Published in final edited form as:

J Magn Reson Imaging. 2018 April ; 47(4): 988–994. doi:10.1002/jmri.25843.

Optimization of Region-of-Interest Sampling Strategies for Hepatic MRI Proton Density Fat Fraction Quantification

Cheng William Hong, MD, MS¹, Tanya Wolfson, MA², Ethan Z. Sy, BS¹, Alexandra N. Schlein, BS¹, Jonathan C. Hooker, BS¹, Soudabeh Fazeli Dehkordy, MD, MPH¹, Gavin Hamilton, PhD¹, Scott B. Reeder, MD, PhD³, Rohit Loomba, MD, MHSc⁴, and Claude B. Sirlin, MD^{1,*}

¹Liver Imaging Group, Department of Radiology, University of California San Diego, San Diego, California, USA

²Computational and Applied Statistics Laboratory, University of California San Diego, San Diego, California, USA

³Departments of Radiology, Medical Physics, Biomedical Engineering, Medicine, and Emergency Medicine, University of Wisconsin Madison, Madison, Wisconsin, USA

⁴NAFLD Research Center, Division of Gastroenterology, Department of Medicine, University of California San Diego, San Diego, California, USA

Abstract

BACKGROUND—Clinical trials utilizing proton density fat fraction (PDFF) as an imaging biomarker for hepatic steatosis have used a laborious region-of-interest (ROI) sampling strategy of placing an ROI in each hepatic segment.

PURPOSE—To identify a strategy with the fewest ROIs that consistently achieves close agreement with the nine-ROI strategy.

STUDY TYPE—Retrospective secondary analysis of prospectively acquired clinical research data.

POPULATION—A total of 391 adults (173 men, 218 women) with known or suspected NAFLD.

FIELD STRENGTH/SEQUENCE—Confounder-corrected chemical-shift-encoded 3T MRI using a 2D multiecho gradient-recalled echo technique.

ASSESSMENT—An ROI was placed in each hepatic segment. Mean nine-ROI PDFF and segmental PDFF standard deviation were computed. Segmental and lobar PDFF were compared. PDFF was estimated using every combinatorial subset of ROIs and compared to the nine-ROI average.

STATISTICAL TESTING—Mean nine-ROI PDFF and segmental PDFF standard deviation were summarized descriptively. Segmental PDFF was compared using a one-way analysis of variance, and lobar PDFF was compared using a paired *t*-test and a Bland–Altman analysis. The PDFF

* Address reprint requests to: C.B.S., Department of Radiology, University of California, San Diego, Altman Clinical and Translational Research Institute, 9452 Medical Center Dr., La Jolla, CA 92037. csirlin@ucsd.edu.

estimated by every subset of ROIs was informally compared to the nine-ROI average using median intraclass correlation coefficients (ICCs) and Bland–Altman analyses.

RESULTS—The study population's mean whole-liver PDFF was $10.1 \pm 8.9\%$ (range: 1.1–44.1%). Although there was no significant difference in average segmental ($P=0.452$) or lobar ($P=0.154$) PDFF, left and right lobe PDFF differed by at least 1.5 percentage points in 25.1% (98/391) of patients. Any strategy with 4 ROIs had ICC >0.995 . 115 of 126 four-ROI strategies (91%) had limits of agreement (LOA) $<1.5\%$, including four-ROI strategies with two ROIs from each lobe, which all had LOA $<1.5\%$. 14/36 (39%) of two-ROI strategies and 74/84 (88%) of three-ROI strategies had ICC >0.995 , and 2/36 (6%) of two-ROI strategies and 46/84 (55%) of three-ROI strategies had LOA $<1.5\%$.

DATA CONCLUSION—Four-ROI sampling strategies with two ROIs in the left and right lobes achieve close agreement with nine-ROI PDFF.

