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Automated Vessel Exclusion Technique for Quantitative Assessment of Hepatic Iron Overload by R2*-MRI

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Abstract

BACKGROUND—Extraction of liver parenchyma is an important step in the evaluation of R2*-based hepatic iron content (HIC). Traditionally, this is performed by radiologists via whole-liver contouring and T2*-thresholding to exclude hepatic vessels. However, the vessel exclusion process is iterative, time consuming, and susceptible to inter-reviewer variability.

PURPOSE—To implement and evaluate an automatic hepatic vessel exclusion and parenchyma extraction technique for accurate assessment of R2*-based HIC.

STUDY TYPE—Retrospective analysis of clinical data.

SUBJECTS—Data from 511 MRI exams performed on 257 patients were analyzed.

FIELD STRENGTH/SEQUENCE—All patients were scanned on a 1.5T scanner using a multi-echo gradient echo sequence for clinical monitoring of HIC.

ASSESSMENT—An automated method based on a multi-scale vessel enhancement filter was investigated for 3 input data types—contrast-optimized composite image, T2* map, and R2* map—to segment blood vessels and extract liver tissue for R2*-based HIC assessment. Segmentation and R2* results obtained using this automated technique were compared with those from a reference T2*-thresholding technique performed by a radiologist.

STATISTICAL TESTS—Dice similarity coefficient was used to compare the segmentation results between the extracted parenchymas, and linear regression and Bland-Altman analyses were performed to compare the R2* results, obtained with the automated and reference techniques.

RESULTS—Mean liver R2* values estimated from all 3 filter-based methods showed excellent agreement with the reference method (slopes 1.04–1.05, $R^2 > 0.99$, $P < 0.001$). Parenchyma areas extracted using the reference and automated methods had an average overlap area of 87–88%. The T2*-thresholding technique included small vessels and pixels at the vessel/tissue boundaries as parenchymal area, potentially causing a small bias (<5%) in R2* values compared to the automated method.

DATA CONCLUSION—The excellent agreement between reference and automated hepatic vessel segmentation methods confirms the accuracy and robustness of the proposed method. This automated approach might improve the radiologist's workflow by reducing the interpretation time and operator dependence for assessing HIC, an important clinical parameter that guides iron overload management.

Keywords

liver iron overload; iron quantification; R2* MRI; whole-liver ROI; Frangi vesselness filter; T2* thresholding

Introduction

Hepatic iron overload is a severe complication in patients with increased gastrointestinal absorption of dietary iron or receiving chronic blood transfusions for sickle cell disease, beta-thalassemia, and myelosuppression during chemotherapy.^{1–5} Accurate assessment of hepatic iron content (HIC) is important to quantify excessive iron accumulation and monitor response to iron chelation therapy. Needle biopsies are considered the reference standard to measure HIC.⁶ Magnetic resonance imaging (MRI) methods based on the effective transverse relaxation rate (R2*) have been used to noninvasively measure HIC. R2* is typically measured by analyzing the exponential signal decay of multi-echo gradient echo (GRE) images of the liver, and HIC is estimated from R2* by using published biopsy HIC/R2* calibration curves.^{7–10} MRI-based HIC quantification can therefore be used to guide iron overload management.

R2*-based HIC usually relies on mean R2* values calculated from manually outlined regions of interest (ROIs). There are two approaches: One method involves drawing one or multiple small (0.5–3 cm²) ROIs in a homogenous area of the liver relatively devoid of vessels.^{11,12} Although this approach shows excellent correlation between R2* values and biopsy-derived HIC values, it is prone to inter-reviewer variability,¹³ and displays measurement errors in patients with heterogeneous iron distribution.^{14,15}

The other approach involves drawing an ROI encompassing the entire liver area in the acquired axial cross-section, followed by post-processing steps to exclude blood vessels, to accurately estimate mean R2* of the segmented iron-loaded tissue. This whole-liver approach yields an overall R2*-based HIC estimate by maximizing the liver ROI area and minimizing the inter-reviewer variability associated with ROI placement. In a comparative study of small and whole-liver ROI with biopsy HIC for R2* measurements,¹³ whole-liver ROI analysis had higher reproducibility and yielded smaller standard errors in R2* measurements than small ROI analysis. Moreover, the whole-liver ROI approach lends itself more readily to automation compared to the small ROI approach, with liver boundaries being for example automatically detected based on contrast intensity changes.

