Fat quantification and analysis of lung transplant patients on unenhanced chest CT images based on standardized anatomic space

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ABSTRACT

Chest fat estimation is important for identifying high-risk lung transplant candidates. In this paper, an approach to chest fat quantification based on a recently formulated concept of standardized anatomic space (SAS) is presented. The goal of this paper is to seek answers to the following questions related to chest fat quantification on single slice versus whole volume CT, which have not been addressed in the literature. What level of correlation exists between total chest fat volume and fat areas measured on single abdominal and thigh slices? What is the anatomic location in the chest where maximal correlation of fat area with fat volume can be expected? Do the components of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) have the same area-to-volume correlative behavior or do they differ? The SAS approach includes two steps: calibration followed by transformation which will map the patient slice locations non-linearly to SAS. The optimal slice locations found for SAT and VAT based on SAS are different and at the mid-level of the T8 vertebral body for SAT and mid-level of the T7 vertebral body for VAT. Fat volume and area on optimal slices for SAT and VAT are correlated with Pearson correlation coefficients of 0.97 and 0.86, respectively. The correlation of chest fat volume with abdominal and thigh fat areas is weak to modest.

Keywords: fat quantification, standardized anatomic space (SAS), unenhanced computed tomography (CT), lung transplantation

1. INTRODUCTION

Obesity and being underweight are contraindications to lung transplantation due to their association with mortality [1, 2]. Chest fat estimation may therefore be important for identifying high-risk lung transplant candidates. Body mass index (BMI), defined as the body mass divided by the square of the body height, expressed in units of kg/m^2, has been commonly adopted for fat measurement. However, BMI cannot describe fat distribution in different body regions and even in healthy adults; BMI fails to identify many patients with obesity [3]. Previous research has shown that BMI alone cannot differentiate between obese phenotypes even though body composition (differences in fat distribution given the same BMI) may indicate different phenotypes of obese subjects [4-6]. Presently, BMI greater than 30 kg/m^2, is considered to be a relative contraindication to lung transplantation due to its associations with early mortality [7-9] and primary graft dysfunction, although recent evidence suggests that BMI is a poor measure of adiposity in patients with advanced lung disease [10].

In this paper, an approach to chest fat quantification based on a recently formulated concept of standardized anatomic space [11] is presented. The goal of this paper is to understand the relationship between total chest fat volume and fat area measured on single slice in the chest, abdomen, and thigh. Such a study has not been reported in the literature. The motivation for such a study is to find effective markers of fat quantity and quality with high efficiency while minimizing radiation exposure [12, 13].

2. MATERIALS & METHODS

Image Data

This is a retrospective image analysis study. It was conducted following approval from the Institutional Review Board at the University of Pennsylvania along with a Health Insurance Portability and Accountability Act waiver. Unenhanced CT image data from forty lung transplant patients, predominantly with idiopathic pulmonary fibrosis (IPF) or chronic obstructive pulmonary disease (COPD) were analyzed. Every subject had an unenhanced chest CT scan as well as research single slice CT scan of the thigh at mid-level and a single slice CT scan of the abdomen at the L5 level. These data had been acquired as part of an NHLBI-funded and IRB-approved prospective study at 3 lung transplant centers: Columbia, Penn, and Duke (R01 HL114626; PI: Christie/Lederer). All participants provided informed consent.

