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## THE ROLE OF IMAGING IN OBESITY SPECIAL FEATURE: FULL PAPER

# Fully automated segmentation and quantification of visceral and subcutaneous fat at abdominal CT: application to a longitudinal adult screening cohort

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**Objective:** To investigate a fully automated CT-based adiposity tool, applying it to a longitudinal adult screening cohort.

**Methods:** A validated automated adipose tissue segmentation algorithm was applied to non-contrast abdominal CT scans in 8852 consecutive asymptomatic adults (mean age, 57.1 years; 3926 M/4926 F) undergoing colonography screening. The tool was also applied to follow-up CT scans in a subset of 1584 individuals undergoing longitudinal surveillance (mean interval, 5.6 years). Visceral and subcutaneous adipose tissue (VAT and SAT) volumes were segmented at levels T12-L5. Primary adipose results are reported herein for the L1 level as mean cross-sectional area. CT-based adipose measurements at initial CT and change over time were analyzed.

**Results:** Mean VAT values were significantly higher in males ( $205.8 \pm 107.5$  vs  $108.1 \pm 82.4$  cm<sup>2</sup>;  $p < 0.001$ ), whereas mean SAT values were significantly higher in females ( $171.3 \pm 111.3$  vs  $124.3 \pm 79.7$  cm<sup>2</sup>;  $p < 0.001$ ).

The VAT/SAT ratio at L1 was three times higher in males ( $1.8 \pm 0.7$  vs  $0.6 \pm 0.4$ ;  $p < 0.001$ ). At longitudinal follow-up CT, mean VAT/SAT ratio change was positive in males, but negative in females. Among the 502 individuals where the VAT/SAT ratio increased at follow-up CT, 333 (66.3%) were males. Half of patients (49.6%; 786/1585) showed an interval increase in both VAT and SAT at follow-up CT.

**Conclusion:** This robust, fully automated CT adiposity tool allows for both individualized and population-based assessment of visceral and subcutaneous abdominal fat. Such data could be automatically derived at abdominal CT regardless of the study indication, potentially allowing for opportunistic cardiovascular risk stratification.

**Advances in knowledge:** The CT-based adiposity tool described herein allows for fully automated measurement of visceral and subcutaneous abdominal fat, which can be used for assessing cardiovascular risk, metabolic syndrome, and for change over time.

## INTRODUCTION

Accurate and reliable measurement of adipose tissue is necessary for studying the epidemiology of obesity in humans. Current common weight metrics such as body mass index (BMI), when taken in isolation, incompletely capture more specific associations between abdominal (central) obesity and metabolic syndrome-related outcomes.<sup>1</sup> Central obesity is better quantified by waist circumference measurements compared to BMI,<sup>2</sup> but this method also has its own limitations related to inter- and intraobserver reproducibility,<sup>3</sup> as well as inability to distinguish visceral from subcutaneous fat compartments.

Adipose tissue is readily identifiable on CT images, and segmentation of adipose tissue on CT images can be performed using a variety of manual and algorithmic methods. More importantly, visceral fat, which studies have shown to be strongly associated with future cardiovascular event risk,<sup>4-9</sup> can be quantified separately from subcutaneous fat on CT images. Visceral fat measurement has also been shown to be an independent predictor of all-cause mortality in males.<sup>10</sup> Studies of visceral and subcutaneous fat volumes quantified by CT have been carried out using a variety of image processing methods.<sup>11-15</sup> However, none to date has been applied to a large-scale set of CT images

on a screening population of patients, including a subset with multiple examinations over time.

Application of automated methods over time could be useful for identifying patients who have an increasing risk for adverse outcomes related to the metabolic syndrome in a screening setting, such individuals undergoing CT colonography (CTC) or lung cancer screening with CT. It could also be applied in settings where long-term imaging monitoring by CT already occurs, such as in oncology patients, as a quantitative measurement of body compositional change. Furthermore, a fully automated tool would not require manual input from the radiologist, increasing efficiency and eliminating subjective measurement differences. The purpose of this study was to apply an automated adipose tissue segmentation algorithm to a large adult screening cohort undergoing CTC to determine the feasibility of population-level visceral fat quantification and monitoring.