Level of Evidence—3

Technical Efficacy—Stage 2

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide, affecting an estimated 20–30% of adults in developed countries, and is highly associated with Type 2 diabetes, obesity, and cardiovascular disease.^{1–3} Liver biopsy is currently the clinical reference standard for the diagnosis and grading of NAFLD. However, it is invasive and prone to sampling error, motivating the development of noninvasive imaging approaches to quantify hepatic steatosis.^{4,5} Proton density fat fraction (PDFF), as measured by quantitative chemical-shift-encoded MRI (CSE-MRI), is emerging as the leading biomarker for quantifying liver fat content.^{6–9}

Due to spatial heterogeneity in hepatic fat deposition, differences in region of interest (ROI) sampling methods can lead to variability in fat quantification.^{10–13} A common approach in clinical trials is to place one ROI in each of the nine Couinaud segments (Fig. 1); however, this laborious method is not possible in some cases due to imaging artifacts, and would not be feasible in clinical care if these ROIs are to be placed by radiologists.^{7,14,15}

Therefore, the purpose of this study was to identify a strategy with the fewest ROIs that consistently achieves close agreement with the nine-ROI strategy.

Materials and Methods

Study Design

This study was a single-site secondary analysis of 391 patients (173 men, 218 women) with known or suspected NAFLD who underwent confounder-corrected CSE 3T MRI for magnitude-based fat quantification as part of prospective clinical studies from 2012 to 2016. Data represented in this work were obtained from subjects described in previously reported studies,^{22–25} but reanalyzed for the purposes outlined above. All patients signed written informed consent, and this study was approved by an Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act. Demographic and anthropometric information was collected.

MRI Acquisition

Patients were scanned supine using a 3T Signa EXCITE HDxt MRI system (GE Healthcare, Waukesha, WI) with an eight-channel torso phased-array coil centered over the liver. A dielectric pad was placed between the coil and the abdomen.

A 2D multiecho spoiled gradient-recalled echo (SPGR) sequence was acquired with full liver coverage in one or two 18–30-second breath-holds. A low flip angle (10°) with 150 msec repetition time (TR) was used to minimize T_1 bias.^{6,16–18} Six echoes were obtained per TR at nominally out-of-phase and in-phase echo times to permit fat-water signal separation and assuming monoexponential signal decay, the estimation of T_2^* . The rectangular field of view was adjusted depending on the patient's body habitus and breath-hold capacity. A previously described fitting algorithm was applied to the source images pixel-by-pixel to create parametric PDFF maps.¹⁸ These maps were reconstructed using a multipeak fat spectral model.¹⁹ Due to the fat-water ambiguity intrinsic to magnitude fitting, water was assumed to be the dominant signal and the PDFF dynamic range was 0–50%. No corrections were necessary for phase errors^{20,21} as reconstruction of PDFF maps was performed with magnitude fitting. MRI parameters are summarized in Table 1.

MRI Postprocessing and Analysis

Source images and the PDFF maps were analyzed using OsiriX software (OsiriX Foundation, Geneva, Switzerland) by several trained research staff (including E.Z.S. and J.C.H.) blinded to clinical data. These analysts all had a minimum of 6 months of experience performing this specific analysis for various research and clinical studies. Each examination was analyzed by a single research analyst, who placed a 1-cm radius ROI in each of the nine Couinaud liver segments while avoiding major vessels, bile ducts, liver edges, and artifacts. The fifth-echo image series was used to place ROIs, as it consistently provided adequate anatomic delineation for this purpose. PDFF values for each hepatic segment were recorded and averaged to obtain an average PDFF value for each patient.

PDFF Segmental Variability

For each patient, the nine-ROI average PDFF and standard deviation of the nine segmental PDFF values were computed. Histograms were generated for the visual assessment of the distributions of the nine-ROI average PDFF and of the standard deviations of the segmental PDFF values. PDFF across hepatic segments was compared using a one-way analysis of variance. PDFF in the left lobe and PDFF in the right lobe was compared using a paired t -test and a Bland–Altman analysis. PDFF from individual segments was plotted for illustration using a representative sample of patients.

ROI Sampling Strategies

For each patient, PDFF was estimated 511 times by averaging the segmental PDFFs using every combinatorial subset of up to eight Couinaud segments: all nine combinations of one ROI, all 36 combinations of two ROIs, 84 combinations of three ROIs, etc. PDFFs estimated from these combinations were informally compared to the nine-ROI average PDFF using ICCs and Bland–Altman analyses. Two thresholds for close agreement were used: an ICC greater than 0.995 and an absolute limits of agreement (LOA) bound less than 1.5

percentage points, which was felt to represent a clinically meaningful difference. A sampling strategy using the minimum number of ROIs required to achieve close agreement with the nine-ROI average was determined.