Blood vessel exclusion for the whole-liver ROI approach can be achieved by T2*-thresholding^{13,16} or vessel segmentation based on fuzzy c-means (FCM) clustering techniques.^{17–19} T2*-thresholding is based on the fact that T2* of blood (approximately 30 ms at 1.5 T) is higher than that of iron-overloaded liver tissue (< 20 ms at 1.5 T). Then, on a

T2* histogram a patient-specific T2* threshold value is chosen that separates the blood pixel distribution from the parenchyma distribution; pixels beyond that value are eliminated.^{13,16} However, this process is iterative, time consuming, and subjective, because mean T2*/R2* results depend on the chosen threshold.

FCM clustering techniques provide automatic vessel segmentation by assigning membership to each data point corresponding to each cluster center by distance between the cluster center and data point. These have been applied to segment the liver parenchyma and vessels by using either a single image at a given TE or R2* map or their combination.^{17–19} However, FCM-based methods are computationally expensive, sensitive to initialization, easily trapped in local optima,²⁰ and segment tissue based on differences in pixel values, without considering spatial or structural information.

Frangi et al.²¹ introduced a multi-scale vessel enhancement filter to accurately visualize and quantify blood vessels. This filter has been primarily used in brain,^{21–23} and has so far been used only in limited abdominal applications.^{24,25} The filter computes the likeliness of an image region to contain vessels by analyzing structural information and enhancing only tubular structures regarded as blood vessels. In this study, we developed a vessel enhancement filter based on Frangi's technique for automatic segmentation of hepatic vessels and parenchyma extraction to assess hepatic iron overload by R2*-MRI. Such a technique will improve the clinical workflow in estimating R2*-based HIC by reducing the operator time and dependence. The purpose of this study was therefore, to validate the proposed automated vessel exclusion technique by comparing with the manual T2*-thresholding performed by an experienced radiologist for R2*-based HIC assessment in a large cohort of patients covering the full clinical spectrum of HIC values.

Materials and Methods

Participants

Our Institutional Review Board, approved with a waiver of informed consent the retrospective review of all consecutive MRI exams performed at the institution for clinical monitoring of hepatic iron overload between August 2011 and June 2016. This study complied with the Health Insurance Portability and Accountability Act. A total of 565 MRI exams from 282 patients with transfusional iron overload (126 male, 156 female; median age at first scan: 13±9 years, range 1–53 years) were identified. Approximately 50% of patients had multiple MRI exams as part of their annual HIC assessment for clinical care: specifically, 157 patients received 1 exam, 39 received 2 exams, 37 received 3 exams, 29 received 4 exams, 17 received 5 exams, and 3 received 6 exams.

Of the 565 MRI scans, 50 cases had to be excluded because of failed T2* fit (more details under Data Analysis). Further, whole-liver regions were not available in 4 cases due to severe motion or susceptibility artifacts compromising the evaluation of the entire liver in the acquired slice; the respective exams were hence excluded from the analysis. Thus, 511 MRI exams from 257 patients with transfusional iron overload were analyzed. The median age at first exam was 13 years (range 1 to 53 years); 70% of the subjects were children and 30% adults (Table 1).

