AUTOMATED MEASUREMENT AND SEGMENTATION OF ABDOMINAL ADIPOSE TISSUE IN MRI

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ABSTRACT

Obesity has become widespread in America and has been identified as a risk factor for many illnesses. Measuring adipose tissue (AT) with traditional means is often unreliable and inaccurate. MRI provides a safe and minimally invasive means to measure AT accurately and segment visceral AT from subcutaneous AT. However, MRI is often corrupted by image artifacts which make manual measurements difficult and time consuming. We present a fully automated method to measure and segment abdominal AT in MRI. Our method uses non-parametric non-uniform intensity normalization (N3) to correct for image artifacts and inhomogeneities, fuzzy c-means to cluster AT regions and active contour models to separate subcutaneous and visceral AT. Our method was able to measure images with severe intensity inhomogeneities and demonstrated agreement with two manual users that was close to the agreement between the manual users.

INDEX TERMS: abdominal MRI, adipose tissue, segmentation, quantification, intensity inhomogeneity.

1. INTRODUCTION

Obesity in humans is widely viewed as a risk factor for several diseases, including diabetes, hypertension, atherosclerosis, and cardiovascular disease [1]. Excess visceral AT (VAT) as opposed to subcutaneous AT (SAT), appears to be more highly associated with metabolic disorders in obesity and obesity related illnesses [2].

Measuring fat by traditional means is often very imprecise and can be invasive. Determining the locations and distribution of adipose tissue (AT) deposits is not possible by methods such as anthropometry and under-water weighing. CT allows for localization of AT deposits, but exposes the subject to radiation. MRI allows for accurate, safe measurement and segmentation of AT. MRI is free from ionizing radiation and minimally invasive, and has been used in multiple studies for fat measurement [3, 4].

On a T1-weighted MRI, AT has higher signal intensity than other body tissues (see figure 1). Hence, many measurement techniques use a threshold to segment out AT followed by generation of contours to separate SAT from VAT. However, intensity inhomogeneities and other image artifacts can make choosing a threshold difficult and inaccurate. Also, manually choosing a threshold and drawing contours can be both time consuming and unreliable. Most previous studies requiring AT measurements have used manual or semi-automated techniques; however, there have been several attempts to fully automate the process. Kullberg et al. used expectation maximization to correct bias fields and gradient masks for segmentation [5]. Brennan et al. used histogram matching and thresholding with a region refining algorithm [6]. Positano et al. used fuzzy c-means (FCM) and adaptive FCM with active contour models (ACM) [7, 8]. We present a fully automated algorithm that segments and measures AT volumes in single abdominal MRI slices. Our method is similar to Positano’s, but includes correction for the severe intensity inhomogeneities encountered in multiple imaging protocols and incorporates anatomical knowledge in segmenting AT and separating VAT and SAT.

2. DATA

We used T1-weighted MR scans from 30 patients from three scanning protocols for fat measurement, from studies of patients with Turner syndrome, systemic lupus erythematosus, and obesity. Both obese and non-obese patients were included. Up to four slices were measured from each patient. 90 slices were measured in total. MR scan parameters varied between protocols (see Table 1). Examples of images from the three protocols are in Figure 1.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field Strength (T)</td>
<td>1.5</td>
<td>1.5</td>
<td>3</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>400</td>
<td>400</td>
<td>100</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>8</td>
<td>9</td>
<td>18.8</td>
</tr>
<tr>
<td>Slice Thickness(mm)</td>
<td>10</td>
<td>10</td>
<td>6</td>
</tr>
</tbody>
</table>

3. METHODS

Our algorithm uses three main techniques, non-parametric non-uniform intensity normalization (N3) [9], Fuzzy C-Means (FCM) [10], and active contour model (ACM) [11], for inhomogeneity correction, pixel classification, and SAT and VAT separation respectively. We describe these briefly and then give an overview of the entire algorithm.