## METHODS AND MATERIALS

### Patient population

This was an IRB-approved, HIPAA-compliant retrospective cohort study. 10,059 adults of any age who underwent initial screening CTC between April 2004 and March 2017 at our single academic medical center were eligible for inclusion. If a patient had a follow-up CTC study during this time, they were also included to assess for longitudinal changes in adipose tissue volumes. All patient CTC images were anonymized before the segmentation algorithm was run.

### CT scanning protocol

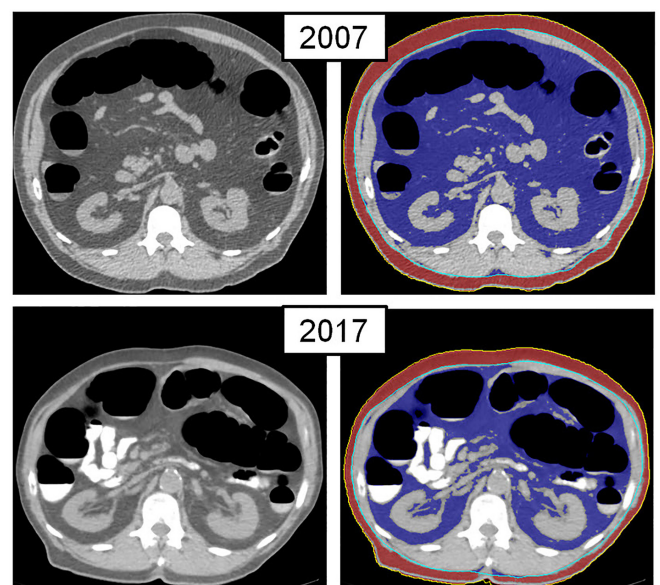
Specifics relating to CTC technique such as bowel preparation and distention have been previously described and are beyond the scope of this study.<sup>16</sup> Breath-hold CT acquisition of the abdomen and pelvis without IV contrast was obtained in both supine and prone positions, but only the former was utilized herein. All CT scans were performed on a variety of 8–64 multi-detector-row scanners (all CT scanners from GE Healthcare; Chicago, Illinois). Scanning was performed at 120 kVp with variable low-dose mA settings (typically modulated). Images were reconstructed with 1.25 mm slice thickness at 1 mm intervals.

### Abdominal adipose compartment measurements

The automated adipose tissue segmentation algorithm utilized in this study represents a modified version of a previously validated tool developed at our institution.<sup>17,18</sup> The CT images were first processed by fully automated spine segmentation and labeling software that identifies the slices that correspond to the top and bottom of each vertebral body from T12–L5.<sup>19</sup> Volumetric slabs of the abdominal CT cross-section were obtained at each of these levels, with craniocaudal slab length based on vertebral height.

Fully automated adipose tissue segmentation of these volumetric slabs consists of five algorithmic steps: body masking, noise reduction, adipose tissue labeling, visceral and subcutaneous adipose tissue (VAT and SAT) separation, and quantification. The body mask is created by a region-growing algorithm on the image background. The region-growing algorithm initially segments the low-intensity pixels outside the body and then,

Figure 1. Example of the automated fat segmentation tool in an asymptomatic 59-year-old male (at time of initial examination) undergoing routine colorectal cancer screening over a period of 10 years. Top row shows an image from initial CTC screening at the L1 level on the left, with the results from the automated fat tool on the right. The external contour is depicted as the yellow outer-most line and the inner contour as the blue line just external to the abdominal wall musculature. Segmented visceral fat is marked blue and subcutaneous fat is marked red. The L1 mean cross-sectional areas for VAT and SAT are 467.8 and 170.2 cm<sup>2</sup>, respectively, with VAT/SAT ratio of 2.75. Bottom row shows similar images from the follow-up study performed 10 years later. Note the marked interval decrease in visceral fat (202.1 cm<sup>2</sup>) relative to subcutaneous fat (103.9 cm<sup>2</sup>). The VAT/SAT ratio has decreased to 1.94. CTC, CT colonography; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.