MRI Measurements

All patients were imaged on a 1.5T scanner (Magnetom Avanto, Siemens Healthineers, Malvern, PA). For hepatic iron overload assessment, a multi-echo GRE sequence was performed on a single transverse slice of the liver at the location of the main portal vein, with the following acquisition parameters: TR 200 ms, TE₁ 1.1 ms, TE 0.82-0.92 ms (small variations due to software upgrades), 20 echoes, bipolar readout gradient, matrix size 128×104, slice thickness 10 mm, bandwidth 1950 Hz/px, flip angle 35°, and FOV 210-450 mm, depending on participant's size. Multi-echo GRE images were acquired in a single breath-hold of ~21 s in patients who could perform the breath-hold maneuver. For sedated patients or for those unable to suspend breathing, 3-6 averages were acquired to minimize respiratory motion artifacts.

Data Analysis

T2*-Thresholding Technique—As part of the clinical HIC reporting, a single, pediatric radiologist (M.B.M.) with 16-years of experience at the beginning of the data collection period, performed the analysis of all 565 exams as follows: The GRE images were post-processed at a computer workstation, using a custom-written program in MATLAB (MathWorks). Quantitative T2* or R2* (=1/T2*) maps were calculated by fitting signal intensity on a pixel-by-pixel basis to a monoexponential decay, using a nonlinear least-squares fit method, which accounts for bias due to Rician noise.^{9,26,27} Noise (N) was estimated from the image background and used in the following signal model equation:

$$S(t) = \sqrt{(S_0 \cdot \exp(-t \cdot R2^*))^2 + N^2}$$
 to estimate R2* as described in Krafft et al.²⁷ No data points were discarded with this method. However, pixels were only fitted, when at least one data value in the decay curve was higher than three times the estimated noise level, otherwise they were labeled as 'not fitted'.

The T2*-thresholding technique consists of 3 steps:¹³ 1) drawing an ROI to outline the entire hepatic cross-sectional area in the acquired transverse slice (magnitude image or T2* map), 2) excluding blood vessels based on T2* histogram analysis by rejecting T2* values over the chosen threshold, and 3) using an image overlay to confirm that exclusion of vessel pixels for the chosen T2* threshold. Steps 2 and 3 are repeated by re-adjusting the T2* threshold until the radiologist visually confirms exclusion of all vessel pixels. Mean liver T2* and R2* values are calculated by taking the pixel-wise mean value of remaining pixels inside the ROI after vessel exclusion. Cases wherein the number of fitted pixels within the ROI is less than 30% of the total number of pixels were considered as failed fit.¹³ The radiologist's T2*-thresholding results served as a standard reference for evaluation and comparison against the automated technique. For inter-observer variability analysis, a second reviewer with 20 years of MRI experience (C.M.H) performed an independent T2*-thresholding analysis on 60 cases (~10% of the study cohort), and the results were compared to the radiologist's and automated analyses (see Supplement).

Automated Filter-Based Technique—An automated method based on multi-scale vessel enhancement filter²¹ was investigated to segment hepatic vessels from MRI images without any user interface for R2*-based HIC assessment. The basic theory of the 2D

vesselness filter is given in the Supplement. First, a simulation study was performed (in Supplement) to determine appropriate filter parameters and evaluate the efficiency of the vesselness filter for a wide range of $R2^*$ values and SNR scenarios under known conditions. The vesselness filter was applied to 3 image inputs: contrast-optimized composite magnitude image, $T2^*$ map, and $R2^*$ map. For the composite image, a median $T2^*$ value of whole-liver ROI was calculated and the 3 TEs producing the highest contrast between parenchyma and vessel in the simulation study for that $T2^*$ range were used (see Supplement). Thus, the contrast-optimized composite magnitude image was generated by averaging the images acquired at the 3 TEs with the highest contrast.²⁸

For all 3 image inputs, the filter was applied to whole-liver ROI drawn by the radiologist in MATLAB. Appropriate filter parameters β (for suppressing blob-like structures) and c (for suppressing background noise) determined from the simulation study were as follows: $\beta=0.5$ for all filters and $c=15\%$ of the median signal for composite image and $T2^*$ map, and 10% for $R2^*$ map. The filter's spatial scale (σ) was varied between 1 and 2.5 pixels to capture vessels with different sizes. Filter parameters chosen were similar to those suggested in previous studies.^{21,29,30} The filter also had a Boolean parameter set either to detect bright vessels on a dark background or dark vessels on a bright background. Vessels appeared bright on the magnitude images and $T2^*$ map, and dark on the $R2^*$ map, and filter options were set accordingly.