3.1 Non-parametric non-uniform intensity normalization (N3)

N3 attempts to correct for intensity inhomogeneities by maximizing high frequency components of the image histogram. Images are modeled by \( \hat{v} = \exp(\hat{b} - \hat{u}) \) where \( \hat{v}, \hat{u} \) and \( \hat{b} \) are the log of \( v, u \) and \( b \) respectively. \( \hat{v} \) is sharpened to give \( u_\ast \), an estimate of \( u \). Then, \( E[\hat{u}_\ast | \hat{v}] \) is computed from the distributions of \( \hat{v}, \hat{u}_\ast \), and an assumed Gaussian distribution for \( \hat{b} \) (see Sled et al. for details of the computation of the expected value [9]). \( \hat{b}_\ast \) is estimated as \( \hat{b}_\ast = \hat{v} - E[\hat{u}_\ast | \hat{v}] \). \( \hat{b}_\ast \) is then smoothed by fitting a b-spline surface to give \( \hat{b}_\ast \). We now have \( u = \exp(\hat{v} - \hat{b}_\ast) \). This method is applied iteratively by replacing \( \hat{v} \) with the new \( u \). We use a version of N3 implemented in ITK [12].
3.2 Fuzzy C-Means (FCM)

FCM is an unsupervised pixel classification technique. It involves minimizing the objective function:

\[ Y = \sum_{k=1}^{C} \sum_{x} m_k(x) \| u(x) - \mu_k \| \]

where \( C \) is the number of clusters, \( u(x) \) is the intensity at position \( x \) and \( m_k(x) \) is the membership of position \( x \) in class \( k \) and \( \mu_k \) is the centroid of class \( k \). \( Y \) is minimized by iterating the following equations:

\[ m_k(x) = \left( \sum_{i=1}^{C} \frac{\| u(x) - \mu_i \|^2}{\| u(x) - \mu_k \|^2} \right)^{-1} \quad \text{and} \quad \mu_k = \frac{\sum_{x} m_k(x) u(x)}{\sum_{x} m_k(x)}. \]

In our implementation, we use two-class (AT and non-AT) FCM for the pixel classification.

3.3 Active Contour Models (ACM)

ACM are used to determine the external contour of an object in an image by iteratively deriving a sequence of candidate external contours, each candidate an improvement on the previous. This is done by applying forces to the initial and each subsequent candidate boundary. The forces that drive the active contour model can be expressed as:

\[ F = w_{id} F_{\text{internal}} + w_{im} F_{\text{image}} + w_{es} F_{\text{external}} \]

where \( F_{\text{internal}} \) is the spline force of the contour, \( F_{\text{image}} \) is the image force, and \( F_{\text{external}} \) is the external force, and \( w_{id}, w_{im}, \) and \( w_{es} \) are the respective weighting parameters. The internal force \( F_{\text{internal}} \) can be written as:

\[ F_{\text{internal}} = \frac{1}{2} \int_0^1 \left( \alpha(s) |x'(s)|^2 + \beta(s) |x''(s)|^2 \right) ds \]

where \( x(s) \) is the curve representing the contour, \( x'(s) \) is the first order derivative of \( x(s) \), and \( x''(s) \) is the second order derivative of \( x(s) \). The spline force is composed of a first-order term controlled by \( \alpha(s) \) and a second-order term controlled by \( \beta(s) \). The internal force is used to guarantee the smoothness and continuity of the contour.

\( F_{\text{image}} \) are forces derived from the image to attract the contour to image features such as edges, iso-values, or boundaries. In our method, we use the gradient of the edge map of the membership function as the image force to drive the deformable contours to the polyp boundary, i.e.

\[ F_{\text{image}} = \nabla \left( \nabla m(x) \right) \]

where \( m(x) \) is the membership map of AT tissue class, \( \nabla \) is the gradient operator.

\( F_{\text{external}} \) are forces added by users for different applications. We add two kinds of external forces. One force is similar to the balloon forces proposed by Cohen et al.\[13\], a force to inflate or deflate the contour from its initial state. The external balloon force at a vertex \( v_i \) can be written as

\[ F_{\text{balloon}} = \frac{v_i - v_s}{\| v_i - v_s \|} \left( \| u_{Lx} - v_{Lx} \| - \| v_s - v_i \| \right) \]

where \( v_s \) is the centroid of the current contour, the direction of \( F_{\text{balloon}} \) can be adjusted to command an inflating force or a deflating force by changing the sign. The second force is a lateral symmetry force which drives the contour to maintain lateral symmetry. The symmetric force can be written as