in a second pass, removes the CT table. Once the body mask is created, an anisotropic diffusion filter is used to reduce noise, and voxels between  $-274$  and  $-49$  HU were labeled adipose tissue. A contour around the outside of the body, the external contour, is then initialized. Active contour models<sup>20</sup> are then used to iteratively modify the external contour to find the inner boundary of the SAT. This results in a contour along the abdominal wall, which is the internal contour. An example of the visual appearance of this segmentation and quantification process is shown in Figure 1.

Volumetric quantification is performed by multiplying voxel counts by the voxel volumes (*i.e.* the pixel area times the slice thickness) to get SAT, VAT, and internal body volumes in each slab volume corresponding to T12–L5 body regions. Visceral adipose volume is defined as the volume of all adipose tissue voxels inside of the internal contour. Subcutaneous adipose volume is defined as the volume of all adipose tissue voxels between the external and internal contours. Segmental body volume was defined at each level as the volume of all voxels within the external contour, excluding air within the GI tract. Exclusion of air allows for true

tissue volumes, and nullifies the impact of colonic insufflation at CTC. In total, the adipose tissue measurement algorithm takes approximately three minutes to process an abdominal-region study (Intel Xeon CPU, 3.4 GHz; Santa Clara, CA).

### Statistical analysis

Descriptive statistics were calculated for patient age and adipose tissue measurements, grouped by gender. For each patient, the adipose tissue volumetric slabs and body volumes ( $\text{cm}^3$ ) at each vertebral level were normalized by dividing the volume by the corresponding vertebral level slab thicknesses (cm), yielding the mean cross-sectional area ( $\text{cm}^2$ ) at each vertebral body level. In patients who had more than one CTC study, changes in adipose tissue areas over time were normalized to annual rates by dividing changes in mean area by the number of years between scans. The number of years between scans was calculated by dividing the number of days between scans by 365.25. Because segmentation at the T12 level was found to be prone to error, we limit our results to the L1–L5 levels. Furthermore, because we have extensively utilized the L1 level for BMD assessment, and because this level is generally included on all thoracic and abdominal CT scans, the main results and data analysis will focus on this level.

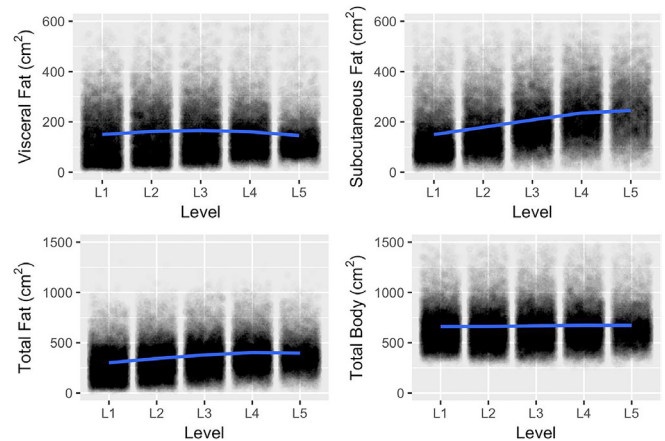
Comparison of mean adipose values between males and females were performed by independent *t*-tests. Comparison of the proportion of male and female patients among those whose VAT/SAT ratio increased between CTC scans was performed with a one-sample proportion test using a null hypothesis value of 0.5. All data processing and statistical analyses were performed using base R (R Core Team, v. 3.4.2; Vienna, Austria) and the *data.table*, *dplyr*, and *ggplot2* packages.