Statistical Analysis

Statistical analysis was performed using R v. 3.3.1 statistical software (2016; R Foundation for Statistical Computing, Vienna, Austria). Demographic, anthropometric, and PDFF data were summarized descriptively. We used two thresholds to define close agreement: intraclass correlation coefficient (ICC) greater than 0.995, and absolute LOA less than 1.5 percentage points. These thresholds were picked a priori to represent clinically meaningful differences.

Results

Patient Population

Their mean age was 49.8 ± 16.5 years (range: 18–85 years). Their mean body mass index (BMI) was 29.4 ± 5.7 kg/m² (range: 16.2–52.5 kg/m²; anthropometric data not recorded for 29 patients), respectively. 44.8% of them (162/362) were obese, using a BMI cutoff of 30 kg/m².

Summary of PDFF by Segments

The mean nine-ROI average PDFF across the cohort was $10.1 \pm 8.9\%$ (range: 1.1–44.1%), with a right-skewed distribution (Fig. 2). Although we did not find a statistically significant difference in segmental PDFFs ($P=0.452$), the highest mean PDFF values of 10.5% (0.5% higher than the nine-ROI average) were recorded in segments seven and eight, whereas the lowest mean PDFF values of 9.2% (0.8% less than the nine-ROI average) were recorded in segment two (Table 2). This is consistent with the general observation that right lobe PDFFs are slightly higher than left lobe PDFFs.²⁶ Mean lobar PDFF in the left lobe (including caudate) and right lobe did not differ significantly on average (bias= -0.125 , LOA= -3.53 to 3.28 , $P=0.154$), but the PDFF in the left and right lobe differed by more than 1.5 percentage points in 25.1% (98/391) of patients (Fig. 3). In this subset of patients who had substantial differences between the left and right lobe PDFF, 65.3% of them (64/98) had higher PDFF in the right lobe, and 34.7% (34/98) had higher PDFF in the left lobe. Similarly, although the standard deviation of the segmental PDFFs was less than 1.5 percentage points for 69% of patients (293/391), some patients exhibited more substantial segmental variability (Fig. 4). Figure 5 shows individual segmental PDFFs for a representative sample of patients.

ICC Analysis

ICCs increased as the number of ROIs used increased (Fig. 6). As summarized in Table 3, none of the sampling strategies with only one ROI had ICC >0.995 . In all, 14 of 36 (39%) sampling strategies with two ROIs had ICC >0.995 ; 74 of 84 (88%) of sampling strategies with three ROIs had ICC >0.995 . All sampling strategies with four or more ROIs had ICC >0.995 .

LOA Analysis

LOA bounds decreased as the number of ROIs used increased (Fig. 7). As summarized in Table 3, one of the sampling strategies with one ROI had $|\text{LOA}| < 1.5\%$ (absolute value). Two of 36 (6%) sampling strategies with two ROIs had $|\text{LOA}| > 1.5\%$; 46 of 84 (55%) of sampling strategies with three ROIs had $|\text{LOA}| < 1.5\%$. In all, 115 of 126 (91%) of sampling strategies with four ROIs had $|\text{LOA}| < 1.5\%$. All sampling strategies with five or more ROIs had $|\text{LOA}| < 1.5\%$.

Sampling Strategies

Since some but not all two-, three-, and four-ROI strategies achieved close agreement with the nine-ROI average, we further examined these subsets to determine if a simple “rule” could identify a sampling strategy that consistently meets the predefined agreement thresholds. Figures 6 and 7 show the ICC and LOA for all ROI sampling strategies based on sampling both hepatic lobes. The darker points represent strategies where both hepatic lobes are represented as equally as possible (“balanced” sampling between the left and right lobes of the liver). For the four-ROI approach, all 60 balanced subsets (two ROIs in the left lobe, two ROIs in the right lobe) achieved close agreement with the nine-ROI average using both agreement thresholds, whereas only 55/66 (83%) of unbalanced subsets achieved close agreement (Fig. 7). For two and three ROI subsets, balanced sampling approaches were more likely to achieve close agreement, but did not do so consistently.