The filter result is a vesselness response of the pixels containing vessels (defined in Supplement). The filter output is high for pixels with high probability of containing a vessel and low for small vessels. The filter might also produce small vesselness values for noise pixels. To exclude noise pixels, a small threshold value of 0.05 of the maximum vesselness response was used as recommended previously.^{24,25} Thus, pixels with vesselness response greater than or equal to the threshold value provide the vesselness mask and those less than the threshold value provide the extracted parenchyma mask. For each image input, parenchyma and vessel masks were created and the mean $R2^*$ value was calculated by taking the pixel-wise mean of the extracted parenchyma $R2^*$ map. Figure 1 summarizes the processing steps for the automated parenchyma extraction technique, using the multi-scale vesselness filter for the 3 image inputs.

For both reference and automated analyses, mean liver $R2^*$ values were converted into HIC estimates (abbreviated as $R2^*$ -HIC), using a previously published $R2^*$ vs. biopsy HIC calibration curve.^{9,13} To investigate the association of the segmentation results of the automated technique with the reference method, a dice similarity coefficient (DC) was used to assess agreement of the extracted parenchyma between both methods:²⁸

$$DC (\%) = \frac{2(A \cap B)}{A + B} \times 100 \quad [1]$$

where A and B represent extracted parenchyma masks by the reference and automated methods, respectively, and $\cap$ and $+$ represent the intersection and addition between the

masks, respectively. DC values of 0% and 100% indicate no overlap and perfect overlap, respectively, between extracted masks obtained by both methods.

Statistical Analysis

Statistical analysis was performed using MATLAB. Mean $\pm$ standard deviation (SD) and range of $R2^*$ and $R2^*$ -HIC values estimated by the reference and automated techniques across the cohort were determined. Mean $R2^*$ values of the extracted liver parenchyma between the reference and automated methods were compared by linear regression and Bland–Altman analyses. Further, the coefficient of variation (CV), calculated by dividing the SD with the mean $R2^*$ value, was compared between the reference and automated methods to assess dispersion in $R2^*$ measurements.

Results

The mean and range of liver $R2^*$ and $R2^*$ -HIC values for the reference threshold-based and the automated parenchyma extraction techniques are summarized in Table 2. Representative examples of extracted parenchyma masks obtained using reference and filter-based methods in mild ($3 < \text{HIC} < 7 \text{ mg Fe/g}$), moderate ($7 < \text{HIC} < 15 \text{ mg Fe/g}$), and high ($\text{HIC} > 15 \text{ mg Fe/g}$) cases of iron overload are shown in Figure 2. For all 3 cases, the reference analysis based on $T2^*$ -thresholding excluded less vessels, and pixels, which are affected by partial volume effects at tissue and vessel boundaries (white arrows, Fig. 2) compared to filter-based methods. This yielded lower $R2^*$ values with the $T2^*$ -thresholding analysis than those obtained by filter-based analysis. Further, compared with filter-based values, the underestimation of $R2^*$ /HIC values with $T2^*$ -thresholding increased with iron overload severity (Fig. 2).

The mean DCs of parenchyma masks that were extracted using reference and filter-based methods were 87–88% (Figure 3). Mean liver $R2^*$ values estimated by all 3 filter-based methods showed excellent correlation ($R^2 > 0.99$, $P < 0.001$) and a slope slightly over 1 (image-based: 1.05, $T2^*$ -based: 1.04, and $R2^*$ -based: 1.05) compared with reference $R2^*$ values (Figure 4). Bland–Altman analysis showed a positive $R2^*$ bias of 3.93% – 4.51% for all filter-based methods compared with the reference method (Figure 4). Analysis of CV of $R2^*$ values measured by radiologist analysis and different filter-based methods showed a slightly higher mean $R2^*$ -CV for the $T2^*$ thresholding technique than that for filter-based methods (Figure 5).

