

Accurate Liver Iron Estimation Using a Novel Single-Breathhold R2* Technique

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Introduction: Iron overload is a relatively common health problem resulting from increased iron absorption syndromes, such as hereditary hemochromatosis, and from excessive transfusion therapy. Liver iron content, assayed from liver biopsy, is often used as a surrogate for total somatic iron burden during iron removal therapy[1]. Unfortunately, liver biopsy is expensive, invasive, and yields little information regarding iron content of other organs. While trends in serum ferritin value provide some guidance for iron removal therapy, concordance between iron burden and serum ferritin is inexplicably poor in some patients and disease states. Since iron increases transverse relaxivity, MRI estimates of liver R2 and R2* have been used to accurately estimate liver iron burden in patients with transfusional iron overload[2-4]. Using a custom, reduced-matrix multiphase single-echo gradient-echo technique, we previously demonstrated strong linear correlation ($r=0.98$) between R2* and liver iron[2]. In this abstract, we compare the performance of that prior method to a novel multiecho gradient echo sequence (General Electric Medical Systems, Milwaukee, WI).

Methods: 33 patients with transfusional iron overload had liver iron assessment during clinically-indicated MRI imaging. Informed consent was obtained to compare the different liver MRI techniques. Images were collected using the torso or cardiac coil on a 1.5 T CVi scanner running version 9.1 system software (General Electric Medical Systems, Milwaukee, WI). Liver R2 was assessed using a custom 120-120 degree spin echo sequence having the following parameters: TR 300 ms, matrix 64 x 64, FOV 48 x 24 cm, bandwidth ± 32 kHz, 4 slices, slice thickness 15 mm, 5 mm gap and 1 NEX. Echo times were 3.5, 5, 8, 12, 18, and 30 ms, collected one per breath-hold (16 seconds each). Liver R2* was assessed using both single and multiecho gradient echo techniques. Single echo technique used an FOV of 48 x 24, TR 25 ms, matrix 64 x 64, 1 NEX, single slice, 15 mm thick, BW 83 kHz. Using the multiphase loop, fifteen echo times (0.92-4.42 by 0.25 ms increments) were collected in a single 16 second breath-hold. The multi-echo gradient echo T2* sequence used a FOV of 36-44 cm, matrix 128 x 128, slice thickness 10 mm, BW ± 125 kHz, and 1 NEX. Eight echoes were collected using an initial TE of 1.59 ms and interecho spacing of 1.76 ms. One to five slices could be collected in a single breath-hold.

R2 and R2* values were calculated on a pixel by pixel basis by fitting signal decay curves to a monoexponential plus a constant offset. R2 and R2* values were converted to estimated iron using previous biopsy-derived relationships [2]

$$[\text{Fe}] = [(R2/3.18)^{1.642} - 21.49]/40.64 \quad (1)$$

$$[\text{Fe}] = (R2^*) \times 0.0246 - 0.5286 \quad (2)$$

R2* values and predicted iron concentrations were compared to one another using linear regression analysis. The single and multi echo gradient echo sequences were also compared to one another using a manganese chloride phantom. Phantom consisted of 12 Nalgene bottles having MnCl₂ concentrations ranging from 0.5 mM to 24 mM. Vials were bathed in a 0.25 mM MnCl₂ solution to decrease boundary artifacts.

Results: R2* values using the multiecho gradient echo sequence were closely correlated to those generated by the single echo sequence for R2* < 1000 sec⁻¹. In the phantom measurements, r was 0.994 with a slope of 1.1 \pm 0.02 (not shown). In-vivo liver R2* correspondence was also excellent with an r value of 0.97 and a slope of 0.988 \pm 0.025 (Figure 1, Left). The multiecho sequence could not calculate R2* > 1000 because the minimum echo time (1.592 ms) was too long to accurately sample initial signal decay.

Predicted hepatic iron concentration (HIC) using the multi-echo R2* technique was compared with HIC estimated by a Hahn single spin echo technique (Figure 1, Right), using calibrations from our prior liver biopsy validation study[2]. Agreement was excellent up to estimated HIC's of 25 mg/g dry weight, with a slope of 0.95 \pm 0.03 and an r-value of 0.94.

Discussion: Although many investigator-derived custom pulse sequences have been written for iron quantitation, including a similar multiecho gradient echo technique[5], the present multi-echo gradient echo sequence represents the first dedicated commercial effort. The sequence can accurately characterize HIC over most of the entire liver in a single breath-hold. Currently, the minimum echo time is too long to characterize iron concentrations greater than 25 mg/g. Clinically, this is not a fundamental problem as HIC's > 15 mg/g are treated aggressively to prevent cardiotoxicity[1]. Higher iron concentrations may be measurable by using a smaller frequency matrix, higher bandwidth, or by using signal intensity ratios; these investigations are ongoing.

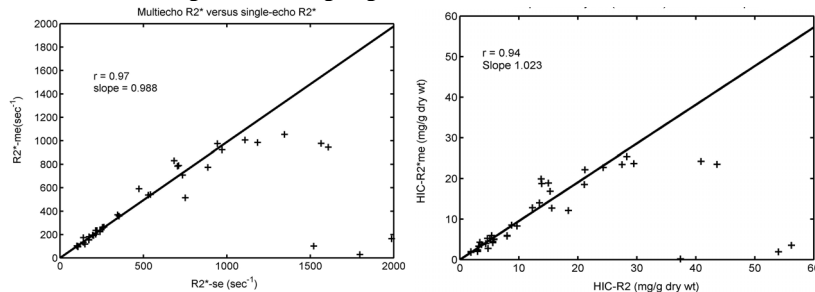


Figure 1: (Left) Comparison of R2* values calculated using the old single echo technique and the new multiecho technique. Good concordance is observed for R2* values up to 1000 sec⁻¹, with an r-value of 0.97 and slope of 0.988 (Right) Predicted hepatic iron concentrations (HIC) using new multiecho gradient echo technique compared with HIC's estimated from Hahn single-spin echo technique. Slope is near 1 with a r-value of 0.94 for HIC's up to 25 mg/g dry weight of liver

References

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