Discussion

The results of this study suggest that if balanced sampling is applied, four ROIs is the minimum number required to achieve close agreement with the nine-ROI PDFF estimate using the >0.995 ICC and $<1.5\%$ LOA thresholds. Using only one ROI achieves neither a sufficiently high ICC nor a sufficiently narrow LOA. Using two or three ROIs achieves sufficiently high ICC and/or a sufficiently narrow LOA only in some cases, but no simple rule permits the selection of ROI strategies that consistently achieve close agreement with the nine-ROI PDFF.

In comparison, for four-ROI strategies, a simple rule that utilizes two ROIs from each hepatic lobe achieves close agreement consistently for all 60 such combinatorial subsets in our study. The high performance of the balanced strategies probably reflects the spatial heterogeneity of fat distribution in the liver, as has been described previously and verified here.¹¹ For example, Bonekamp et al found that right lobe and left lobe segments had different amounts of fat; segment eight had the highest segmental PDFF and segment two had the lowest segmental PDFF.¹¹ While our results were not statistically significant, we similarly found that two right lobe segments (segments seven and eight) had the highest segmental PDFF point estimates and a left lobe segment (segment two) had the lowest. Importantly, although the left and right lobes had similar PDFF at the population average level, they differed by more than 1.5 percentage points (the LOA benchmark) in 25% of patients. As such, there can be substantial differences in lobar PDFFs in certain patients even if there is little difference in the mean lobar PDFF across the entire study population. Thus, having at least two ROIs in each lobe provides a reasonably representative assessment of the

whole liver, while reducing the burden of sampling every hepatic segment. The large number of exploratory comparisons precluded statistical testing of individual sampling strategies, but the agreement for all 60 of these strategies was high. This suggests that the exact choice of ROIs can be made based on other considerations such as the need to avoid major vessels, bile ducts, and imaging artifacts.

Prior studies demonstrated that sampling strategies that included more segments, used larger ROIs, or sampled both lobes of the liver had significantly improved correlation with liver mean PDFF, and that the repeatability of liver PDFF measurements improves as the size and number of ROIs increase.^{13,27} Vu et al demonstrated that sampling strategies that sampled the right lobe exclusively estimated significantly different PDFF values compared to sampling strategies that sampled both lobes of the liver.¹³ Campo et al suggested that placing four ROIs (one in each of the anterior, posterior, medial, and lateral segments of the liver) may be a reasonable compromise between minimizing time burden and maximizing reader agreement.²⁷ Our study adds to those studies by demonstrating that a simple sampling strategy of placing two ROIs in each lobe provides high accuracy for whole liver PDFF estimation using the nine-ROI average as the reference standard.

The strengths of our study were the relatively large sample size, and the comprehensive comparison between all possible combinations of ROIs. Additionally, by setting a priori thresholds for close agreement, our study was able to identify a specific clinically applicable sampling strategy using four ROIs. This is useful because prior studies have suggested that more ROIs is better but do not systematically evaluate the tradeoff between the number of ROIs and accuracy. Since our thresholds are arbitrary, clinicians and researchers may prefer to use different thresholds to identify adequate sampling strategies based on Figs. 6 and 7.

Limitations of this study include the use of the nine-ROI sampling method as the standard for comparison. Although it has been used as an accepted biomarker in multiple clinical studies, it has not been completely validated. Whole-liver segmentation and PDFF calculation would have been a more accurate gold standard, but this is impractical and time-consuming to perform manually, and software to perform this automatically is not yet widely available. In addition, this study design involved hundreds of informal comparisons, and hence the results are only suggestive and require further validation. We did not examine the effect of ROI size, which may also impact the agreement of ROI sampling strategies, as other studies have shown that larger ROIs improve agreement. We also did not directly compare the time spent by the analysts drawing ROIs using these strategies. Finally, this was a single-center study of adults with known or suspected NAFLD, which may limit the generalizability of our results to children, populations in other geographic regions, and adults without NAFLD.

