MRI assessment of changes in adipose tissue parameters after bariatric surgery

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Abstract

Bariatric surgery and other therapeutic options for obese patients are often evaluated by the loss of weight, reduction of comorbidities or improved quality of life. However, little is currently known about potential therapy-related changes in the adipose tissue of obese patients. The aim of this study was therefore to quantify fat fraction (FF) and T1 relaxation time by magnetic resonance imaging (MRI) after Roux-en-Y gastric bypass surgery and compare the resulting values with the preoperative ones. Corresponding MRI data were available from 23 patients (16 females and 7 males) that had undergone MRI before (M0) and one month after (M1) bariatric surgery. Patients were 22–59 years old (mean age 44.3 years) and their BMI ranged from 35.7–54.6 kg/m^2 (mean BMI 44.6 kg/m^2) at M0. Total visceral AT volumes (V_{VAT-T}, in L) were measured by semi-automatic segmentation of axial MRI images acquired between diaphragm and femoral heads. MRI FF and T1 relaxation times were measured in well-defined regions of visceral (VAT) and subcutaneous (SAT) adipose tissue using two custom-made analysis tools. Average BMI values were 45.4 kg/m^2 at time point M0 and 42.4 kg/m^2 at M1. Corresponding V_{VAT-T} values were 5.94 L and 5.33 L. Intraindividual differences in both BMI and V_{VAT-T} were highly significant ($p<0.001$). Average relaxation times $T1_{VAT}$ were 303.7 ms at M0 and 316.9 ms at M1 ($p<0.001$). Corresponding $T1_{SAT}$ times were 283.2 ms and 280.7 ms ($p = 0.137$). Similarly, FF_{VAT} differences (M0: 85.7%, M1: 83.4%) were significant ($p <0.01$) whereas FF_{SAT} differences (M0: 86.1, M1: 85.9%) were not significant ($p = 0.517$). In conclusion, bariatric surgery is apparently not only related to a significant reduction in common parameters of adipose tissue distribution, here BMI and total visceral fat volume, but also significant changes in T1 relaxation time and fat fraction of visceral adipose tissue. Such quantitative MRI measures may potentially serve as independent biomarkers for longitudinal and cross-sectional measurements in obese patients.

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Introduction

In western countries, obesity is a growing healthcare problem and also associated with meta-bolic and cardiovascular diseases. Adipose tissue (AT) is a metabolically active organ that is highly affected by obesity and chronic low-grade inflammatory processes in obese AT have been reported to contribute significantly to the development of obesity-related morbidities [1]. One focus of medical research is therefore the development of effective anti-obesity therapies. Bariatric surgery and Roux-en-Y gastric bypass (RYGB) surgery in particular have shown sig-nificant therapeutic effects in the treatment of morbid obesity [2]. Besides the marked weight loss and reduced amounts of abdominal visceral (VAT) [3–5] and subcutaneous (SAT) [3–5] adipose tissue, bariatric surgery may reduce co-morbidities like type 2 diabetes and cardiovas-cular diseases [6,7]. The underlying mechanisms that ultimately improve the health of patients after such interventions are still not well understood. Intraoperative and follow-up biopsies are a direct way to assess the inflammatory [8,9] or morphological [10] response of adipose tissue to excessive weight. On the downside, invasive tissue sampling requires good patient compli-ance and has side effects, in particular for biopsies in visceral fat regions. There is consequently a need for a relatively simple, safe and reliable technique to assess and monitor the effects of bariatric surgery on adipose tissue.

Over the last decade, different magnetic-resonance techniques have been applied to charac-terize adipose tissue in vivo. Magnetic resonance spectroscopy (MRS) essentially probes the distribution of fatty acid components [11–13] whereas chemical shift-encoded water-fat MR imaging (MRI) may quantify the fat fraction (FF) in white or brown adipose tissue [14–16]. In a recent study, measurements of T1 relaxation times in adipose tissue have revealed significant differences between obese and healthy lean subjects [17].

The purpose of this work was to assess T1 relaxation time and fat fraction changes by MRI in visceral and subcutaneous AT of patients before and after Roux-en-Y gastric bypass (RYGB) surgery.

Materials and methods

This study was performed within the Integrated Research and Treatment Center on adiposity diseases (IFB *AdiposityDiseases* at Leipzig University Hospital, Leipzig, Germany) and approved by the institutional review board (IRB No. 363-11-ff-07032011, Faculty of Medicine, University of Leipzig). Written informed consent was obtained from all subjects.

All patients underwent standard laparoscopic RYGB with a small pouch (20 cm^3), an ali-mentary limb of 150 cm and a biliopancreatic limb of 50 cm. Surgery was performed following applicable German and IFSO guidelines. Twenty-three patients (16 females and 7 males, mean age 44.3 years, mean BMI 45.4 kg/m^2, both at M0) were included. Anthropometrics were recorded for both MRI time points.

All patients were examined in a 1.5-T MRI (Philips Achieva XR, Best, Netherlands) at time points before (M0) and one month (M1) after surgery. Fat volumetry involved axial in-phase/opposed-phase gradient echo images with 10 mm thickness and 0.5 mm gap that were acquired between diaphragm and femoral heads (typically 50 slices) in breath-hold technique (expiration). Other imaging parameters were: repetition time (TR) 76 ms, first/second echo time (TE$_1$/TE$_2$) 2.3/4.6 ms, flip angle (FA) 70, slice thickness (ST) 10 mm, interslice gap (ISG) 0.5 mm, field of view (FOV) 530 mm × 530 mm, acquisition matrix (M$_{ACQ}$) 216 × 177, recon-struction matrix (M$_{REC}$) 480 × 480. The total acquisition time (TA) was 10 x 16 seconds plus the intervals for breathing. All MRI data were acquired with the integrated whole-body coil.

