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A Single MRI Slice Does Not Accurately Predict Visceral and Subcutaneous Adipose Tissue Changes During Weight Loss

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Abstract

Previous cross-sectional studies found that a single magnetic resonance imaging (MRI) slice predicts total visceral and subcutaneous adipose tissue (VAT and SAT) volumes well. We sought to investigate the accuracy of trunk single slice imaging in estimating changes of total VAT and SAT volume in 123 overweight and obese subjects who were enrolled in a 24-week CB-1R inverse agonist clinical trial (weight change, −7.7±5.3 kg; SAT change, −5.4±4.9 L, VAT change, −0.8±1.0 L). VAT and SAT volumes at baseline and 24 weeks were derived from whole body MRI images. The VAT area 5–10 cm above L_4–L_5 ($A_{+5–10}$) (R^2=0.59–0.70, P<0.001) best predicted changes in VAT volume but the strength of these correlations were significantly lower than those at baseline (R^2=0.85–0.90, P<0.001). Furthermore, the L_4–L_5 slice poorly predicted VAT volume changes (R^2=0.24–0.29, P<0.001). Studies will require 44–69% more subjects if ($A_{+5–10}$) is used and 243–320% more subjects if the L_4–L_5 slice is used for equivalent power of multi slice total volume measurements of VAT changes. Similarly, single slice imaging predicts SAT loss less well than cross-sectional SAT (R^2=0.31–0.49 vs. R^2=0.52–0.68, p<0.05). Results stayed the same when examined in men and women separately. A single MRI slice 5–10 cm above L_4–L_5 is more powerful than the traditionally used L_4–L_5 slice in detecting VAT changes, but in general single slice imaging poorly predicts VAT and SAT changes during weight loss. For certain study designs, multi-slice imaging may be more cost effective than single slice imaging in detecting changes for VAT and SAT.

Keywords

Visceral adipose tissue; subcutaneous adipose tissue; clinical trial; magnetic resonance imaging; computed tomography; body composition

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INTRODUCTION

Computerized axial tomography (CT) and magnetic resonance imaging (MRI) are increasingly being used to quantify regional adipose tissue, including visceral and subcutaneous adipose tissue (VAT and SAT). Because of the relatively high cost of MRI analysis and the radiation exposure of CT attributed to multi-slice imaging, a single slice image is often used as a compromise between accuracy, safety and cost (1–8). Previous studies have evaluated the relationship between single slice imaging and total VAT and SAT volume in cross-sectional subject samples (9–19). Most of these studies, including some with large sample sizes, have found that single slice images in the upper abdomen best predict total VAT as opposed to the traditionally used L_4–L_5 slice (9, 16–18).

Currently, there is a lack of large scale studies that evaluate how accurately a single slice predicts changes in VAT and SAT. A report of 39 postmenopausal women showed that a single slice area at L_2–L_3 better predicts changes in VAT than a slice at L_4–L_5 after 6 months of supervised exercise intervention (10). However, in this study there was no change in VAT so it is unknown which slice location best predicts VAT loss. Furthermore, it is also unknown how the relatively large measurement errors associated with the use of single slice imaging in estimating VAT changes influence study design and power estimates (10).

The present study is the first to evaluate how a single image slice predicts total VAT and SAT changes in a randomized, double-blind weight loss clinical trial. We use a relatively large sample of overweight and obese men and women to determine how single slice estimation errors influence sample size estimation.

METHODS

Protocol and subjects

The study aims were carried out by evaluating the relationships between changes in single cross-sectional image areas and changes in the volumes of total body SAT and VAT in overweight and obese subjects. The study sample is a sub-set of subjects from a 24 week, double-blind, randomized, placebo-controlled study of the CB-1R inverse agonist Taranabant. Subjects included in the present study all had baseline and 24 week whole body MRI scans acquired. Subject characteristics are similar between the whole sample and the sub-set that had whole body MRI acquired (Table 1, **Table S1**).

