Liver Iron Content Quantification via Single Breath-Hold MR Imaging at 3.0 Tesla

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Introduction: Iron overload due to either increased gastrointestinal absorption and/or transfusions is key to the underlying pathophysiology of organ dysfunction and decreased patient survival for those with hematological disorders. Chelation therapy effectively reduces the iron burden, decreases iron-associated complications, and improves patient survival.[1] To optimize chelator effectiveness and minimize toxicity, a safe, accurate, and easily performable means of measuring the degree of iron overload is essential. Liver iron content (LIC) correlates with total body iron load.[2] The current gold standard for the quantification of LIC in iron-overloaded states is liver biopsy. Biopsy is, however, an invasive procedure with attendant risks, and is imperfect due to sampling bias (which increases in the presence of fibrosis, cirrhosis, and elevated iron), small sample size and technical error. Fortunately, MR imaging is a non-invasive, readily available, and potentially accurate alternative to quantifying LIC.[3,4] The primary goals of our study are to acquire the LIC information within one single breath-hold at 3.0 T, calculate LIC maps rapidly and robustly, and compare the results to liver biopsy.

Methods: We modified a multi-echo, multi-slice, spoiled gradient-recalled echo (SPGR) sequence to acquire 16 echoes spaced 224 μs apart in a single 18 s breath hold, and calculated the LIC, in mg of iron per gram of dry liver weight (mg/g), according to methods established by Wood[4] and Storey.[5] Fourteen chronic transfusion-dependent patients (suffering from β-thalassemia major, β-thalassemia intermedia, or pure red cell aplasia) underwent liver biopsy and abdominal MR imaging on a 3.0 T scanner (Discovery 750; GE Healthcare, Waukesha, WI) using a 32-channel torso phased-array coil. R2* maps were generated using Functool's R2Star feature (GE Healthcare), and further processed to produce LIC maps. The MR-based LIC values were compared to the single-sample biopsy LIC estimates using the Student's paired *t*-test.

Results: The biopsy samples of two patients were mishandled, while a third patient had an excessively large amount of iron such that no MR liver signal could be detected. For the remaining eleven patients, the Student's paired *t*-test yielded a mean LIC difference of 2.5 mg/g between MR and biopsy, or equivalently a mean difference of about 14.1%. The minimum detectable differences (MDD), assuming 95% confidence level and 80% statistical power, were 2.6 mg/g and 20.8%, respectively. Considering that biopsy estimates have an inherent associated error/bias of ±25%, the MR- and biopsy-derived LIC values are not statistically different.

Conclusion: Despite our small sample size, the MR quantification at 3.0 T provided LIC estimates that correlated well with biopsy. These MR-based LIC measurements covered the entire liver volume, and potentially represent more accurate and faithful estimates than those obtained from a small single sample of liver tissue biopsy. Note that clinically, LIC classification in steps of 5 mg/g or so are typically adequate for diagnosis. Thus, although our MR-to-biopsy MDD was about 2.5 mg/g, and taking biopsy biases into consideration, this MR-based method represents a viable LIC paradigm. Moreover, MR-derived measurements can be done quickly and efficiently within a single breath-hold, are non-invasive, are well tolerated by most patients, provide LIC maps in meaningful absolute units (like biopsy), and can be performed repeatedly.

References: [1]Brittenham, et al. *N Engl J Med* 1994;331:567. [2]Angelucci, et al. *N Engl J Med* 2000;343:327. [3]St-Pierre, et al. *Blood* 2005;105:885. [4]Wood, et al. *Blood* 2005;106:1460. [5]Storey, et al. *J Magn Reson Imaging* 2007;25:540.

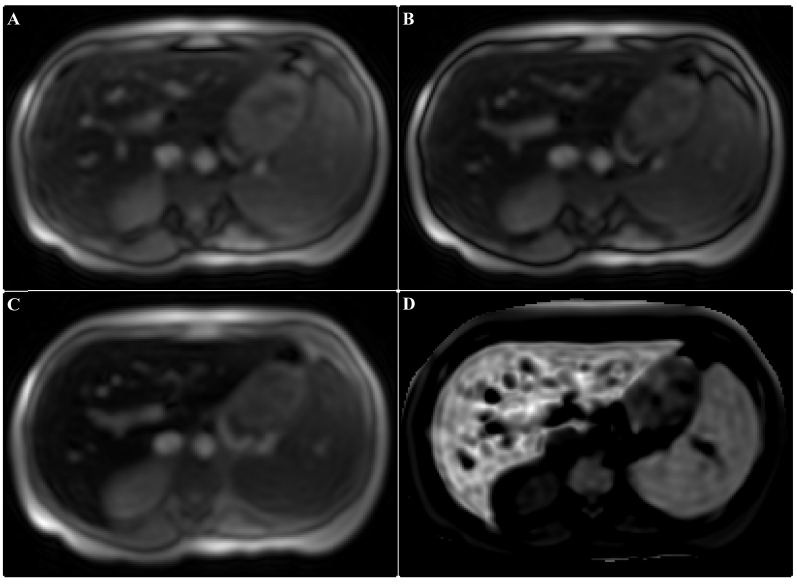

Figure 1: Source SPGR images and derived LIC map for one patient. The SPGR images at (A) echo1 with TE = 1.0 ms, (B) echo3 with TE = 1.45 ms, and (C) echo5 with TE = 1.90 ms are at identical windowing levels and show significant signal loss in the liver due to the iron overload. (D) The LIC map (in mg/g), whereby the values are only meaningful in the liver.