Total abdominal VAT volumes (V$_{VAT}$) were then evaluated by a semiautomatic fat segmen-tation tool (under Matlab). Automatic contouring used k-means clustering to detect the outer

body (SAT) boundary and an iterative active-contours (snakes) algorithm in combination with region growing to define an inner SAT as well as a VAT boundary. A detailed description can be found in a previous work [18]. Incorrect portions of the automatic contours were simply corrected for by redrawing along the proper tissue boundary–effectively overwriting the wrong portions. Quantification of fat volumes involved a histogram-based analysis of the area under the fat-related peak structures (at higher signal intensities). This approach involves slightly more user interaction but also eliminates the need for highly accurate VAT boundary definition. Inter-observer reliability and reproducibility of that method have previously been found to be high [19]. Total SAT volumes were not considered because the SAT regions of several patients extended beyond the scanner's field of view.

T1 relaxation times were derived from a single-shot fast spin-echo sequence (TR/TE = 5,000/60 ms, FOV 500 mm × 500 mm, M_{ACQ} 296 × 295, ST 10 mm) with inversion recovery preparation at different inversion times TI (100, 150, 250, 500, 750 and 1,000 ms) [20]. A custom-made software tool under Matlab tool was used to compute the T1 time by fitting the TI-dependent signal intensities *SI* to the following model function

$$SI(TI) = \sqrt{S_0^2 \left(1 - 2 \cdot e^{-\left(\frac{TI}{T1}\right)} + e^{-\left(\frac{T_{SAT}}{T1}\right)^2} + C^2 \right)} \tag{1}$$

with calibration constant S_0, noise-related constant C and saturation time T_{SAT} (4,500 ms). Further technical details can be found in the original work by de Bazelaire et al. [21]. Fig 1 shows an example of a resulting T1 map with SAT and VAT regions of interest (ROI) used for quantification. VAT ROIs were generally placed within the mesentery at some distance away from signal heterogeneities, sparing intestines, peritoneum and vessels.

Reliability of ROI-based T1 measurement was then estimated by inspecting the distribution of individual T1 times and computing the coefficient of variation CV_{T1} as the ratio of mean TI intensity μ_{T1} and standard deviation σ_{T1} (Fig 2). Reported T1 times for VAT and SAT are then mean values μ_{T1} of the respective ROI.

For evaluation of the so-called proton density fat fraction in adipose tissue, chemical shift-encoded water-fat MRI was carried out using a multiecho Dixon sequence (3D spoiled gradient echo, TR 8.7 ms, TE 0.92–7.55 ms, 11 echoes, echo spacing 0.66 ms, FOV 384 mm × 288 mm, M_{ACQ} 128 × 96, FA 5˚, 18 slices, ST 10 mm, TA 19.3 s) in breathhold technique. Fat fraction (FF) and T2* time were then estimated by least-squares fitting the mean ROI signal intensities at all echo times TE to the model function

$$SI(TE) = |S_W + e^{i \cdot 2\pi \Delta f \cdot TE} \cdot S_F| \cdot e^{-TE/T2*} \tag{2}$$

with S_W and S_F as complex signal contributions of water and fat, respectively, and Δf as the frequency difference between the main lipid (1.3 ppm) and water peaks (4.7 ppm), approximately 220 Hz at 1.5 T. Computations were performed under Matlab (MathWorks, Natick, MA) and verified against an independent code under IDL (Exelis Visual, Boulder, CO).