Eligible patients included men and women age ≥18 years with a BMI between 30 and 43 kg/m^2, inclusive, or patients with a BMI ≥27 kg/m^2 and < 30kg/m^2, but only if they had obesity-related comorbidities (e.g., hypertension, dyslipidemia, sleep apnea, etc.). Exclusion criteria included a history or presence of a major psychiatric disorder, severe hypertension, diabetes mellitus, or any other clinically significant disorder including cardiovascular, pulmonary, hepatic, renal, gastrointestinal, neurological, malignancy <5 years, or endocrine diseases (20). This study included a total of 123 subjects, 99 women and 24 men who were predominantly white (n=113) (Table 1).

The original study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study was approved by an institutional review board or independent ethics committee and all patients provided written informed consent. The exempt status of the present analysis was reviewed and approved by the Institutional Review Board of St. Luke's-Roosevelt Hospital.

Magnetic Resonance Imaging

Whole-body MRI was carried out as previously reported by our group using 1.5 T MR systems (21–22). All subjects were scanned with a T1-weighted, spin-echo sequence, with a 300 ms repetition time and an 11 ms echo time. A field of view 48 cm and a 256×256 matrix was used. The protocol involved acquisition of approximately 40 axial images of 10 mm thickness and at 40 mm intervals from fingers to toes with the subject in a supine position (23). The L_4–L_5 intervertebral disc was used as the point of origin. Following acquisition, VAT and SAT were segmented by trained, quality-controlled technicians using image analysis software (SliceOmatic, Tomovision Inc., Montreal, Canada) at the Image Reading Center of the New York Obesity Nutrition Research Center. The intraclass correlation coefficient for volume rendering of VAT and SAT by different technicians at our center is 0.95 and 0.99. The VAT and SAT volumes were calculated as:

$$V=(t+h)\sum_{i=1}^{N}A_i$$

where V is volume, A_i is each scan's cross-sectional area, h is the between-slice interval, t is the thickness of each slice, and N is the number of total slices. Abdominopelvic VAT volumes were calculated using all slices between the dome of the liver and the bottom of the pelvis (abdominopelvic region), while abdominal VAT was calculated using all slices between the dome of the liver to one slice below the L_4–L_5 level. Abdominal and abdominopelvic VAT were chosen in this study because they were the most frequently measured compartments in previous studies. Shen *et al.* provide an extended critical review of VAT definitions and the use of VAT estimations in clinical research (24).

Statistical methods

Group data are presented as the mean ± SD. The correlations among single slice VAT or SAT areas and VAT or SAT volumes were calculated in baseline and follow up data in all subjects, as well as in men and women groups. The results were used to identify the trunk slice location with the highest correlation with VAT or SAT. Similarly, these correlations were also calculated for VAT and SAT changes. Since a majority of earlier studies reported abdominal rather than abdominopelvic VAT (25–29), we simplify our presentation of results by providing illustrative examples mainly for abdominal VAT, although we carried out analyses for both with similar results.

The slice showing the highest correlation between adipose tissue area and adipose tissue volume was chosen as the best slice for use in regression models. A simple regression model was then applied to determine the coefficients for the observed relations between adipose

tissue volume and adipose tissue area separately for the selected slice and the L_4–L_5 level slice. The variances of the residuals from the regression using L_4–L_5 versus using the best single slice were compared using Pitman's test for correlated variances (30). Differences between correlated correlation coefficients were tested using the method of Steiger (31).

All statistical analyses were carried out using SAS 9.2 package (SAS Institute. Inc., Cary, NC, USA). Two-tailed (α=0.05) tests of significance were used.

RESULTS

Relationship between single slice area and total adipose tissue volumes

At baseline, the highest correlation between single slice abdominal VAT area and abdominal VAT volume was located 5 – 10 cm above the L_4–L_5 level (r = 0.947 and 0.948, respectively, significantly greater than r = 0.850 at the L_4–L_5 level at P < 0.001) (Table 2). Similar results were observed for abdominopelvic VAT (Table 2).