For the $T2^*$ -thresholding technique, the inter-observer variability analysis produced slopes close to unity (0.987, 0.990) and excellent correlation coefficients ($R^2 = 0.998$) between $R2^*$ values obtained by the 2 reviewers (see Figure S3 and explanation provided in the Supplement). However, there is a small positive $R2^*$ bias of ~3% on Bland–Altman suggesting the use of slightly different $T2^*$ thresholds by the reviewers. Further, filter-based methods produced similar slopes (reviewer-1: 1.04 – 1.06, reviewer-2: 1.04 – 1.07) and slightly different mean biases (reviewer-1: 1.67 – 2.46%, reviewer-2: 4.6 – 5.28%) compared to $R2^*$ values calculated by the 2 reviewers using the $T2^*$ -thresholding technique (see Figure S4 and explanation provided in Supplement).

Discussion

Accurate assessment of HIC by R2*-MRI is critical for managing patients with iron overload. The current approach for R2*-MRI iron quantitation using whole-liver ROI requires manual steps of excluding blood vessels in the ROI and radiologists take about 3-7 min per case to perform the vessel exclusion. Also, this process introduces potential inter-observer variability, given the need for the subjective reviewer's visual inspection of vessel pixels to be excluded (see Supplement). In this study, we tested an automatic vessel segmentation technique that substantially reduces processing time (< 1 s per case) and operator dependence, thereby improving the clinical workflow and diagnostic confidence of R2*-MRI based HIC measurements while removing potential inter-observer variability. This technique was robust and yielded accurate R2* measurements in patients with a wide range of HICs (0.4 – 26.5 mg Fe/g) when compared with the conventional T2* thresholding technique.

Mean liver R2* values estimated by all 3 filter-based methods and by the reference method showed excellent agreement across a wide range of HICs. The reference analysis based on T2* thresholding, produced on an average ~13% more parenchymal area compared to filter-based methods (i.e., DC ~87%). This is because parenchyma extracted by the reference analysis included more small vessels and pixels at tissue and vessel boundaries than that extracted by filter-based methods. This lower number of vessels excluded by the reference method also led to R2* underestimation compared to filter-based methods (slope over 1 on linear regression and positive bias on Bland-Altman analyses), because blood has a lower R2* than iron-overloaded tissue. Further, R2*/HIC underestimation was higher for cases of high iron overload because of considerable difference between the R2* of vessels and liver parenchyma with severe iron overload. The lower number of extracted vessel pixels also increased the SD in R2* values, leading to higher CV for the reference method than for filter-based methods.

Although all filter-based methods performed equally well, irrespective of input data types used for parenchyma extraction, each has advantages and limitations. The composite image is calculated by averaging the 3 TE images with highest contrast between vessel and parenchyma. Thus, the image-based filter output depends on the TEs selected, which should be determined using simulation studies prior to in-vivo application. Further, the filter output based on magnitude images is susceptible to signal intensity inhomogeneities, which might affect vessel segmentation. Applying the filter on quantitative T2*/R2* maps removes the effect of intensity inhomogeneities. However, filter outputs based on T2*/R2* maps depend on the fitting accuracy of the signal decay. Fitting is a major concern in cases of high iron overload, as the signal decays so fast that sampled echoes are predominated by noise that affects accurate T2*/R2* quantification.³¹ Applying filters on magnitude images is advantageous for vessel segmentation in such scenarios but not if the fitting is imprecise, because the goal is to accurately estimate R2* to assess HIC. Finally, despite subtle differences among different input data types, results obtained by all 3 filter-based methods compared to reference method were similar. These findings support the robustness of the automated vesselness filter and offer clinicians the flexibility to apply it on magnitude images, T2*/R2* maps, or their combination.