Statistical evaluation was performed with SPSS (Version 24, IBM SPSS). Statistical significance was assumed at p<0.05. All data sets–six individual parameters at both time points (M0 and M1) as well as six percent changes (M1 vs. M0)–were tested for normal distribution using Shapiro-Wilk tests. Percent changes relative to M0 were then analyzed with a one sample Wilcoxon signed-rank test against a hypothetical median of 0% or with a one-sample t-test against a 0% mean depending on the p-values of the Shapiro-Wilk tests.
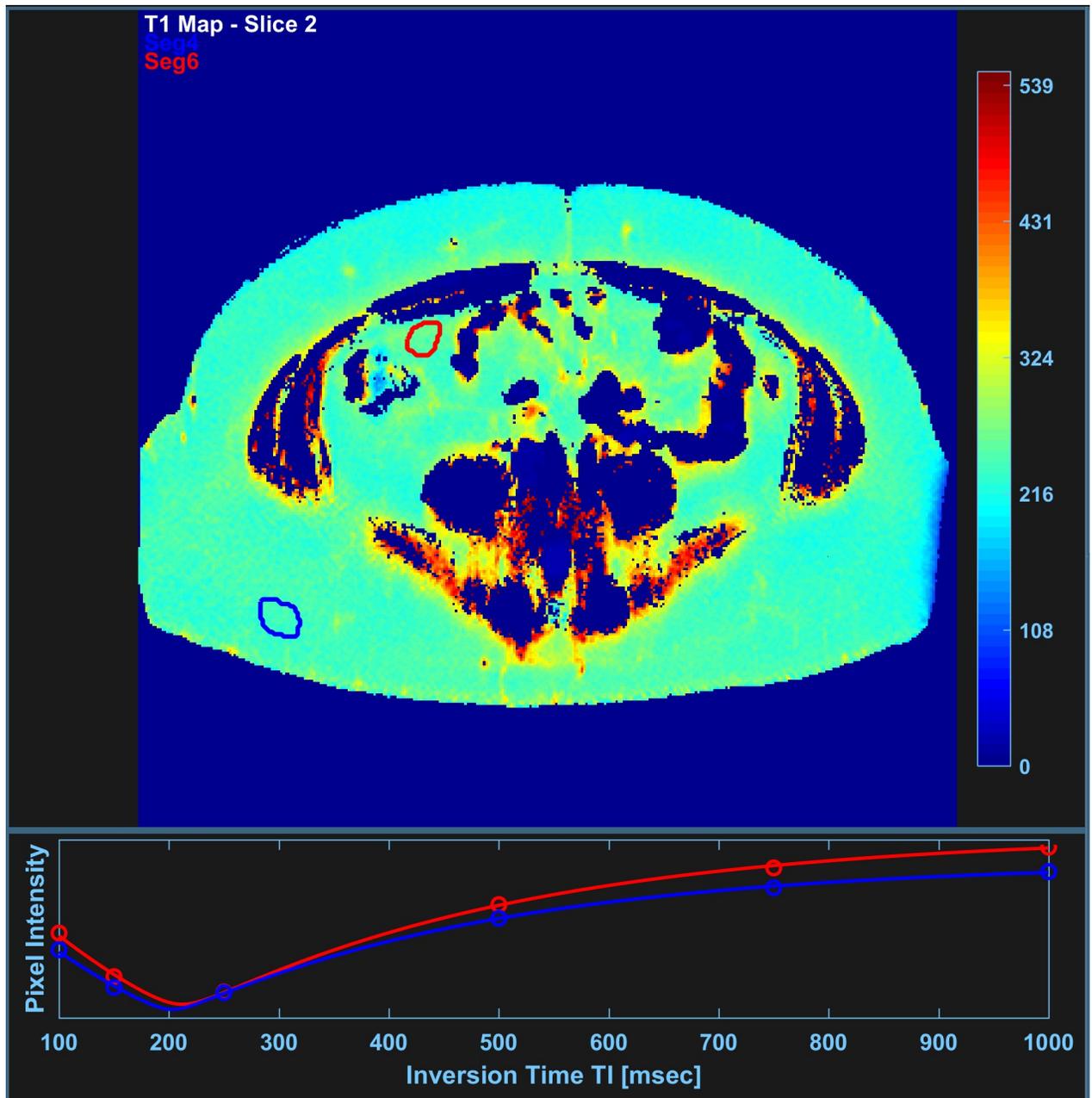
Fig 1. Screenshot of custom-made software tool for the quantification of T1 relaxation times in selected regions of interest. Display shows presurgical axial T1 map of an obese, 31-year-old female patient with a BMI of 41.1 kg/m^2. T1 values were determined in VAT (174 pixels) and SAT ROI (237 pixels) by fitting mean signal intensities (SI) in arbitrary units (a.u.) of single-shot fast spin-echo sequence with inversion recovery preparation at different inversion times TI to model function [17].

