches based on Compressed Sensing (CS). In CS, the transform-sparsity of MR images is exploited to reconstruct images from reduced data samples (e.g. acquired below Nyquist limit). Less k-space sampling translates to shorter scan times. Specifically in CS, the sparsity of an image in an alternative domain (e.g. spatial finite-differences (FD), wavelet) is sought. According to CS theory, images with sparse representations can be recovered if their k-space is undersampled. Random data sampling introduces noise-like incoherence and interference. However, the most significant coefficients can still be isolated from the noise in the sparse transform domain. As a result, the image can be recovered with little loss in quality using constrained (e.g. L1 norm) data reconstruction. The equations below and FIG. 4 illustrate the CS-IDEAL approach.

\[
\begin{align*}
\text{min} \quad & \| k \cdot \Phi y - y^c \|_1 + \lambda_1 \| c_w \|_1 + \| c_f \|_1 \\
\text{subject to} & \quad \| \mathbf{A} \psi \mathbf{x} \|_2 \leq 1
\end{align*}
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II. FAT IMAGE SEGMENTATION and REGISTRATION

The application of 3D IDEAL-MRI to more than 100 CORC subjects has generated a rich data base of whole-abdomen images (6,000+) that require further analysis and quantification. Manual image segmentation by a trained operator is very time intensive, and requires about 1 hour per subject. We are currently developing semi-automated image segmentation tools that will allow an operator to efficiently label and tag the fat depots and organs of interest (FIG. 5).

CORC studies are often longitudinal, requiring each subject to obtain multiple IDEAL-MRI scans at 2-3 months intervals. In this manner, the efficacy of various therapeutic interventions targeting a decrease in body fat can be evaluated. We are developing automated image segmentation methods for fat quantification. For example, a data set from an individual’s first IDEAL-MRI exam will be manually segmented by an expert, and the resultant labels will serve as the subject’s reference. Subsequent IDEAL-MRI data of the same individual at later time points will then be automatically segmented, with corresponding labels generated by applying rigid and non-rigid registration deformations to the initial reference label set. We are also investigating a more challenging scenario, where an individual’s IDEAL-MRI data set will be automatically segmented by using a reference labels from a different individual --- but with a similar body shape --- that is chosen from a large pre-established label data base. We are currently building this data base and investigating a variety of selection criteria.

III. MRI of BROWN FAT

Two types of fat exist in mammals: white and brown. White fat is the constituent of subcutaneous, visceral, and ectopic fat, and is an energy reservoir. Brown fat in contrast, is involved in energy expenditure. It is responsible for heat generation; it is a highly metabolically active tissue; and in mice, it is protective against weight gain and obesity. We are currently investigating MRI-based approaches for the imaging of brown fat in humans, and recently demonstrated with IDEAL that brown fat has a much lower fat fraction than white fat.

Contact Information

Please contact Prof. Harry Hu (houchunh@usc.edu) for more information, or to learn how you can get involved. MREL website – http://mrel.usc.edu/