Slice location did not have a strong influence on the relationship between a single slice SAT area and total SAT volume. The highest correlation between a single slice SAT area and SAT volume was located at 10 cm below L_4–L_5 (r = 0.824, P<0.001) (Table 2), but was not significantly different (P = 0.35) from a slice acquired at L_4–L_5 (r = 0.795, P<0.001).

For VAT changes between baseline and 24 weeks, the slices located 5–15 cm above the L_4–L_5 level predict volume changes significantly better (P < 0.001) than the slice at L_4–L_5 (r = 0.796 – 0.834 vs. r = 0.488, P<0.001), with the slice located at 10 cm above L_4–L_5 having the highest correlation with changes in VAT volume (Table 2). Similar results were observed for abdominopelvic VAT. When VAT was examined in white subjects only, the results remained the same with the slices located 5–15 cm above the L_4–L_5 level predicting volume changes significantly better (P < 0.001) than the slice at L_4–L_5 (r = 0.795 – 0.831 vs. r = 0.481, P<0.001). When VAT changes were examined separately in men and women, the results remained the same except that the correlations were higher for men than women in the upper abdomen (i.e., 5–15 cm above L_4–L_5)(r = 0.858 – 0.940 and 0.691 – 0.732, respectively, all P<0.001) but were similar at L_4–L_5 (r = 0.510 and 0.477 respectively, all P<0.05).

Slice location did not appear to have a strong influence on the relationship between a single slice SAT area change and total SAT volume change. The highest correlation between a single slice SAT area change and SAT volume change was located 10 cm below L_4–L_5 (r = 0.702) (Table 2), but was not significantly different (P = 0.08) from a slice acquired at L_4–L_5 (r = 0.590, P < 0.001). When SAT was examined in white subjects only, the results remained the same with the highest correlation between a single slice SAT area change and SAT volume change located 10 cm below L_4–L_5 (r = 0.699). When SAT changes were examined separately in men and women, the results remained the same except that the correlation was highest in the upper abdomen in men (20 cm above L_4–L_5, r = 0.682, P < 0.001) but in the pelvis in women (10 cm below L_4–L_5, r =0.721, P<0.001).

All correlations between single slice and total VAT or SAT volume changes were significantly lower ($P < 0.05$) than their counterparts at baseline, with the exception of a slice taken 20 cm above the L_4–L_5 level for abdominal VAT ($P = 0.06$).

Weight, BMI and waist circumference predicts changes of VAT and SAT similar to single slice imaging at L_4–L_5 (VAT, r = 0.503–0.535 vs. 0.488–0.540, p = 0.548–0.945; SAT, r = 0.485–0.665 vs. 0.590, p = 0.158–0.273).

Power estimates for different anatomic locations

If VAT volume as measured by the multiple slice protocol is taken as the "true" value, and the squared correlations between individual slice locations and VAT volume are considered to be estimates of the reliability of the individual slice, then we can calculate the relative loss of power from using a single slice (32). In order to achieve equivalent power, a study with multiple slice measures of abdominal VAT volume as the dependent variable would require 11% more subjects if a single slice area is measured +10 cm above L_4–L_5 and 38% more subjects if a slice area is measured at L_4–L_5. In contrast, achieving an equivalent power with measures of VAT volume change would require 44% more subjects if a single slice area is measured +10 cm above L_4–L_5 and 320% more subjects if a slice area is measured at L_4–L_5. Similar patterns of sample size increase for single slice imaging were observed for abdominal-pelvic VAT.

For SAT, the sample size increase using a single slice versus total volume measurement was also larger when SAT volume changes was the outcome of interest, rather than baseline SAT (103% – 187% vs. 47–58%).

DISCUSSION

Two main findings emerge from this study conducted on a large, randomized, weight-loss clinical trial. The first finding is that a single MRI slice in the upper abdomen better predicts changes in VAT volume compared to the traditionally used L_4–L_5 slice. The second finding is that the accuracy of single slice imaging is much lower for estimating longitudinal changes in VAT volume than for estimating the cross-sectional amount of VAT.