### RESULTS

10,059 patients were initially eligible for inclusion. The final study cohort consisted of 8852 individuals (mean age, 57.3 years; 3926 males, 4926 females). Exclusions were due to spine segmentation failure ( $n = 102$ ), adipose tissue classification failure ( $n = 80$ ), and unavailability of the thin-section supine series images from our picture archiving and communications system (PACS) ( $n = 1025$ ).

A comparison of the spread of all CT-based adipose tissue and body size measurements across L1–L5 vertebral levels in this population is shown in Figure 2. For reasons noted in the Methods, we focus primarily on the L1 values for further analysis. Summary statistics for adipose tissue measurements at the L1 level at initial CT evaluation are provided in Table 1. Adipose tissue measurements are reported as mean cross-sectional area ( $\text{cm}^2$ ) at the L1 vertebral level. For SAT at L1, males had significantly lower mean cross-sectional area than females, with mean values of  $123.8 \text{ cm}^2 (\pm 75.1)$  and  $171.0 \text{ cm}^2 (\pm 109.8)$ , respectively ( $p < 0.001$ ). For visceral adipose tissue, males had significantly greater mean cross-sectional area than females, with mean values of  $205.5 \text{ cm}^2 (\pm 105.5)$  and  $108.0 \text{ cm}^2 (\pm 82.3)$ , respectively ( $p < 0.001$ ). The ratio of visceral to subcutaneous fat (VAT/SAT) at the L1 vertebral level at initial CTC was three times higher in males compared with females on average, with values of  $1.8 (\pm 0.7)$  and  $0.6 (\pm 0.4)$ , respectively ( $p < 0.001$ ). Mean VAT/SAT values at the L4 vertebral level for males and females

Figure 2. Jitter plots showing the distribution of adipose tissue measurements according to vertebral level at initial CT in 8854 adults. The transparency of individual points is linearly related to the degree of over-plotting (100 overlapping points required for complete opacity). The Loess smoother lines connect the mean volumes at each vertebral level. The blue line represents the mean values at each vertebral level.



were  $1.0 (\pm 0.6)$  and  $0.6 (\pm 0.8)$ , respectively. The population-based distribution of SAT, VAT, and total adipose tissue measurements between males and females are shown in Figure 3.

A total of 1584 patients had multiple CTC examinations with a mean time difference of  $5.6 (\pm 2.0)$  years between the initial and follow-up study. Summary statistics for mean annual changes in adipose tissue measurements between initial and follow-up CTC are given in Table 2. There were no significant differences

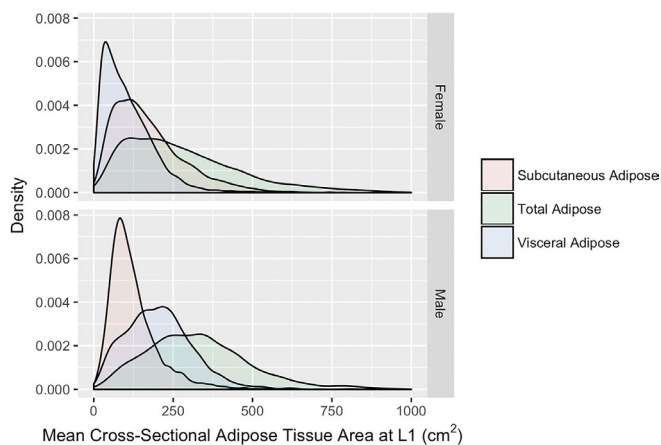
Table 1. Summary statistics for adipose measurements at initial CT (L1 level) in 8854 adults