\[ F_{\text{symetric}} = \frac{u_s - v_s}{\| u_s - v_s \|} \left( \| u_{Lx} - v_{Lx} \| - \| v_s - v_i \| \right) \]

where \( u_s \) and \( u_{Lx} \) are the vertex and its symmetric vertex on the initial contour and \( v_s \) and \( v_{Lx} \) are the vertex and its symmetric vertex on the current contour. The symmetric force is only applied if \( \| u_s - v_{Lx} \| \) is large which indicates the internal contour is not adhering to the symmetry property of the abdominal wall. The forces are exerted on the contour until either an equilibrium position is reached or a maximum number of iterations is reached.

ACM is used twice in our algorithm, once to extract the exterior body boundary and once to fit the boundary separating SAT and VAT.

3.4 Algorithm Details

Our algorithm is composed of four stages: (1) body masking, (2) preprocessing, (3) SAT and VAT separation, and (4) tissue classification and quantification.

3.4.1 Body Masking

FCM is performed on the whole image with two classes (body and background) giving fuzzy memberships \( m_{\text{Bad}} \) and \( m_{\text{BG}} \) and centroids \( \mu_{\text{Bad}} \) and \( \mu_{\text{BG}} \). The FCM centroids are used in a region growing algorithm which establishes an initial body mask. The mask is divided into connected components. The convex hull of the largest (or two largest, if the second is at least half the size of the first) connected component gives the final body mask (inside yellow contour in Figure 2a). We use the two largest components in some images since severe artifact may sometimes separate the body regions as illustrated in Figure 1c where the dark artifact divides the SAT in half.
3.4.2 Preprocessing
The goal of the preprocessing stage is to reduce image artifacts such as noise and intensity inhomogeneity. FCM is performed again with clusters AT and non-AT (NAT). We calculate the membership weighted standard deviation of voxels in the AT cluster:

$$\sigma_{AT} = \sqrt{\frac{\sum_i (m_{AT}(x)\mu(x) - \mu_{AT})^2}{\sum_i m(x)}}. \quad (8)$$

We then truncate the extremely high intensity pixels which are mostly artifact, by truncating pixels with intensity greater than $\mu_{AT} + 2\sigma_{AT}$. We run the N3 algorithm for several iterations and after each run compare the corrected image to the truncated image and keep the higher intensity for each voxel. We also perform anisotropic diffusion filtering to reduce noise. Figure 2a illustrates the image after the preprocessing step performed on 1c.

3.4.3 SAT and VAT Separation
The separation is achieved by generating two contours, the external contour which separates the body from the background, and the internal contour which separates the subcutaneous adipose tissue from the internal body cavity. The initial value of the external contour is the convex hull of the body mask (Figure 2a). An ACM is applied to this initial contour with a search range of 10 pixels to closely fit the external contour to the body. Following this step an internal contour can be initialized in two ways FCM is performed with two classes, AT and NAT, and we set $t = \frac{\mu_{AT} + \mu_{NAT}}{2}$. Pixels brighter than $t$ create an approximate AT mask. The mask is split into connected components. If only one connected component borders the external contour, the internal contour is initialized as the external contour reduced by 10mm. Otherwise it is initialized as the convex hull of the remaining components. In the first method, the balloon force is a deflating force, while in the second method it is an inflating force. Figure 2b illustrates the first initialization method. The ACM algorithm is then performed on the internal contour. Search ranges are set by measuring the distance inward (or outward in the case of the second initialization method) from the initial contour to a voxel with intensity less than $\frac{\mu_{AT} + \mu_{NAT}}{2}$ are found. The search range is set to 1.5 times the maximum distance. After ACM, the internal contour is ensured to be at least 10mm inwards of the external contour by shifting vertices points which violate this criterion. Finally, we smooth the contour by fitting the internal contour with degree 3 b-splines. Figure 2b shows the initial contour for the internal contour and it converges in Figure 2c.