The present study, carried out in a large longitudinal sample of overweight and obese subjects, observed that the slice that best predicts VAT changes is located 5 to10 cm above the L_4–L_5 level. Our results are consistent with most previous cross-sectional studies showing that a single image slice in the upper abdomen better predicts total VAT volume than the L_4–L_5 slice (9, 11–12, 14–18, 33). In addition, we found that slice location did not appear to have a strong influence on the relationship between a single slice SAT area change and total SAT volume change and this observation is consistent with that previously reported in cross-sectional studies (18). Our findings are also consistent with a previous report of 39 postmenopausal women showing that a single slice area at L_2–L_3 better predicts VAT changes than the slice at L_4–L_5 following a 6 month supervised exercise intervention (10). However, unlike the previous study that found no VAT loss (i.e., -0.09 ± 0.33 L), the present study showed a significant reduction in VAT from baseline (i.e., -0.78 ± 0.96 L). In addition, the present study demonstrated that using a single slice at the upper abdomen can

reduce the sample size compared to using a slice at L_4–L_5. For example, using the best single slice can reduce sample size by 276% compared to using L_4–L_5 (i.e., 320% − 44% =276%, Table 3). This reduction in sample size is much larger than that in the baseline cross-sectional sample (i.e., 38% − 11% = 27%, Table 3).

An important finding of the present study is that a single image slice poorly predicts VAT or SAT changes, with the correlations between single slice area and total volume significantly lower for VAT or SAT changes than for baseline VAT or SAT. The results have important implications for study designs when using a single image slice in longitudinal studies. The increase in sample size is much larger for changes in total VAT than for baseline VAT (i.e., baseline VAT, 11–38%; VAT change, 44–320%). If a study design includes a single slice method to measure VAT, it is important to use a slice 5–10 cm above the L_4–L_5 level rather than the L_4–L_5 level. In addition, whether to choose a single slice method or a multi-slice total volume measurement method depends on the tradeoff between increase in image slice numbers and increase in subject number for longitudinal study designs (Figure 1). Depending on the non-imaging study cost, subject recruitment and image analysis cost (Figure 1), it is possible that whole body MRI may be counter-intuitively more cost effective than single slice studies. It should be noted that image analysis labor costs are influenced by scan quality and whether additional body components are segmented (i.e., intermuscular adipose tissue, skeletal muscle, etc.). In addition, cost for quality control procedures, including sorting whole body MRI scans (i.e., for scans acquired with re-positioning) should also be considered.

An example of how future studies can be designed using this information is shown in Table 3. If by power calculation, a cross-sectional study measuring total VAT volume needs to recruit 100 subjects, a study that uses a single slice measured at the best location only needs to include 11 more subjects to achieve the same power. On the other hand, if a longitudinal study measuring total VAT volume needs to recruit 100 subjects, a study using a single slice at the best location needs to include 44 more subjects to achieve the same study power. Similarly, if a longitudinal study measuring total SAT volume needs to recruit 100 subjects, a study using a single slice at the best location needs to include 103 more subjects to achieve the same study power. These results imply that a single slice image's efficiency is much lower in estimating VAT or SAT volume changes than in estimating cross-sectional VAT or SAT. If the cost to recruit new subjects and the cost of non-imaging studies are higher than the cost of image analysis and the cost of image acquisition (Figure 1), it is possible that a total VAT or SAT volume measurement study will be more cost effective than a single slice study (Figure 1). L_4–L_5 is a poor choice for estimating changes in total VAT, since 320 more subjects need to be included in a longitudinal study to achieve the same study power as a volume measurement study (Table 3). Using a single slice at L_4–L_5 level is an inefficient approach for detecting changes in VAT. Interestingly, we found that the predictive value of L_4–L_5 single slice imaging is as weak as weight, BMI and waist circumference when determining total VAT and SAT volume changes. Although many studies have used single slice imaging as a reference method for VAT and SAT measurement to validate other techniques, our results suggest that it is not appropriate to use single slice imaging as a reference method to validate other methods (i.e., BMI, waist circumference, etc.) when VAT or SAT changes are examined, especially when the slice is acquired at L_4–L_5.