Applying the vesselness filter to detect bright vessels on a dark background, as seen in image-based and T2*-based data types, requires an extra processing step to eliminate liver boundary outliers, because the filter output also includes a small strip around the liver into the vessel mask due to the extreme contrast difference at liver boundaries. To avoid this problem, background signal and T2* values for both image-based and T2*-based methods were made similar to those in the parenchyma before applying the filter. However, this was not a problem for R2*-based filters, as they detect dark vessels on a bright background. At liver boundaries, the R2*-based filter output will include a small strip from the dark background into the vessel mask, but this strip can easily be excluded as it is outside the whole-liver ROI. Overall, the R2*-based filter seems to be the most robust and easiest to implement and apply.

Our study has some limitations. It was a retrospective analysis of liver MRI exams from patients with different diseases. However, we included a large number of exams, all centrally reviewed by one single radiologist. The automated technique, although an advance due to the reduction in user interface and subjectivity, is not fully automated, as the reviewer must still outline the whole-liver ROI as with T2*-thresholding. Nevertheless, the process of outlining the liver is quick and straightforward although leaning itself to higher inter-reviewer variability (see Figure S3 in Supplement with different whole-liver ROIs). A possible future improvement is to entirely eliminate user interaction by incorporating automatic liver-contouring techniques based on region-growing methods or using information from additional imaging data (e.g., fat/water or T1 maps). Our patients did not have diffuse or focal liver diseases or other hepatic pathologies; hence, the usability of filters in such scenarios could not be tested. Our automated filter-based methods seem to be over-conservative in vessel segmentation, but excluding as many vessels as possible is more important than maximizing the extraction of parenchyma for accurate liver R2* measurement. The smallest vessel diameter that can be detected by the filter is limited by the spatial resolution of the image, which is equally a limitation for T2*-thresholding. Decreasing the slice thickness and increasing the in-plane resolution in future prospective studies could reduce potential partial volume effects that currently hinder extraction of smaller vessels. In this study, R2* was estimated using a mono-exponential signal model and presence of fat in the liver may confound R2* measurements. However, the majority of our patients had low body mass index and were primarily iron-overloaded with no prior evidence of steatosis. Moreover, as the same R2* model is used for both, manual and automated parenchyma extraction methods, potential fat contamination would only affect the true iron R2* calculation but be irrelevant for the comparisons between the vessel extraction methods.

In this study, some cases were excluded as failed fit, likely because of massive iron overload ($\text{HIC} > 25 \text{ mg Fe/g dry weight}$), which causes the signal to decay rapidly before the first possible TE of 1.1 ms achieved with our conventional GRE sequence. To provide accurate R2* quantification for massive iron overload, TE₁ should be significantly reduced in future prospective studies, e.g. by using ultra short TE (UTE) sequences (TE₁ ~0.1 ms).³²

Lastly, to be able to provide the clinicians with HIC values for treatment decisions, our acquisition method and R2* fitting model had to be matched to those of a validated biopsy

HIC vs. $R2^*$ calibration study that was derived in a large pediatric population.⁹ We are aware of several recently proposed $R2^*$ models that may show superior fit performance in low SNR and/or severe iron overload scenarios.^{31,33} An advantage of the presented automated vessel exclusion technique is, however, that it does not require the use of a particular fitting model or acquisition method (e.g., 2D/3D, GRE/UTE, single-slice/multi-slice acquisition), and only depends on good contrast between vessel and parenchyma. Future work could investigate this aspect further.

In conclusion, we found our automatic vessel exclusion technique is equivalent to the conventional technique and can be applied to extract the entire liver parenchyma in the acquired cross-sectional image while substantially reducing operator time and input. This method can improve the radiologist's workflow while potentially reducing inter-rater variability in HIC measurements and optimizing management of patients with iron overload.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Processing diagram for automated parenchyma extraction based on a vesselness filter for the 3 input data types: contrast-optimized composite image (first column), T2* map (second column), and R2* map (third column). For all 3 image inputs, the filter was applied to the whole-liver ROI drawn by the radiologist. The filter output was calculated using appropriate filter parameters derived from the simulation study (Supplement). Pixels with a vesselness response greater than or equal to the threshold value (0.05 of the maximum vesselness

response) provide the vesselness mask, and those less than the threshold value provide the extracted parenchyma mask. ROI, region of interest.