3.4.4 Pixel Classification and AT Quantification
FCM is run on the body mask with two classes (AT and NAT) in two iterations. First iteration computes the initial membership value and centroids $\mu_{AT}$ and $\mu_{NAT}$. The second iteration excludes voxels that are brighter than $\mu_{AT} + 2\sigma_{AT}$, where $\mu_{AT}$ and $\sigma_{AT}$ are the centroid and weighted standard deviation for the AT cluster, calculated from the first FCM run. The second run results in centroids $\nu_{AT}$ and $\nu_{NAT}$. We set the intensity threshold $t_{AT} = \frac{\nu_{AT} + \nu_{NAT}}{2}$, corresponding to AT membership threshold of 0.5. Any voxels between the external contour and the internal contours with intensity greater than $t_{AT}$ are SAT and those voxels inside the internal contour with intensity greater than $t_{AT}$ are VAT. Volumes are computed by multiplying the number of SAT or VAT voxels times the voxel volume. SAT and VAT classification are shown in Figure 2c.

3.5 Manual AT Measurement
The manual AT Measurement was conducted similar to clinical practice. The user first draws a contour separating the body from the background. The user then chooses a single lower-bound threshold which masks the AT voxels. Finally a second contour is drawn separating VAT from SAT. The AT voxels are summed up to give the manual measurement. Figure 3a and b show examples of manual segmentations from User 1 and 2 respectively.

4. RESULTS AND DISCUSSION
Automatic measurements and manual measurements from two raters were performed on all slices. Also, the times used to make
the measurements were recorded for each technique. Of the two manual users, User 1 is an experienced medical imaging technologist and User 2 is a new trainee.

Figure 4 illustrates comparisons between the different measurements as Bland-Altman plots. They show the average versus difference of measurements for each patient. Table 2 shows the means and standard deviations of the differences between the raters. Agreement is highest between User 1 and the automatic method (Auto), with the smallest limits of agreement for both SAT and VAT measurement. Agreement between User 2 and Auto is close to agreement between the two manual users. This shows that our method performs similarly to how a third manual user might perform. It would be advantageous to have two expert raters in future work to have a better reference.

Table 2: Means and standard deviations of differences between the three raters.

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<thead>
<tr>
<th></th>
<th>User1-User2</th>
<th>Auto-User1</th>
<th>Auto-User2</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAT</td>
<td>.64±11.99</td>
<td>-3.46±8.13</td>
<td>-2.81±12.66</td>
</tr>
<tr>
<td>VAT</td>
<td>-.76±25.26</td>
<td>3.34±15.35</td>
<td>4.59±19.14</td>
</tr>
</tbody>
</table>

Auto measurement slightly overestimates the VAT and underestimates the SAT on average relative to both manual users. This is partially due to over smoothing of the internal contour which sometimes results in SAT being marked as VAT.

Protocols 1 and 2 had some intensity inhomogeneity problems but no severe issues. As a result, agreement was similar between the three comparisons. User 1 had mean VAT measurements which were less overall than Auto and User 2. In contrast, protocol 3 was corrupted by severe bias fields which were manifest by a darkened area running vertically through the center of the image (Figure 1c). For this protocol, User 2 underestimated both SAT and VAT by an average of 6 cm³ and 15 cm³ respectively, relative to both Auto and User 1. However, Auto and User 1 had mean differences of less than 1 cm³ and limits of agreement of approximately 6.5 cm³ for both SAT and VAT. This suggests that an experienced user can compensate for certain image artifacts in their selection of thresholds.

From the Bland-Altman plots, the automated method showed a moderate dependence on SAT quantity when compared to user 2 (r=.554, p=.0015) (Figure 4c). However, no other rater comparisons showed a significant correlation of between difference and average size of the measurements.

Median times were 48, 66, and 105 s per slice for Auto, User 1 and User 2 respectively. Though not a large difference, the Auto times include preprocessing, an extra step not taken by manual users. In future work we plan to have manual users measure preprocessed images in order to compare both times and measurements more accurately. Additionally, our algorithm can be run in the background using no clinician time.

5. CONCLUSION

We have developed an algorithm for automated segmentation of SAT and VAT in abdominal MRI. In contrast with existing techniques, we have included a multi-iteration N3 method to correct severe image inhomogeneity and a symmetry force in an ACM to exploit knowledge of abdominal anatomy. Our algorithm is able to successfully measure SAT and VAT on images with severe image artifacts. The agreement between its measurements and those of the two manual users is close to the agreement between the measurements of the two users.

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REFERENCES