In conclusion, our study demonstrates that in a large cohort of adults with a wide range of hepatic PDFF values due to known or suspected NAFLD, four-ROI sampling strategies can achieve close agreement with sampling all nine hepatic segments. Two ROIs should be placed in each hepatic lobe to ensure representative sampling. With further validation, this simplified strategy may become a new practical standard for assessing hepatic PDFF in clinical trials and clinical practice.

Acknowledgments

Contract grant sponsor: National Institutes of Health; contract grant numbers: T32 EB005970-09, R01 DK106419-02, R01 DK083380, K24 DK102595, and R01 DK100651-03.

We thank GE Healthcare, who provides research support to UCSD and UW-Madison.

References

1. Preiss D, Sattar N. Non-alcoholic fatty liver disease: An overview of prevalence, diagnosis, pathogenesis and treatment considerations. *Clin Sci (Lond)*. 2008; 115:141–150. [PubMed: 18662168]
2. Lazo M, Clark JM. The epidemiology of nonalcoholic fatty liver disease: A global perspective. *Semin Liver Dis*. 2008; 28:339–350. [PubMed: 18956290]
3. Vernon G, Baranova A. Systematic review: The epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther*. 2011; 34:273–285.
4. Ratziu V, Charlotte F, Heurtier A, et al. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. *Gastroenterology*. 2005; 128:1898–1906. [PubMed: 15940625]
5. Vuppalanchi R, Unalp A, Van Natta ML, et al. Effects of liver biopsy sample length and number of readings on sampling variability in nonalcoholic Fatty liver disease. *Clin Gastroenterol Hepatol*. 2009; 7:481–486. [PubMed: 19162235]
6. Yokoo T, Shiehorteza M, Hamilton G, et al. Estimation of hepatic proton-density fat fraction by using MR imaging at 3.0 T. *Radiology*. 2011; 258:749–759. [PubMed: 21212366]
7. Tang A, Tan J, Sun M, et al. Nonalcoholic fatty liver disease: MR imaging of liver proton density fat fraction to assess hepatic steatosis. *Radiology*. 2013; 267:422–431. [PubMed: 23382291]
8. Reeder SB, Sirlin CB. Quantification of liver fat with magnetic resonance imaging. *Magn Reson Imaging Clin N Am*. 2010; 18:337–357. ix. [PubMed: 21094444]
9. Reeder SB, Cruite I, Hamilton G, Sirlin CB. Quantitative assessment of liver fat with magnetic resonance imaging and spectroscopy. *J Magn Reson Imaging*. 2011; 34:729–749. [PubMed: 21928307]
10. Larson SP, Bowers SP, Palekar NA, Ward JA, Pulcini JP, Harrison SA. Histopathologic variability between the right and left lobes of the liver in morbidly obese patients undergoing Roux-en-Y bypass. *Clin Gastroenterol Hepatol*. 2007; 5:1329–1332. [PubMed: 17702661]
11. Bonekamp S, Tang A, Mashhood A, et al. Spatial distribution of MRIdetermined hepatic proton density fat fraction in adults with nonalcoholic fatty liver disease. *J Magn Reson Imaging*. 2014; 39:1525–1532. [PubMed: 24987758]
12. Merriman RB, Ferrell LD, Patti MG, et al. Correlation of paired liver biopsies in morbidly obese patients with suspected nonalcoholic fatty liver disease. *Hepatology*. 2006; 44:874–880. [PubMed: 17006934]
13. Vu K-N, Gilbert G, Chalut M, Chagnon M, Chartrand G, Tang A. MRI-determined liver proton density fat fraction, with MRS validation: Comparison of regions of interest sampling methods in patients with type 2 diabetes. *J Magn Reson Imaging*. 2016; 43:1090–1099. [PubMed: 26536609]
14. Hines CDG, Frydrychowicz A, Hamilton G, et al. T(1) independent, T(2) (*) corrected chemical shift based fat-water separation with multi-peak fat spectral modeling is an accurate and precise measure of hepatic steatosis. *J Magn Reson Imaging*. 2011; 33:873–881. [PubMed: 21448952]
15. Bastati N, Feier D, Wibmer A, et al. Noninvasive differentiation of simple steatosis and steatohepatitis by using gadoteric acid-enhanced MR imaging in patients with nonalcoholic fatty liver disease: A proof-of-concept study. *Radiology*. 2014; 271:739–747. [PubMed: 24576046]
16. Yokoo T, Bydder M, Hamilton G, et al. Nonalcoholic fatty liver disease: Diagnostic and fat-grading accuracy of low-flip-angle multiecho gradient-recalled-echo MR imaging at 1.5 T. *Radiology*. 2009; 251:67–76. [PubMed: 19221054]