Image Processing

Image segmentation: For all subjects, the thoracic body region was defined as extending from 15 mm superior to the apex of the lungs to 5 mm inferior to the base of the lungs. All CT images were accordingly trimmed to include just this body region. The interface between SAT and VAT in the abdomen (and thigh) is much easier to define and delineate than in the chest [13, 14]. When axial CT images were seen to pass through the lower thorax and upper abdomen simultaneously, the visualized portions of the diaphragm were used to separate abdominal from thoracic VAT. In particular, visceral fat located external or superior to the diaphragm was considered to be part of the thoracic VAT, whereas visceral fat located internal or inferior to the diaphragm was considered to be part of the abdominal VAT. For chest SAT, we use the axial slice at the inferior aspect of the thoracic region as the demarking level. The Livewire tool in the open source software system CAVASS [15] was used for delineating the SAT-VAT interface in all three body regions. Subsequently segmentations of
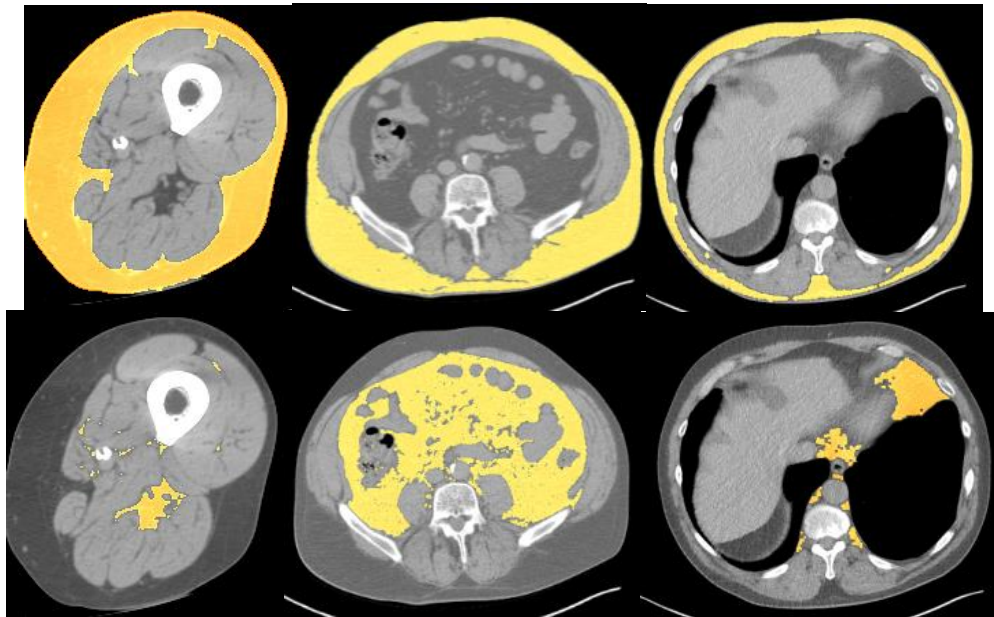

Figure 1. From left to right: SAT (top) and VAT (bottom) components segmented and overlaid on a slice display for thigh, abdomen, and chest from a study data set.

the SAT and VAT components were obtained by thresholding the marked regions. Figure 1 shows an example of the segmented SAT and VAT components in the three body regions.

Standardized anatomic space and selecting slices at homologous locations: In analyzing volume-to-area correlations, it becomes important to make sure that the slice used for correlation analysis comes from the same anatomic location in every subject. Otherwise, the analysis becomes meaningless [11]. Even though the superior-most and inferior-most slices are fixed by the body region definition given above, if the remaining slices are mapped in a linear fashion as often done

[16] to make sure that there is 1:1 correspondence among slices from different subjects, the mapped corresponding slices may not, and usually do not, match in anatomic locations [11]. This can be overcome by a non-linear mapping of the slice locations into a standard anatomic space as described in [11] based on landmarks chosen on the vertebrae in their 3D renditions. That method, which will be referred to as *Standardized Anatomic Space* (SAS) approach, has been employed in this paper to map the slice locations.

The volumes and areas in each study were normalized by dividing volume by L^3 and area by L^2, where L denotes the diagonal of the box that just encloses the thoracic skeleton derived from the study.

Area-to-volume correlations

Once SAS mapping has been accomplished, for each given anatomic axial slice location, it becomes possible to find the correct matching slice in each of the 40 subjects. SAT and VAT areas for that location are then computed from the segmentations, and the Pearson correlation coefficients (PCC) between the 40 area measures and the 40 volume measures are computed. From these estimated correlations, a single slice location that yields the best correlation is determined separately for SAT and VAT. These slices will be referred to as "best slices" for SAT and VAT. The correlation between the SAT and VAT areas on the best slice and the corresponding SAT and VAT areas on the slices imaged in the abdomen and the thigh are evaluated as well.

Correlation coefficient from PCC between two random variables A and B will be denoted by $\rho(A, B)$. A and B were selected from among fat slice-area in chest, abdomen, and thigh, and fat volume in chest. The variables will be codified by the symbol XY_Z, where X = S (for SAT) or V (for volume); Y = A (for area) or V (for volume); and Z = C (for chest), A (abdomen), or T (for thigh). As an example, $\rho(VV_C, VA_A)$ denotes PCC between VAT volume in chest and VAT area in abdominal slice. The variables are summarized in Table 1.