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Figure 2.

Quantitative T2* maps of the acquired slice (first column) and extracted parenchyma T2* maps obtained after vessel exclusion using manual, histogram-based T2*-thresholding performed by a radiologist (second column) and different filter-based methods (last 3 columns) in cases of mild ($3 < \text{HIC} < 7 \text{ mg Fe/g}$, top row), moderate ($7 < \text{HIC} < 15 \text{ mg Fe/g}$, middle row), and high ($\text{HIC} > 15 \text{ mg Fe/g}$, bottom row) iron overload. Mean liver R2* and associated R2*-HIC values calculated using the calibration curve^{9,13} for the extracted liver parenchyma for each technique are also given. R2* underestimation seen in T2*-thresholding analysis, caused by inclusion of small vessels and pixels affected by partial volume effects (PVE) (white arrows), can be seen in all 3 cases but is more pronounced in cases of moderate and high HIC.

Figure 3.

Dice similarity coefficients (DCs) for parenchyma masks extracted using T2*-thresholding and 3 filter-based methods (A-C). Mean DCs were $87.3 \pm 2.7\%$ for composite image-based, $88.0 \pm 2.9\%$ for T2*-based, and 87.8 ± 2.9 for R2*-based methods.

Figure 4.

Linear regression (A, C, E) and Bland–Altman (B, D, F) analysis of mean liver $R2^*$ values obtained by conventional $T2^*$ -thresholding and 3 filter-based methods. For regression plots, solid lines represent regression lines and the dashed line represents the unity line. For Bland–Altman plots, solid lines represent mean bias and dashed lines represent 95% confidence intervals ($\pm 1.96 \times SD$). Regression equations, correlation coefficients (R^2), and mean biases are also included in the respective plots.

Figure 5.

Scatter plots showing the coefficient of variation (CV) of $R2^*$ values obtained by conventional T2*-thresholding (A) and 3 filter-based methods (B–D). $R2^*$ -CV ranged from 7.8% to 35.1% (mean, $16.4 \pm 4.4\%$) for the conventional method, from 6.5% to 35.5% (mean, $13.7 \pm 3.9\%$) for the image-based filter, from 6.3% to 34.2% (mean, $13.4 \pm 3.9\%$) for the T2*-based filter, and from 6.1% to 35.2% (mean, $13.0 \pm 3.7\%$) for the $R2^*$ -based filter.

Table 1

Patient Demographics and Disease Characteristics

Characteristic	N (%)
Total MRI exams	565
Evaluable MRI exams	511
Number of patients	257
Adult patients (>18 years old)	79 (30%)
Pediatric patients (≤ 18 years old)	178 (70%)
Age at first exam (years)	
Median (min. – max.)	13 (1–53)
Gender	
Male	117 (46%)
Female	140 (54%)
Diagnosis	
Sickle cell disease	94 (37%)
β-thalassemia	24 (9%)
Cancer	105 (41%)
Others (Bone marrow failure syndromes, histiocytosis, hereditary hemochromatosis, pyruvate kinase deficiency)	34 (13%)

Table 2

Liver R2* and R2*-HIC Values Obtained with Reference and Automated Parenchyma Extraction Techniques

	Reference		Automated	
	T2*-thresholding	Image-based	T2*-based	R2*-based
Mean R2*± SD	271 ± 172	283 ± 180	282 ± 178	285 ± 181
Range (s⁻¹)	31–854	31–870	31–868	31–875
Mean R2*-HIC ± SD	7.8 ± 5.3	8.2 ± 5.6	8.2 ± 5.5	8.2 ± 5.6
Range (mg Fe/g)	0.4–25.9	0.4–26.4	0.4–26.3	0.4–26.5

Abbreviation: SD, standard deviation.