17. Kühn J-P, Hernando D, Mensel B, et al. Quantitative chemical shift-encoded MRI is an accurate method to quantify hepatic steatosis. *J Magn Reson Imaging*. 2014; 39:1494–1501. [PubMed: 24123655]
18. Bydder M, Yokoo T, Hamilton G, et al. Relaxation effects in the quantification of fat using gradient echo imaging. *Magn Reson Imaging*. 2008; 26:347–359. [PubMed: 18093781]
19. Hamilton G, Schlein AN, Middleton MS, et al. In vivo triglyceride composition of abdominal adipose tissue measured by (1) H MRS at 3T. *J Magn Reson Imaging*. 2017; 45:1455–1463. [PubMed: 27571403]
20. Hernando D, Hines CDG, Yu H, Reeder SB. Addressing phase errors in fat-water imaging using a mixed magnitude/complex fitting method. *Magn Reson Med*. 2012; 67:638–644. [PubMed: 21713978]
21. Yu H, Shimakawa A, Hines CDG, et al. Combination of complex-based and magnitude-based multiecho water-fat separation for accurate quantification of fat-fraction. *Magn Reson Med*. 2011; 66:199–206. [PubMed: 21695724]
22. Loomba R, Sirlin CB, Ang B, et al. Ezetimibe for the treatment of nonalcoholic steatohepatitis: Assessment by novel magnetic resonance imaging and magnetic resonance elastography in a randomized trial (MOZART trial). *Hepatology*. 2015; 61:1239–1250. [PubMed: 25482832]
23. Cui J, Philo L, Nguyen P, et al. Sitagliptin vs. placebo for non-alcoholic fatty liver disease: A randomized controlled trial. *J Hepatol*. 2016; 65:369–376. [PubMed: 27151177]
24. Paige JS, Bernstein GS, Heba E, et al. A pilot comparative study of quantitative ultrasound, conventional ultrasound, and MRI for predicting histology-determined steatosis grade in adult nonalcoholic fatty liver disease. *Am J Roentgenol*. 2017; 208:W168–W177. [PubMed: 28267360]
25. Loomba R, Schork N, Chen C-H, et al. Heritability of hepatic fibrosis and steatosis based on a prospective twin study. *Gastroenterology*. 2015; 149:1784–1793. [PubMed: 26299412]
26. Bonekamp S, Ghosh P, Crawford S, et al. Quantitative comparison and evaluation of software packages for assessment of abdominal adipose tissue distribution by magnetic resonance imaging. *Int J Obes (Lond)*. 2008; 32:100–111. [PubMed: 17700582]
27. Campo, CA., Hernando, D., Bookwalter, CA., Schubert, TB., Reeder, SB. Standardized approach for region-of-interest-based measurements of proton-density fat-fraction and R2* in the liver. *Proc 24th Annual Meeting ISMRM*; Singapore. 2016.

FIGURE 1.

Comprehensive nine-ROI sampling strategy, where an ROI (green circle) is placed in each of the nine hepatic segments on multiple slices through the liver on the PDFFF map.

FIGURE 2.
Histogram demonstrating distribution of PDFF values across the study cohort.

FIGURE 3.

Bland–Altman plot between left and right lobe PDFF values. The x-axis is a plot with a logarithmic scale. Although the mean bias of -0.125 (solid line) is small, a quarter of patients had a lobar difference of greater than 1.5 percentage points (dashed lines).

FIGURE 4.