Scanning time can be significantly reduced for whole body MRI on newer MR scanners, especially when total imaging matrix (TIM) technology and state-of-the-art fast imaging technique are used (34–37). For these fast whole body scans that can be carried out during one positioning, the image acquisition cost of a whole body scan is of minimal concern. With increasing availability of these new technologies, whole body MRI acquisition is a future direction for adipose tissue quantification. Nonetheless, acquiring one or a few slices image may still be favored by studies that use CT and in multi-center clinical trials that may include data collected with older MRI systems or that can only implement simple acquisition protocols.

There are some limitations of the present study. Although we found that VAT areas 5 and 10 cm above the L_4–L_5 level had the highest correlations with VAT volume changes, we do not have continuous scans and the exact location of the slice with the highest correlation cannot be determined, and we cannot study landmarks such as L_2–L_3 or L_3–L_4. (10). In addition, we do not have clinical outcome data and therefore cannot relate slice location choice to morbidity and mortality. Nonetheless, the present study is largest to date investigating single slice imaging in estimating changes in VAT and SAT. Results from the present study have important implications for future study designs. Another limitation of the present study is that 74% subjects in the present study were White women. Although our previous study in a cross-sectional sample did not find a strong influence of gender or race on how single slice imaging predicts total VAT volume, future multi-race samples with a similar sample size of men and women are needed to clarify potential race and gender differences in the anatomical location and predicbility of single slice imaging in detecting VAT and SAT changes (16, 38).

CONCLUSIONS

A slice 5–10 cm above the L_4–L_5 level is more powerful than the traditionally used L_4–L_5 slice in detecting changes in VAT volumes, but in general single slice imaging poorly predicts changes in VAT and SAT during weight loss. Depending on the tradeoff between increasing subject numbers and image slice numbers, multi-slice imaging may be more cost effective than single slice imaging in detecting changes in VAT and SAT.

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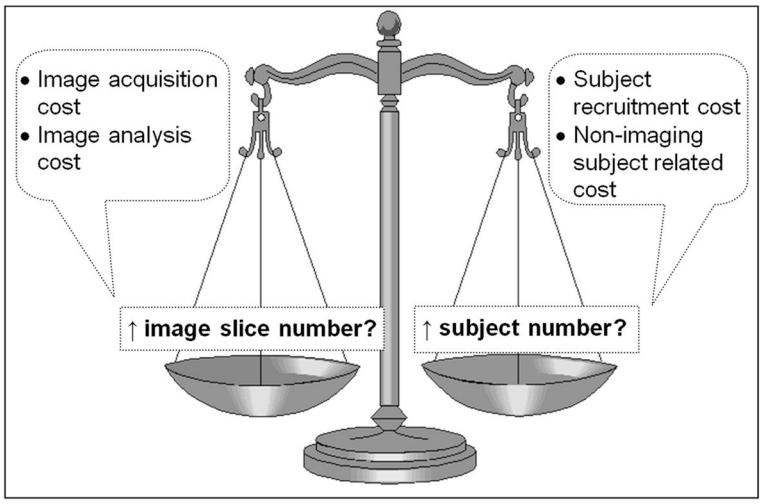

Figure 1.
The tradeoff between increase in subject number and image slice number in designing a study involving MRI imaging measurement.