Results

Table 1 provides a summary of the main results. All parameter sets but percent V_{VAT-T} change were in line with the assumption of a normal distribution. Fig 3 shows a plot of the percent changes for all six parameters after one month (M1 vs. M0). The BMI reduction of nearly –7% was significant (p<0.001). The most prominent relative effect of nearly –11% was observed for total VAT volume, again significant (p<0.001). T1 coefficients of variation (CV) over all
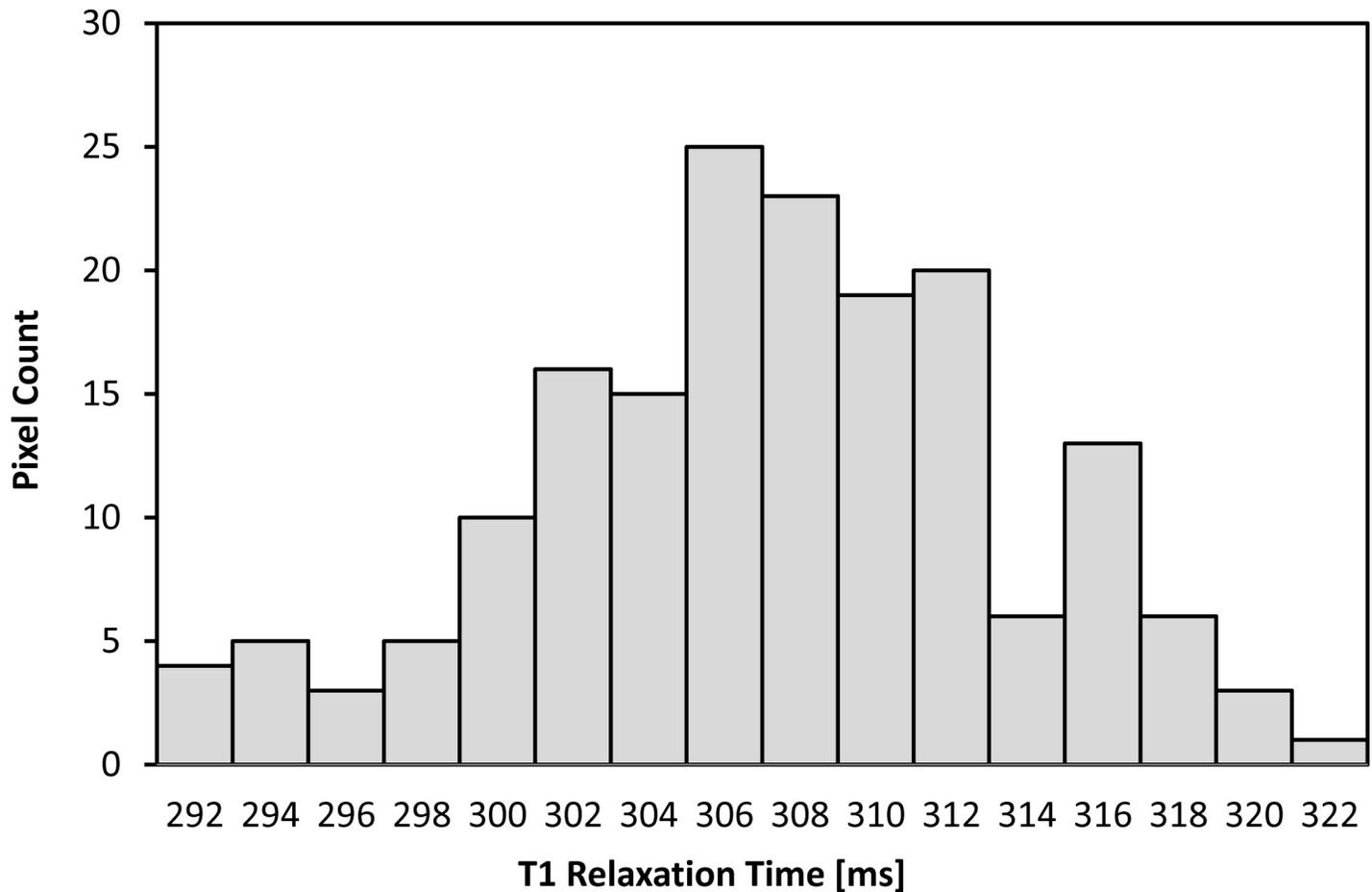
Fig 2. Distribution of individual T1 times for VAT ROI from Fig 1. Corresponding coefficient of variation CV_{T1} is taken as a quantitative estimate for the reliability of ROI-based T1 measurement, here 2.1%.

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subjects and both time points were 1.8±0.3% (range 1.1–2.4%) for SAT and 2.2±0.8% (range 1.3–4.8%) for VAT.

Table 1. Body mass index (BMI) and MRI-derived parameters of obese patients before (M0) and one month after bariatric surgery (M1).

Measure	Month 0 [M0]	Month 1 [M1]
BMI [kg/m^2]	45.4 ± 5.7	42.4 ± 5.9 (−6.8 %) ***
V_{VAT-T} [L]	5.94 ± 2.24	5.33 ± 2.21 (−10.9 %) ***
$T1_{VAT}$ [ms]	303.7 ± 9.7	316.9 ± 14.1 (+4.4 %) ***
$T1_{SAT}$ [ms]	283.2 ± 8.2	280.7 ± 10.4 (−0.9 %)
FF_{VAT} [%]	85.7 ± 2.8	83.4 ± 2.9 (−2.6 %) **
FF_{SAT} [%]	86.1 ± 1.8	85.9 ± 2.0 (−0.2 %)

V_{VAT-T}, total visceral VAT volume; FF, fat fraction; T1, T1 relaxation time
$p \geq 0.05$
*, $p < 0.05$
**, $p < 0.01$ and
***, $p < 0.001$.