Histogram demonstration distribution of standard deviations of segmental PDFF values across the study cohort. Although the standard deviation of the segmental PDFFs was less than 1.5 percentage points for 69% of patients (293/391), some patients exhibited more substantial segmental variability.

FIGURE 5.

Plot demonstrating PDF values (y-axis) vs. segment (x-axis) for a representative sample of patients. Each line represents an individual patient in the cohort. Patients were sorted according to rank-order of increasing standard deviation of segmental PDF, and every 10th patient is shown. Darker lines correspond to patients with greater standard deviation of segmental PDF values.

FIGURE 6.

ICCs (y-axis) shown for sampling strategies by the number of ROIs used. Each dot represents a particular sampling strategy (511 total). ICCs increased as the number of ROIs increased. Strategies where the number of ROIs in the left and right hepatic lobes differed by no more than one (ie, balanced) are color-coded with darker colors. These balanced strategies tended to achieve better agreement with the nine-ROI average.

FIGURE 7.

LOA bounds (y-axis) shown for sampling strategies by the number of ROIs used. Each dot represents a particular sampling strategy (511 total). LOA bounds decreased (closer agreement) as the number of ROIs increased. Strategies where the number of ROIs in the left and right hepatic lobes differed by no more than one (ie, balanced) are color-coded with darker colors. These balanced strategies tended to achieve better agreement with the nine-ROI average. In this study, 91% of four-ROI strategies achieved close agreement by the LOA metric, but 100% of balanced four-ROI strategies achieved close agreement.

TABLE 1

MRI Parameters for Confounder-Corrected Chemical-Shift-Encoded Magnitude-Based Proton Density Fat Fraction Multiecho GRE Sequence

Parameter	Values
Pulse sequence	2D spoiled GRE
Slice thickness	6–8 mm
Flip angle	10°
Interslice gap	0 mm
TE	1.15, 2.30, 3.45, 4.60, 5.75, 6.90 ms
TR	120 msec
Image matrix	224 × 192 base matrix
FOV	44 × 44 cm base
NEX	1
Parallel imaging accelerating factor	1.25
BW	±142 kHz

GRE=gradient recalled echo; TR=reppetition time; TE= echo time; FOV=field of view; NEX=number of excitations; BW=bandwidth (units are kHz).

TABLE 2

Mean PDFF Values by Hepatic Segment

Segment(s)	Mean PDFF (%)
1	10.2 ±8.7
2	9.2 ±8.4
3	9.9 ±9.0
4a	10.3 ±8.7
4b	10.2 ±9.0
5	9.7 ±9.5
6	9.6 ±9.2
7	10.5 ±9.2
8	10.5 ±9.4
Whole liver (all segments)	10.0 ±8.9

The lowest PDFF values were recorded in segment 2 and the highest PDFF values were recorded in segment 7.

TABLE 3

ICCs and LOA Bounds by Number of ROIs

Number of ROIs	Proportion with ICC > 0.995	Average ICC	Lowest ICC	Highest ICC	Proportion with $ LOA < 1.5\%$	Average $ LOA $	Minimum $ LOA $	Maximum $ LOA $
1	0% (0/9)	0.987	0.974	0.992	0% (0/9)	3.08	2.23	4.36
2	38.9% (14/36)	0.994	0.988	0.997	5.6% (2/36)	2.01	1.39	2.95
3	88.1% (74/84)	0.997	0.993	0.998	54.7% (46/84)	1.52	1.06	2.19
4	100% (126/126)	0.998	0.995	0.999	91.3% (115/126)	1.20	0.77	1.80
5	100% (126/126)	0.999	0.997	1.000	100% (126/126)	0.96	0.62	1.44
6	100% (84/84)	0.999	0.999	1.000	100% (84/84)	0.76	0.53	1.09
7	100% (36/36)	1.000	0.999	1.000	100% (36/36)	0.57	0.40	0.84
8	100% (9/9)	1.000	1.000	1.000	100% (9/9)	0.38	0.29	0.55

$|LOA|$ refers to the highest absolute value of either side of the bound. The proportion of sampling strategies that achieved close agreement with the 9-ROI average by either threshold, as well as the range of corresponding ICCs and LOA bounds among those sampling strategies, is shown.