Table 1

Characteristics of the subjects who had whole body MRI scans (n=123)

	Baseline	Follow up (24 weeks)	Changes
Age (yrs)	49.5 ± 12.5 (19.0–79.0)	-	-
Gender; n (%)			
Female	99 (80.5%)	-	-
Male	24 (19.5 %)	-	-
Race; n (%)			
White	113 (91.9%)	-	-
Black	5 (4.1%)	-	-
Hispanic	2 (1.6%)	-	-
Other	3 (2.4%)	-	-
Weight (kg)	95.8 ± 14.4 (70.9 – 133.7)	88.2 ± 14.0** (61.6 – 122.6)	−7.7 ± 5.3 (−21.9 – 3.7)
BMI (kg/m^2)	34.4 ± 3.8 (27.1 – 44.0)	31.7 ± 3.8** (22.5 – 41.0)	−2.8 ± 1.9 (−7.8 – 1.5)
Abdominal-pelvic Visceral adipose tissue (L)	4.6 ± 2.0 (0.8 – 10.5)	3.8 ± 1.9* (0.6 – 11.9)	−0.8 ± 1.0 (−3.6 – 3.8)
Subcutaneous adipose tissue (L)	41.5 ± 10.5 (20.2 – 70.6)	36.2 ± 9.6** (16.5 – 63.7)	−5.4 ± 4.9 (−27.0 – 14.9)

Age, weight, BMI, VAT and SAT are presented as mean ± SD (ranges);

*, **, Significantly different from baseline by paired *t* test:

*, P < 0.01;

** P < 0.001.

Table 2

Pearson correlations between adipose tissue volume and adipose tissue areas for individual transverse slices below (−) or above (+) the L_4–L_5 level

		−15 cm	−10 cm	−5 cm	L_4–L_5	+5 cm	+10 cm	+15 cm	+ 20 cm	Weight	BMI	WC
Abdominal VAT	**Baseline**	-	-	0.787	0.850	0.947^{Δ}	0.948^{Δ}	0.894	0.669	0.508	0.293	0.569
	Changes	-	-	0.462^{*}	0.488^{*}	$0.796^{\Delta,*}$	$0.834^{\Delta,*}$	$0.813^{\Delta,*}$	0.514	0.533	0.503	0.516
Abdominal pelvic VAT	**Baseline**	0.493	0.754	0.820	0.857	0.927^{Δ}	0.920^{Δ}	0.873	0.664	0.503	0.281	0.580
	Changes	0.247^{*}	0.440^{*}	0.554^{*}	0.540^{*}	$0.780^{\Delta*}$	$0.770^{\Delta*}$	$0.733^{\Delta*}$	0.449^{*}	0.535	0.508	0.531
SAT	**Baseline**	0.720	0.824	0.780	0.795	0.776	0.816	0.814	0.752	0.523	0.705	0.408
	Changes	0.644^{*}	0.702^{*}	0.658^{*}	0.590^{*}	0.563^{*}	0.623^{*}	0.645^{*}	0.554^{*}	0.652	0.665	0.485

WC, waist circumference; all correlation coefficients are significantly different from 0 at $P<0.01$;

$^{\Delta}$, significantly higher than L_4–L_5 slice at $P<0.001$;

*, significantly lower than the same slice location at baseline at $P<0.05$.

Table 3

Calculation of increase in sample size for single image slice versus total adipose tissue volume

		Explained variance**		Increase in sample size***	
		Best single slice*	L_4–L_5 slice	Best single slice*	L_4–L_5 slice
Abdominal VAT	**Baseline**	0.90	0.72	11%	38%
	Changes	0.70	0.24	44%	320%
Abdomino-pelvic VAT	**Baseline**	0.86	0.73	16%	36%
	Changes	0.61	0.29	64%	243%
SAT	**Baseline**	0.68	0.63	47%	58%
	Changes	0.49	0.35	103%	187%

*, Slice 10 cm above the L4–L5, 5 cm above the L4–L5, and 10 cm below the L4–L5 have been selected as the images as the best single slice to estimate abdominal VAT, abdomiopelvic VAT, and SAT volume change, respectively.

**, Explained variance by a single slice of total VAT or SAT volume changes

***Increase in sample size related to total VAT or SAT measurement if a single slice is used.