Fully automated, user-independent "screening" of the liver for diffuse steatosis/iron overload using a two-point Dixon pulse sequence

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Purpose: Non-alcoholic fatty liver disease (NAFLD) is pandemic in the United States, affecting 20-80 million people. In the past, the detection of NAFLD and accurate quantification of severity of hepatic steatosis relied on percutaneous liver biopsy. While biopsy remains the reference standard for liver fat assessment, quantitative chemical shift-based (qCS) MRI techniques are gaining acceptance in both research and clinical arenas as accurate, reproducible measures of hepatic steatosis (1). When left untreated, NAFLD can progress to non-alcoholic steatohepatitis (NASH), a progressive necroinflammatory state which ultimately results in cirrhosis. NAFLD can be clinically silent, and a large proportion of the cases of "cryptogenic" cirrhosis are now thought to be due to chronic undiagnosed NAFLD/NASH.

qCS techniques have potential to function as noninvasive screening and diagnostic methods for NAFLD and NASH. Unfortunately, qCS techniques cannot be substituted for standard pulse sequences in a structural MRI examination because they are proton-density weighted, and therefore cannot replace either T1- or T2-weighted sequences due to differences in contrast. Additionally, because they are 2D techniques, they require relatively long repetition times (TRs) compared with 3D T1-weighted sequences, resulting in lower in-plane or through-plane spatial resolution. As a result of these limitations, qCS techniques must be performed as additional pulse sequences in an MRI examination. Performing these qCS sequences in every abdominal MRI lengthens acquisition time and is unnecessary in most patients, who do not have hepatic steatosis. An optimal imaging algorithm would separate patients with hepatic steatosis from normals during their MRI scan, and would subsequently perform qCS only when necessary.

Many institutions perform in- and opposed-phase T1w imaging with two-point Dixon reconstruction as part of their standard abdominal MRI protocols. This pulse sequence can be used to perform both fully automated liver sampling and preliminary evaluation for hepatic steatosis (and iron overload) (2,3). We have implemented the sampling/analysis algorithm to run inline on the MR console and display a message to the MR operator performing the scan recommending that dedicated quantification pulse sequences are performed when the algorithm deems it appropriate. The purpose of this study is to compare the performance of expert readers with the performance of this algorithm in detecting and correctly characterizing diffuse hepatic deposition disease (steatosis, iron overload, and a combination of both).

Materials and Methods: Our institutional review board approved this retrospective Health Insurance Portability and Accountability Act–compliant study. We refer to the combined sampling/analysis algorithm described above as the “screening algorithm.”

Forty-four consecutive patients were identified who had undergone abdominal MRI at 1.5T including in- and opposed-phase imaging with two-point Dixon reconstruction using the screening algorithm. The patients also had liver fat quantification (using a multi-echo T1-insensitive T2*-corrected technique) and liver iron quantification (using a multi-echo short-TE-interval technique), as part of routine imaging. As the reference standard, a normal fat percentage was considered to be <5.6% (based on the Dallas heart study) (4), while a normal R2* value was considered >70 Hz.

Three expert radiologists (with 12, 5, and 2 years of post-fellowship experience in abdominal MRI) reviewed the in- and opposed-phase data set with two-point Dixon reconstruction and were asked to record the following conclusions: (a) presence or absence of diffuse deposition disease; (b) type of disease, if present (fat, iron, or both); (c) confidence for the presence of disease. Reader performance and the automated conclusion generated by the screening algorithm were compared against the reference standard using descriptive statistics.

Results: Of the 44 patients included, 15 had diffuse deposition disease (12 steatosis, 2 iron, 1 combined). The 12 patients with only steatosis had the following diagnoses or risk factors: 4 – no known risk factors; 3 – known non-alcoholic steatohepatitis; 2 – metabolic syndrome; 1 – alcohol abuse; 1 – new liver function test elevation; 1 – known glycogen storage disease. The two patients with isolated iron overload had a history of multiple blood transfusions for sickle cell disease or myelodysplastic syndrome, respectively. The patient with combined disease had hemochromatosis and relapsed acute lymphocytic leukemia, and was being treated with an antineoplastic agent known to increase the risk of hepatic steatosis.

Readers performed well, with an average sensitivity for disease of 91% and specificity of 90%. The screening algorithm, however, was 100% sensitive for the presence of the disease, and equally specific (90%; 3 false positives). When disease was present, the screening algorithm correctly characterized the disease state in every case. For the 15 patients with disease, readers mischaracterized an average of 1.7 cases each: two readers mischaracterized a patient with mild steatosis (7.6% by qCS) as normal, and two readers characterized the patient with combined disease as having steatosis.

Discussion/Clinical Relevance: The screening algorithm detected every case of diffuse deposition disease in our study population, with a 100% negative predictive value; no patients with disease were missed, and all would have undergone dedicated quantification pulse sequences.

Implementation of such an algorithm in a clinical abdominal MRI practice would provide on-the-spot identification of diffuse liver disease. As a result, additional quantification sequences could be performed when necessary, but only when necessary. This methodology has a number of potential applications: (a) detection and immediate expert radiologist review of unsuspected diffuse liver disease in individuals; (b) population-based screening for diffuse liver disease as part of a routine liver MR examination. Population-based screening may improve our understanding of the clinical relevance of hepatic steatosis and the course from silent, asymptomatic NAFLD to progressive NASH/cirrhosis. In addition, the detection of hepatic steatosis in its silent state may allow successful treatment of affected individuals prior to progression to irreversible cirrhosis.

References