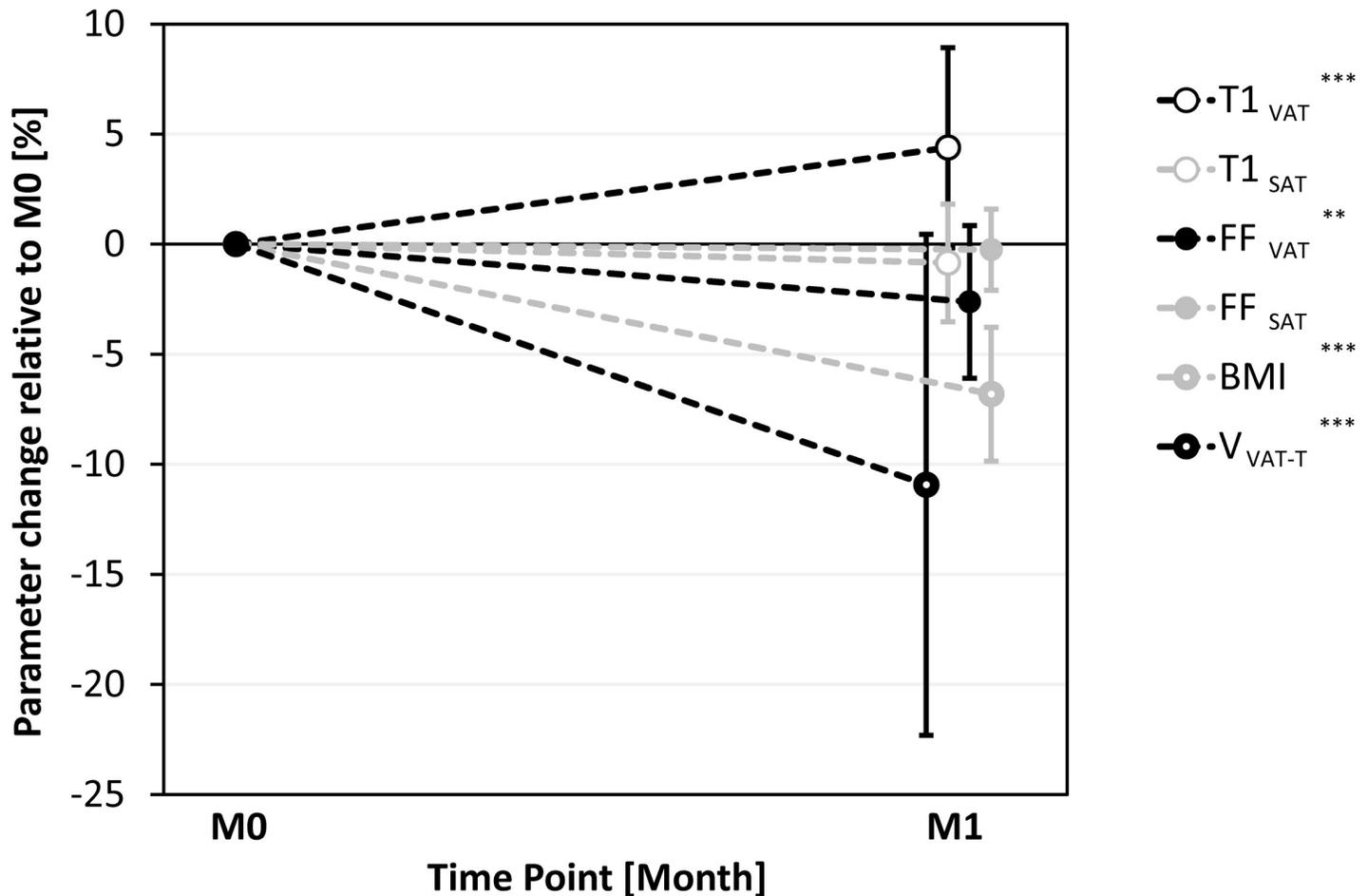https://doi.org/10.1371/journal.pone.0206735.t001

Fig 3. Plot of relative changes in adipose tissue parameters for 23 obese patients one month after bariatric surgery. Symbols show mean percent changes in BMI, total abdominal VAT volume (V_{VAT-T}), regional fat fraction in visceral and subcutaneous adipose tissue (FF_{VAT} and FF_{SAT}), and corresponding T1 relaxation times ($T1_{VAT}$ and $T1_{SAT}$) one month after (M1) relative to before bariatric surgery (M0). Error bars indicate 95% confidence intervals. Asterisks denote level of significance: * (p<0.05), ** (p<0.01), *** (p<0.001). Some symbols have been slightly offset to improve readability.

At the ROI level, T1 relaxation times were significantly longer in VAT (+4.4%, p<0.001) but not in SAT (–0.9%, p = 0.141). Fig 4 illustrates the intraindividual T1 changes in VAT. The early relative changes in fat fraction were significant for VAT (–2.6%, p<0.01) but not for SAT (–0.2%, p = 0.564). Detailed information is provided in S1 Table.

Discussion

Quantification of VAT and SAT by MRI is increasingly used to monitor body fat parameters during obesity interventions [4,5]. Previous studies have found changes in both VAT volume and body composition using anthropometry [22], dual X-ray absorptiometry [23,24], computed tomography [23] or MRI [25].