Table 1. Definition of variables employed in correlative analysis.		
Variable		**Description**
Normalized area	SA_A	SAT area in abdominal slice
	SA_T	SAT area in thigh slice
	SA_C	SAT area in a slice in the chest
	VA_A	VAT area in abdominal slice
	VA_T	VAT area in thigh slice
	VA_C	VAT area in a slice in the chest
Normalized volume	SV_C	SAT volume in chest
	VV_C	VAT volume in chest

3. RESULTS

For all CT images, the image size was 512×512×50-70. Pixel size varied from 0.70×0.70 mm^2 to 0.97×0.97 mm^2. The slice thickness and spacing was 5 mm. The mean age of the participants is 58.0 yrs (±11.7 yrs) with a mean BMI of 26.4 kg/m^2 (±4.3). The significant anatomic variability that exists among subjects is illustrated in Figure 2 where we plot schematically the locations of the midlevel of vertebral bodies in the cranio-caudal (vertical) direction for all 40 subjects considered in the study. The top and the bottom of the vertical line for each subject indicate the extent of the thoracic body region in relation to the vertebral bodies. In all subjects, the thoracic region starts from roughly the T1 vertebra. However, the locations of the inferior boundary show significant variability. As shown in [11], any linear mapping will not properly handle the non-linearity that exists in slice locations. Figure 3 illustrates this point for VAT by plotting by "*" the locations of the best single slice found by the SAS method for different subjects in comparison to linear mapping. The behavior is similar for SAT.

Table 2 lists volume-to-area correlations for the best slices found as well as their anatomic locations separately for SAT and VAT.
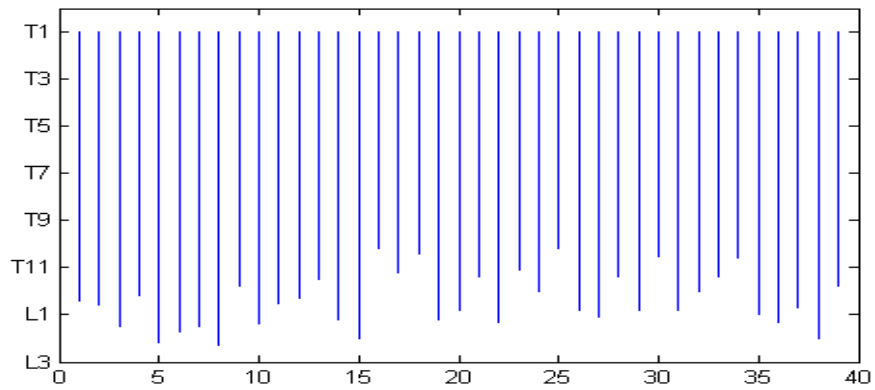
Figure 2. Anatomic locations of chest slices for 40 subjects. Abscissa shows subject number and ordinate indicates the extent of the thorax in cranio-caudal direction for different subjects.
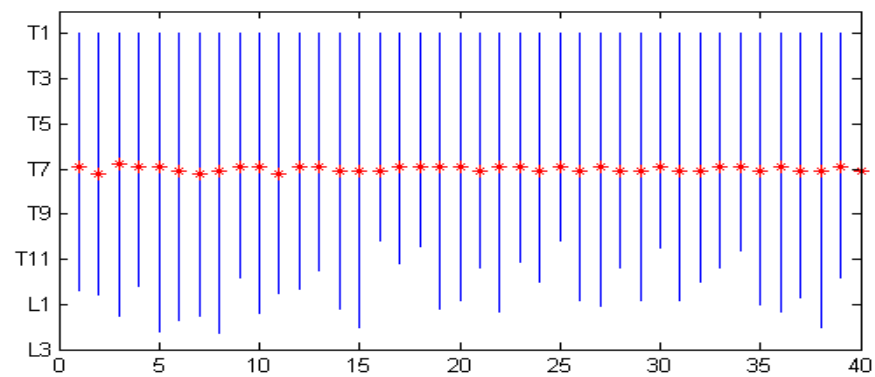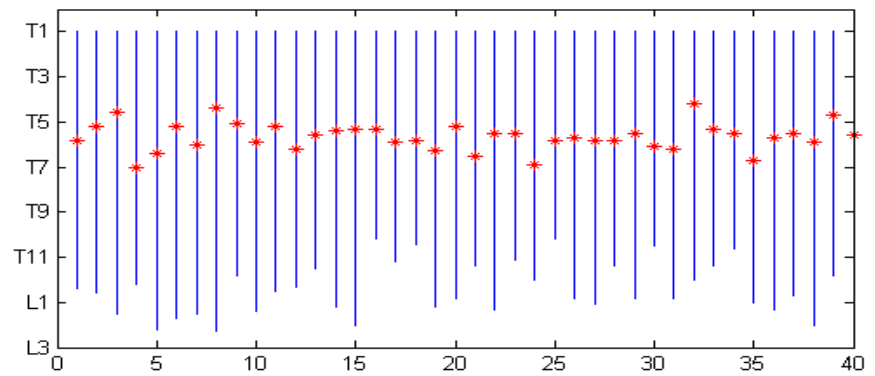