	Sex	Mean	SD	Median
Age (years)	M	57.3	7.8	56
	F	56.9	7.7	55
Total body area ( $\text{cm}^2$ )	M	734.1	183.8	707.6
	F	606.2	201.4	558.5
Subcutaneous adipose ( $\text{cm}^2$ ) (SAT)	M	123.8	75.1	105.4
	F	171.0	109.8	147.3
Visceral adipose ( $\text{cm}^2$ ) (VAT)	M	205.5	105.5	199.7
	F	108.0	82.3	89.4
Total adipose tissue ( $\text{cm}^2$ ) (TAT)	M	329.3	164.3	314.1
	F	278.9	179.7	240.9
VAT/SAT	M	1.8	0.7	1.7
	F	0.6	0.4	0.6

SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue.

Summary statistics for CT-based adipose measurements at the L1 level, according to gender. Adipose volumes at L1 were normalized by dividing by slab thicknesses, yielding mean cross-sectional area. Total body area represents the entire cross-sectional area at the L1 level, excluding gas within bowel.

Figure 3. Density plot comparing the distributions of subcutaneous, visceral, and total adipose tissue measurements at the L1 vertebral level, according to gender. Density values are analogous to the probability of a random patient's adipose tissue volume being at a single point on each respective density curve. Total adipose tissue was the measurement with the broadest distribution in both males and females. The measurement with the highest probability density peak for females was visceral adipose tissue, while for males it was subcutaneous adipose tissue.



in the mean annual rates of change in VAT, SAT, or VAT/SAT in males compared to females ( $p = 0.06, 0.96, 0.20$ , respectively). Interestingly, the average VAT/SAT ratio change was positive in males, but negative in females. However, among patients whose mean annual  $\Delta(\text{VAT}/\text{SAT})$  ratio was  $>1$  (i.e. visceral change was greater than subcutaneous change), 333 (66.3%) were males and 169 (33.7%) were females ( $p < 0.001$ ). A comparison of mean annual  $\Delta\text{VAT}$  against mean annual  $\Delta\text{SAT}$  in all patients who underwent more than one CTC is shown in Figure 4. A total of 786 patients (366 males, 421 females) gained in both VAT and SAT on the follow-up CT. Among patients who gained in both VAT and SAT, 91.2% of males showed an increase in the VAT/SAT ratio, compared with 40.1% of females.

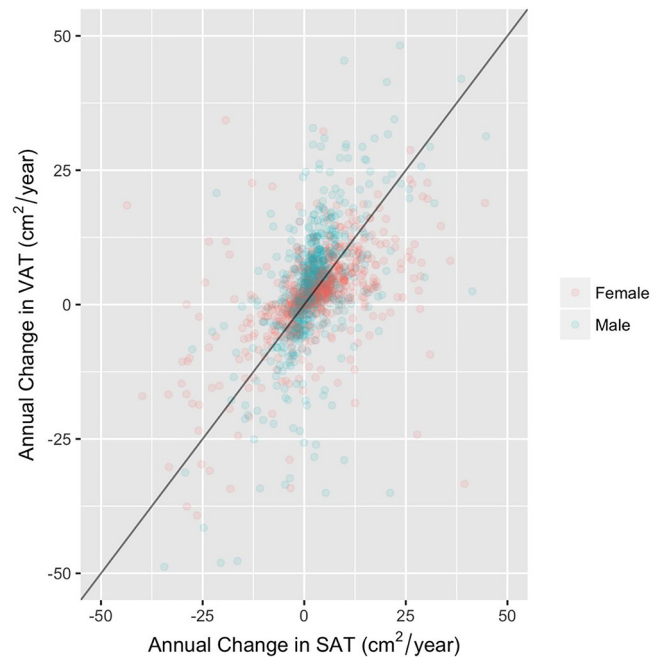
Table 2. Summary statistics for mean annual changes in adipose measures in 1585 adults