The presented in-vivo MRI work is among the first to report on significant early changes in VAT parameters one month after RYGB, specifically in regional fat fraction (decrease) and T1 relaxation time (increase). So far, VAT composition has been studied mainly ex vivo, either by biopsy or autopsy. Tissue samples of adipose tissue during elective laparoscopy have indicated that specific metabolic genetic programming in VAT and SAT was associated with BMI. That data suggested that BMI promotes de novo lipogenesis in VAT [26].
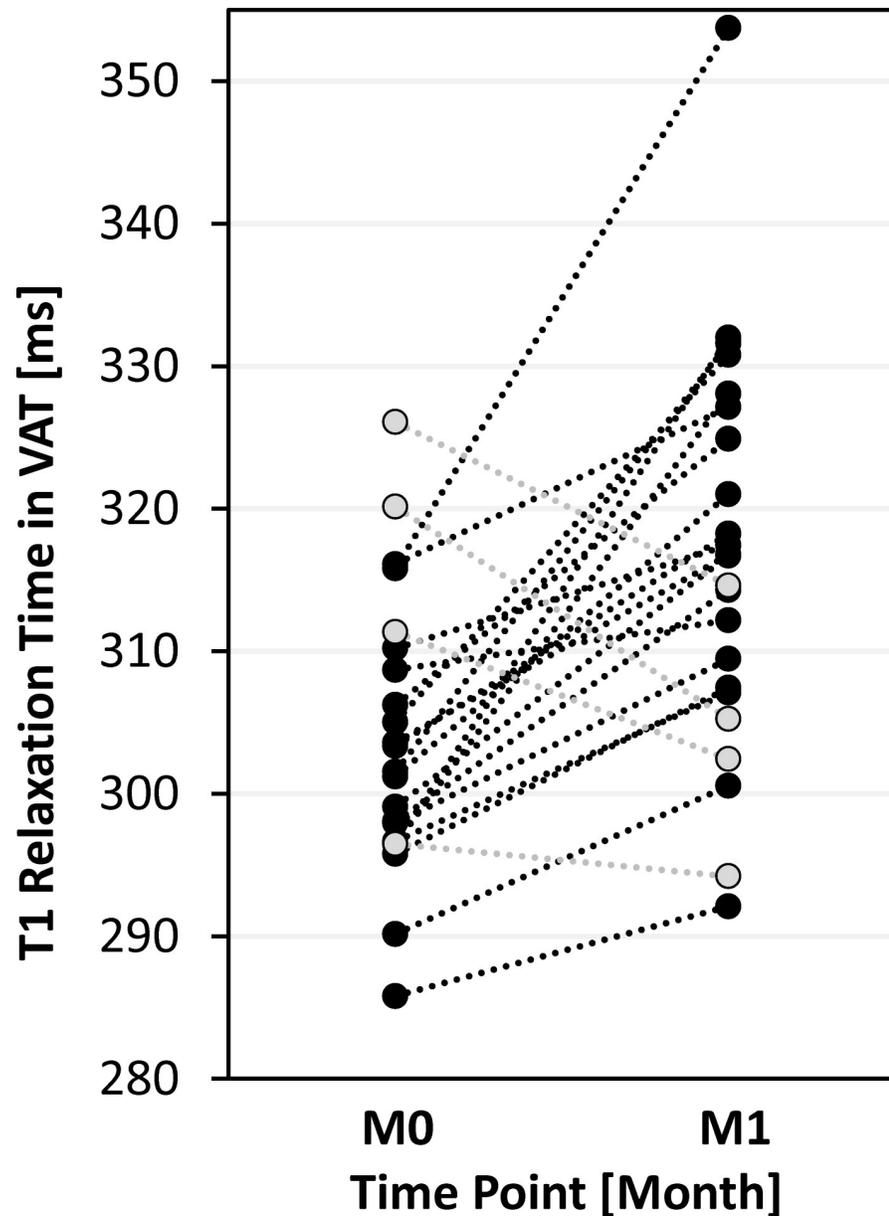
Fig 4. Intra-individual T1 relaxation times (at 1.5 T) in visceral adipose tissue (VAT) of 23 obese patients one month after (M1) relative to before bariatric surgery (M0). Black circles indicate patients with increased T1 time ($n_+ = 18$) and gray circles those with either reduced ($n_- = 4$) or same T1 time ($n_0 = 1$). Overall increase was highly significant ($p < 0.01$).

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In contrast, our data revealed no significant differences in SAT parameters. It is still largely unknown which structural and functional processes in adipose tissue are responsible for the observed changes in FF and T1 after surgery also because of insufficient data from dedicated biopsy studies. Bariatric surgery has been reported to improve the inflammatory state [8,9] and reduce adipocyte volume [10]. Another study has reported a significant correlation between T1 time and mean adipocyte cell size in SAT [17]. It is also worth noting that unlike tissue samples, MRI information can be obtained non-invasively but interpretation is generally complicated by the difference in scale–microscopic versus macroscopic.

Water-fat MRI studies in human subjects have generally focussed on brown adipose tissue but some have also addressed white adipose tissue [14–16]. Leporq et al. [16], for example, have seen differences in FF_{VAT} between two healthy obese (84.3%) and three non-obese (BMI < 30 kg/m^2) subjects (89.5%) with liver steatosis while the corresponding FF_{SAT} values were the same (93.0%). In a different study, Hu et al [14] have observed a higher mean FF_{SAT} for overweight or obese children (90.3%, n = 22) than for children with normal weight (80.9%, n = 17). An earlier comparison of relaxation times in adipose tissue had found T1 times in healthy lean subjects (mean BMI of 21.5 kg/m^2, n = 10) to be larger than in severely obese patients (41.4 kg/m^2, n = 20) for both VAT (360 versus 294 ms, +66 ms) and SAT (301 versus 275 ms, +26 ms) [17].

The individual changes in BMI, V_{VAT}, FF_{VAT} and $T1_{VAT}$ found here were all significant. The largest relative effect was seen for V_{VAT} (about -11%) followed by BMI (-7%). In addition, the mean absolute values (304 and 317 ms for VAT, 283 and 281 ms for SAT) happen to fall within the previously measured range between healthy lean subjects and severely obese patients (294–360 ms for VAT and 275–301 ms for SAT). The $T1_{VAT}$ increase (+4.4% or +13.2 ms) is therefore in line with a shift towards T1 values previously measured in healthy lean subjects. In contrast, the measured $T1_{SAT}$ and FF_{SAT} differences were not significant, which is most likely explained by the more subtle SAT effect. Also note that the intraindividual BMI difference was just 3 kg/m^2 after one month compared to nearly 20 kg/m^2 between the subject groups referred to above.