Figure 3. Optimal slice locations derived from linear mapping and SAS for VAT, linear mapping in top row, and SAS in bottom row.

Table 2. Volume-to-area correlations and the found locations for "best" single and double slices for SAT and VAT.

Number of best slices	SAT	VAT
One	0.97 (T8)	0.86 (T7)
Two	0.97 (T6-T7, T9-T10)	0.92 (T2, T5-T6)

Results from Table 2 and Figure 3 show that the best slice locations in the chest for SAT and VAT assessment are different; SAT and VAT areas measured on best slices are highly correlated with the corresponding 3D volumes, with correlations for SAT being higher than for VAT. The same approach was used to find "best two slices" whose fat area sum correlated maximally with total fat volume. Note that in this case the two slices need not be contiguous. Table 2 lists the correlations and locations for this case as well. Interestingly, the correlations did not improve for SAT with two best slices, but did improve for VAT.

Table 3 summarizes volume-to-area correlations for chest, abdomen, and thigh. Chest fat volume to abdominal slice area correlations are modest at best and are much lower than volume-to-area correlations for best slice in chest. Chest fat volume to thigh slice area correlation is quite low, especially for the VAT component. When two best slices are considered in the chest, these disparities are even greater.

Table 3. Summary of correlations.			
Group	**Variables**		$\rho(.)$
Volume-to-area	SV_C, SA_A		0.73
	SV_C, SA_T		0.52
	SV_C, SA_C	1 sl	0.97
		2 sl	0.97
	VV_C, VA_A		0.75
	VV_C, VA_T		0.37
	VV_C, VA_C	1 sl	0.86
		2 sl	0.92
Area-to-area	SA_C, SA_A		0.74
	SA_C, SA_T		0.59
	VA_C, VA_A		0.41
	VA_C, VA_T		0.4

4. CONCLUSIONS

In this paper, based on the SAS approach previously developed for abdominal fat quantification, we demonstrated a method of consistently and optimally selecting specific slices in the chest whose measurements may be used as markers of similar measurements made on the whole chest volume. The optimal slice locations found in the chest via SAS mapping have better anatomic consistency compared with those from linear mapping. The best slice locations in the chest for SAT and VAT assessment are different. In thoracic studies involving lung transplant surgery and other applications, the best slice taken at the mid-level of the T8 and T7 vertebral bodies may be sufficient for reliably estimating SAT and VAT components, respectively. SAT and VAT areas measured on best slices are highly correlated with the corresponding 3D volumes, with correlations for SAT being higher than for VAT. For VAT, double best slice strategy improves this correlation although not for SAT. Chest fat volume to abdomen and thigh slice area correlations are modest to weak, these being lower for the thigh, especially for the VAT component.

One limitation of this study is the small sample size considered. This was dictated by the manual labor involved in defining the SAT-VAT interface in the thorax, which is a challenging problem. Our future work will focus on developing anatomy-model-based strategies with the goal of bringing this step to a production-mode level. Other future work will include investigation of image-derived parameters, preferably from a few optimally selected slices, which have the best predictive ability to prognosticate clinical parameters and outcome for lung transplantation surgery.

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