	Sex	Mean	Median	IQR
$\Delta\text{VAT}$ ( $\text{cm}^2 \text{ year}^{-1}$ )	M	4.72	3.65	9.53
	F	2.46	2.12	5.81
$\Delta\text{SAT}$ ( $\text{cm}^2 \text{ year}^{-1}$ )	M	2.26	1.62	5.61
	F	1.65	2.52	8.13
$\Delta(\text{VAT}/\text{SAT})$ (per year)	M	0.015	0.005	0.07
	F	0.005	0.006	0.03

SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; IQR, interquartile range

Summary statistics for mean annual changes in visceral (VAT), subcutaneous (SAT), and VAT/SAT between initial and subsequent CTC at the L1 vertebral level, grouped by gender.  $\Delta\text{VAT}$  and  $\Delta\text{SAT}$  are given in units of mean cross-sectional area at the L1 vertebral level ( $\text{cm}^2 \text{ year}^{-1}$ ). The ratio change is unit-less (per year).

Figure 4. Scatter plot of annualized changes in VAT and SAT between the initial and follow-up CT in the subset of 1585 patients with multiple scans. The line indicates a ratio of  $\Delta(\text{VAT}/\text{SAT}) = 1$ . Patient gender is indicated by the point color. Note how more males showed a relative increase in visceral vs subcutaneous fat over time, whereas the reverse was true for females. SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.



## DISCUSSION

In this study, we quantified abdominal adipose tissue in a large adult screening population using a validated and fully automated segmentation algorithm. We believe this unique study is the first to provide normative population-based data, which may prove valuable for assessing cardiometabolic risk in the near future. To our knowledge, this is also the first study to use an automated segmentation algorithm to assess temporal changes in abdominal adipose tissue volumes over time in the clinical setting. This allowed us to identify a subset of patients who showed a significant increase in VAT/SAT over time. Given the predictive value of visceral fat measurement for cardiovascular risk,<sup>4-9</sup> and for all-cause mortality in males,<sup>10</sup> use of such an automated tool might prove useful at abdominal CT evaluation, regardless of the specific indication.

We found that males in our sample had significantly higher VAT cross-sectional areas and significantly higher VAT/SAT ratios than females at the L1 vertebral level. Although this comparison was not statistically controlled for differences in age, mean ages were similar for males and females in our screening cohort (mean age for males =  $57.3 \pm 7.8$  years, females =  $57.0 \pm 7.7$  years). Overall, our results demonstrate that an automated measurement method for VAT and VAT/SAT in a large CT screening population can reliably be used to generate and test hypotheses regarding the association of adipose tissue compartments and adverse patient outcomes.

While there have been no studies of the relationship between changes in the volume or area of abdominal adipose tissue on CT and adverse outcomes, several have noted that, when measured at a single point in time, a significant association between visceral adiposity, metabolic syndrome risk factors, and increased risk of future cardiovascular events exists.<sup>7-9,11,21</sup> In one study, increased VAT and SAT areas measured at cardiac CT were associated with increased risk of all-cause mortality, myocardial infarction, and the need for coronary revascularization at least one month after image acquisition independent of clinical cardiovascular risk factors. However, the outcomes were all combined into one category and competing risks analysis was not performed, so the association of visceral adiposity with specific outcomes was not reported. Contradicting evidence about the role of visceral adiposity and future cardiac events also exists,<sup>22</sup> which may be due to the retrospective nature of most studies and sampling variation. Ultimately, prospective studies using large CT-based screening cohorts would provide the least-biased estimates of the association between visceral adiposity and significant adverse patient outcomes.