This retrospective study is limited by various factors. The relatively small number of patients from a single institution precluded subgroup analyses for variables like age or gender. Furthermore, the analysis did not involve histological validation of our results because repeated biopsies during follow-up examinations are limited for ethical and medical reasons. Another limitation is given by the consideration of the main fat peak only (at 1.3 ppm) when modeling the TE dependence of the MR signal intensity (Eq 2). A previous phantom study has shown MRI estimation of FF [27] to be accurate but has assumed eight individual fat resonances instead. Wang et al. have studied the effect of the number of included peaks in more detail [28] and have found that the use of one peak leads to an underestimation of the obtained fat fraction. In a single-peak model, a change in FF may theoretically also be due to a mere change in fat composition and could then be misinterpreted. Further studies on a larger number of subjects or with the addition of suitable histopathologic markers, such as adipocyte size or inflammation markers, are required to improve statistical power and understanding of the underlying processes.

In conclusion, there were detectable MRI changes in T1 relaxation time and fat fraction of VAT one month after bariatric surgery. Besides the widely used morphological measures derived from fat volumes, these potential MRI markers for the tissue response in obese patients deserve further attention.

Supporting information

S1 Table. The individual data for both timepoints M0 and M1.
(XLSX)

Acknowledgments

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Validation: Nicolas Linder, Roland Stange, Harald Busse.

Visualization: Nicolas Linder, Roland Stange, Harald Busse.

Writing – original draft: Nicolas Linder, Nikita Garnov, Harald Busse.

Writing – review & editing: Nicolas Linder, Arne Dietrich, Thomas Kahn, Harald Busse.

References

1. Blüher M. Adipose tissue dysfunction in obesity. Exp Clin Endocrinol Diabetes Off J Ger Soc Endocrinol Ger Diabetes Assoc. 2009; 117: 241–250. https://doi.org/10.1055/s-0029-1192044 PMID: 19358089

2. Maghrabi AH, Wolski K, Abood B, Licata A, Pothier C, Bhatt DL, et al. Two-year outcomes on bone density and fracture incidence in patients with T2DM randomized to bariatric surgery versus intensive medical therapy. Obes Silver Spring Md. 2015; 23: 2344–2348. https://doi.org/10.1002/oby.21150 PMID: 26193177

3. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Brethauer SA, Navaneethan SD, et al. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. N Engl J Med. 2014; 370: 2002–2013. https://doi.org/10.1056/NEJMoa1401329 PMID: 24679060

4. Blüher M. [Pharmacological therapy versus bariatric surgery for patients with obesity and type 2 diabetes]. Internist. 2015; 56: 143–148, 150–152. https://doi.org/10.1007/s00108-014-3534-6 PMID: 25636953

5. Gaborit B, Jacquier A, Kober F, Abdesselam I, Cuisset T, Boullu-Ciocca S, et al. Effects of bariatric surgery on cardiac ectopic fat: lesser decrease in epicardial fat compared to visceral fat loss and no change in myocardial triglyceride content. J Am Coll Cardiol. 2012; 60: 1381–1389. https://doi.org/10.1016/j.jacc.2012.06.016 PMID: 22939560

6. Toro-Ramos T, Goodpaster BH, Janumala I, Lin S, Strain GW, Thornton JC, et al. Continued loss in visceral and intermuscular adipose tissue in weight-stable women following bariatric surgery. Obesity. 2015; 23: 62–69. https://doi.org/10.1002/oby.20932 PMID: 25384375

7. Otto M, Färber J, Haneder S, Michaely H, Kienle P, Hasenberg T. Postoperative Changes in Body Composition—Comparison of Bioelectrical Impedance Analysis and Magnetic Resonance Imaging in Bariatric Patients. Obes Surg. 2015; 25: 302–309. https://doi.org/10.1007/s11695-014-1382-z PMID: 25096342

8.   Poitou C, Perret C, Mathieu F, Truong V, Blum Y, Durand H, et al. Bariatric Surgery Induces Disruption in Inflammatory Signaling Pathways Mediated by Immune Cells in Adipose Tissue: A RNA-Seq Study. PloS One. 2015; 10: e0125718. https://doi.org/10.1371/journal.pone.0125718 PMID: 25938420

9.   Alvehus M, Simonyte K, Andersson T, Söderström I, Burén J, Rask E, et al. Adipose tissue IL-8 is increased in normal weight women after menopause and reduced after gastric bypass surgery in obese women. Clin Endocrinol (Oxf). 2012; 77: 684–690. https://doi.org/10.1111/j.1365-2265.2011.04322.x PMID: 22168600

10. Andersson DP, Eriksson Hogling D, Thorell A, Toft E, Qvisth V, Näslund E, et al. Changes in subcutaneous fat cell volume and insulin sensitivity after weight loss. Diabetes Care. 2014; 37: 1831–1836. https://doi.org/10.2337/dc13-2395 PMID: 24760260

11. Lundbom J, Hakkarainen A, Fielding B, Söderlund S, Westerbacka J, Taskinen M-R, et al. Characterizing human adipose tissue lipids by long echo time 1H-MRS in vivo at 1.5 Tesla: validation by gas chromatography. NMR Biomed. 2010; 23: 466–472. https://doi.org/10.1002/nbm.1483 PMID: 20099371

12. Hamilton G, Smith DL, Bydder M, Nayak KS, Hu HH. MR properties of brown and white adipose tissues. J Magn Reson Imaging. 2011; 34: 468–473. https://doi.org/10.1002/jmri.22623 PMID: 21780237

13. Lundbom J, Hakkarainen A, Lundbom N, Taskinen M-R. Deep subcutaneous adipose tissue is more saturated than superficial subcutaneous adipose tissue. Int J Obes 2005. 2013; 37: 620–622. https://doi.org/10.1038/ijo.2012.72 PMID: 22641063

14. Hu HH, Yin L, Aggabao PC, Perkins TG, Chia JM, Gilsanz V. Comparison of brown and white adipose tissues in infants and children with chemical-shift-encoded water-fat MRI. J Magn Reson Imaging JMRI. 2013; 38: 885–896. https://doi.org/10.1002/jmri.24053 PMID: 23440739

15. Hu HH, Perkins TG, Chia JM, Gilsanz V. Characterization of human brown adipose tissue by chemical-shift water-fat MRI. AJR Am J Roentgenol. 2013; 200: 177–183. https://doi.org/10.2214/AJR.12.8996 PMID: 23255760

16. Leporq B, Lambert SA, Ronot M, Vilgrain V, Van Beers BE. Quantification of the triglyceride fatty acid composition with 3.0 T MRI. NMR Biomed. 2014; 27: 1211–1221. https://doi.org/10.1002/nbm.3175 PMID: 25125224

17. Garnov N, Linder N, Schaudinn A, Blüher M, Karlas T, Schütz T, et al. Comparison of T1 relaxation times in adipose tissue of severely obese patients and healthy lean subjects measured by 1.5 T MRI. NMR Biomed. 2014; 27: 1123–1128. https://doi.org/10.1002/nbm.3166 PMID: 25066754

18. Thörmer G, Bertram HH, Garnov N, Peter V, Schütz T, Shang E, et al. Software for automated MRI-based quantification of abdominal fat and preliminary evaluation in morbidly obese patients. J Magn Reson Imaging. 2013; 37: 1144–1150. https://doi.org/10.1002/jmri.23890 PMID: 23124651

19. Schaudinn A, Linder N, Garnov N, Kerlikowsky F, Blüher M, Dietrich A, et al. Predictive accuracy of single- and multi-slice MRI for the estimation of total visceral adipose tissue in overweight to severely obese patients: MRI prediction of visceral fat volumes. NMR Biomed. 2015; 28: 583–590. https://doi.org/10.1002/nbm.3286 PMID: 25808071

20. Kang B-K, Yu ES, Lee SS, Lee Y, Kim N, Sirlin CB, et al. Hepatic fat quantification: a prospective comparison of magnetic resonance spectroscopy and analysis methods for chemical-shift gradient echo magnetic resonance imaging with histologic assessment as the reference standard. Invest Radiol. 2012; 47: 368–375. https://doi.org/10.1097/RLI.0b013e31824baff3 PMID: 22543969

21. de Bazelaire CMJ, Duhamel GD, Rofsky NM, Alsop DC. MR imaging relaxation times of abdominal and pelvic tissues measured in vivo at 3.0 T: preliminary results. Radiology. 2004; 230: 652–659. https://doi.org/10.1148/radiol.2303021331 PMID: 14990831

22. Søvik TT, Aasheim ET, Taha O, Engström M, Fagerland MW, Björkman S, et al. Weight loss, cardiovascular risk factors, and quality of life after gastric bypass and duodenal switch: a randomized trial. Ann Intern Med. 2011; 155: 281–291. https://doi.org/10.7326/0003-4819-155-5-201109060-00005 PMID: 21893621

23. Olbers T, Björkman S, Lindroos A, Maleckas A, Lönn L, Sjöström L, et al. Body composition, dietary intake, and energy expenditure after laparoscopic Roux-en-Y gastric bypass and laparoscopic vertical banded gastroplasty: a randomized clinical trial. Ann Surg. 2006; 244: 715–722. https://doi.org/10.1097/01.sla.0000218085.25902.f8 PMID: 17060764

24. Otto M, Elrefai M, Krammer J, Weiß C, Kienle P, Hasenberg T. Sleeve Gastrectomy and Roux-en-Y Gastric Bypass Lead to Comparable Changes in Body Composition after Adjustment for Initial Body Mass Index. Obes Surg. 2016; 26: 479–485. https://doi.org/10.1007/s11695-015-1792-6 PMID: 26189734

25. Heath ML, Kow L, Slavotinek JP, Valentine R, Toouli J, Thompson CH. Abdominal adiposity and liver fat content 3 and 12 months after gastric banding surgery. Metabolism. 2009; 58: 753–758. https://doi.org/10.1016/j.metabol.2008.05.021 PMID: 19375765

26. Alves MG, Moreira Â, Guimarães M, Nora M, Sousa M, Oliveira PF, et al. Body mass index is associated with region-dependent metabolic reprogramming of adipose tissue. BBA Clin. 2017; 8: 1–6. https://doi.org/10.1016/j.bbacli.2017.05.001 PMID: 28567337

27. Peterson P, Månsson S. Simultaneous quantification of fat content and fatty acid composition using MR imaging. Magn Reson Med. 2013; 69: 688–697. https://doi.org/10.1002/mrm.24297 PMID: 22532403

28. Wang X, Hernando D, Reeder SB. Sensitivity of Chemical Shift-Encoded Fat Quantification to Calibration of Fat MR Spectrum. Magn Reson Med. 2016; 75: 845–851. https://doi.org/10.1002/mrm.25681 PMID: 25845713