Several other computational methods for automatically quantifying abdominal adipose tissue from CT images exist,<sup>12,23-30</sup> and computational methods vary between these different algorithms. Our approach was to first identify the L1-L5 vertebral bodies and create separate slabs from which to make adipose volume measurements; this approach enhances inpatient reproducibility by identifying relatively un-changing anatomical landmarks. Then, body masking using region-growing was performed, followed by noise reduction, adipose tissue classification, and separation of visceral and subcutaneous compartments using active contour models. Volume calculations were made by summing the number of voxels classified as adipose tissue within each vertebral slab. Finally, mean adipose cross-sectional areas for each vertebral level were calculated in individual patients in order to remove the correlation of adipose tissue volumes with patient height (due to larger vertebral bodies and subsequently greater slab thickness). No studies comparing different adipose tissue quantification algorithms on the same imaging dataset have been performed, which limits the ability to directly compare different studies and perform meta-analyses. A prior review of methods for measuring body composition using various imaging modalities exists,<sup>31</sup> but several new methods have been introduced since its publication. An updated critical systematic review comparing recently published algorithms for adipose tissue quantification from CT images would assist with development of new standards and future research.

CTC screening affords an opportunity to perform opportunistic screening for multiple conditions that already have established diagnostic criteria, such as osteoporosis, abdominal aortic aneurysm, and metabolic syndrome. When adipose tissue quantification is combined with other screening examinations, such as asynchronous QCT,<sup>32</sup> trabecular attenuation measurement,<sup>33-36</sup> or finite element analysis<sup>37</sup> for osteoporosis screening and fracture-risk prediction, significant value can be added to CTC studies with little additional costs or time on the part of the radiologist.<sup>38</sup> Additional potential examples of

automated CT-based opportunistic screening might include abdominal aortic calcium scoring and muscle mass assessment (for sarcopenia). Ideally, screening for a wide variety of conditions would help referring providers to initiate management plans for patients with positive screening results. Identification of such patients whose VAT/SAT ratio increases over time could be useful for studying the relationship between visceral adiposity and outcomes related to the metabolic syndrome, such as adverse cardiovascular events. To date, no studies have established a relationship between changes in visceral adiposity over time and clinical outcomes.

Our study has some limitations. Spine segmentation and adipose tissue measurement failed in 102 and 78 cases, respectively, and we did not determine what specifically caused them. Spine segmentation failure can be due to excessive spinal hardware or severe compression fractures, which can lead to mislabeling of the vertebrae. Adipose tissue classification failures in 78 cases were signified by cross-sectional area measurements of either 0 cm<sup>2</sup> or anomalously large values. Also, in a small number of patients, the identified vertebral level was off by  $\pm 1$  level (*i.e.* T12 or L2 instead of L1) due to difficulty in accurately detecting the 12th rib that served as a landmark. In a clinical setting, quality assurance could be performed at the time of spine segmentation or adipose quantification failure when it occurs. However, future work will focus on improving the robustness of the algorithm against computational errors. Comparison of manual and automated adipose area measurements were also not performed since prior validation work has shown them to be nearly equivalent.<sup>18,39</sup> A final limitation of our study was that we did not attempt to correlate the automated fat measures for future cardiovascular events. However, we intend to embark on such a study in the near future.

In summary, we quantified cross-sectional areas of abdominal adipose tissue in a large screening CTC population using a validated, automated segmentation algorithm at longitudinal CT. We found significant elevations in VAT and VAT/SAT in males compared to females. Our results demonstrate that an automated adipose tissue measurement method for VAT and VAT/SAT in a large CT screening population can reliably be used to quantify changes in visceral adiposity. Ultimately, it may be possible to translate this opportunistic information into cardiovascular risk stratification, regardless of the indication for the abdominal CT scan.

## COMPETING INTERESTS

Perry Pickhardt, MD is an Advisor to Bracco and a shareholder in Elucent, SHINE, and Celectar. Ronald Summers, MD, PhD receives patent royalties from iCAD, research support from Ping An and NVidia, and royalties for software licenses to ScanMed, Philips, Imbio, Zebra Medical, and Ping An.

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## ETHICS APPROVAL

This study was approved by the University of Wisconsin Institutional Review Board.

## PATIENT CONSENT

Patient consent for this retrospective study was waived by the University of Wisconsin Institutional Review Board.

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