Assessment of hepatic steatosis, iron overload and combined disease with 3 Tesla MR three-dimensional T1w two-point Dixon Imaging: In-vivo Validation and In-vitro Calibration of Decomposition Technique

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SUMMARY

Steatosis hepatis functions as an inducer of hepatic iron metabolism dysregulation. 3 Tesla MR two-point Dixon T1w imaging with subsequent comprehensive four-phase decomposition analysis facilitated not only metabolite decomposition of intrahepatic lipids and iron ions in isolated steatosis hepatis and hepatic iron overload, but also allowed decomposition of metabolites in combined disease in a standardized in-vitro liver phantom with in-vivo patient validation.

INTRODUCTION

Metabolites most commonly associated with diffuse liver disease are triglycerides and iron ions. Its sensitivity for identifying and quantifying hepatic metabolites such as lipids and paramagnetic metal ions non-invasively, predestined abdominal MRI with dual-echo imaging sequences for characterization of diffuse liver disease by exploiting chemical shift phenomena as well as pronounced T2*-effects, respectively.

Recent discoveries in assessing hepatic fat and iron metabolism pathways, however, were able to prove that regulation mechanisms essential for systemic fat and iron uptake and distribution appear to converge in the liver in a mutual-dependent fashion: Steatosis hepatis functions as an inducer of iron metabolism dysregulation. The detection and quantification of each individual disease component may prove essential in order to quantify disease severity, clarify disease component interdependencies and characterize degree of hepatic fibrosis itself. The task of decomposition of underlying intrahepatocellular lipid and iron storage in clinical scenarios of combined-disease, however, may be complicated by non-differentiable simultaneous signal loss on in-phase as well as opposed-phase MR imaging based on simultaneously occurring pronounced T2*-effects and chemical shift phenomena.

The original concept of the two-point Dixon method has been known for over two decades, however, recent technical development allowed the acquisition and implementation of clinical Dixon processing. Acquired in- and opposed-phase MR data series in concert with two-point Dixon processing, results in two additional ‘water-only’ and ‘fat-only’ data series; each voxel of the three-dimensional dual-echo MR acquisition scheme is subsequently characterized by four intensity parameters.

This study was designed to test the hypothesis that clinical 3 Tesla MR two-point Dixon T1w imaging with subsequent comprehensive four-phase decomposition analysis will enhance diagnostic accuracy to characterize steatosis hepatis, hepatic iron overload and combined disease beyond the capabilities of clinical sole dual-echo MR acquisition schemes in a standardized in-vitro liver phantom with in-vivo patient validation.

METHODS

45 patients were included in our study; of which 15 patients were diagnosed with steatosis hepatis, 15 patients had hepatic iron overload, and 15 patients were included without any known medical history of liver disease as normal control group.

Acrylamide-based liver phantom development aimed to reproduce typical MR relaxation times of physiologic hepatic parenchyma; additionally, fatty liver disease was simulated by admixture of triglycerides, hepatic iron overload was simulated by admixture of ferrumoxides. Combined disease was simulated by joint admixture of triglycerides and ferrumoxides at various individual concentrations.

3 Tesla whole-body, breath-hold MR imaging (Magnetom TimTrio, Siemens, Erlangen, Germany) was performed utilizing a clinical three-dimensional in- and opposed-phase Volumetric Interpolated Breath-hold Examination (VIBE) sequence using TR / TE\textsubscript{in-phase} / TE\textsubscript{opposed-phase} of 4.19 / 1.25 / 2.46 ms, respectively. Water- and fat-decomposition was achieved by Dixon-based raw-data calculation algorithms by means of subtraction and summation in combination with region-growing schemes such as next-neighbor and vote-counting calculations to compensate for phase-shift effects.

Hepatic in/opposed phase ratios and fat/water phase ratios were calculated according to:

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\frac{S_{in-phase}}{S_{opposed-phase}} \quad \text{and} \quad \frac{S_{fat-only}}{S_{water-only}}
\]

Graphical and statistical cluster analysis was utilized to identify and characterize voxel clusters representing physiologic liver parenchyma, steatosis hepatis, hepatic iron overload, and combined disease.

RESULTS

Graphical and statistical assessment proved that the decomposition coordinates of patients with steatosis hepatis and hepatic iron overload as well as the coordinates of the normal control group formed three specific voxel clusters with unique hepatic in/opposed phase ratios and fat/water phase ratios in concordance with underlying disease entities as well as for the control group, Figure 1. An imaging artifact falsely mimicking increased fatty infiltration was observed in patients with iron deposition on fat-only images.

Assessment of the liver phantom simulating steatosis hepatis, hepatic iron overload and normal control group confirmed the clustering observed in the two-dimensional assessment of patients. A one-dimensional analysis solely of the in/opposed phase ratio would not have identified a mix of lipids and iron in the combined disease phantom. Only the two-dimensional analysis plotting voxels according to their in/opposed phase and fat/water phase ratios was able to resolve an accurate tissue decomposition allowing the identification and quantification of combined steatosis hepatis and hepatic iron overload utilizing the combined-disease phantom, Figure 2.

CONCLUSION

Our pilot study has proven the basic capability of 3 Tesla MR two-point Dixon T1w imaging to facilitate metabolite decomposition of intrahepatic lipids and iron ions in a standardized in-vitro liver phantom with in-vivo patient validation: the proposed two-dimensional decomposition analysis was able to identify precise correlations of disease severity and magnitude of calculated in/opposed and fat/water ratios for steatosis hepatis, hepatic iron overload and combined disease and furthermore identified an imaging artifact which falsely mimics an increased hepatic fat content in patients with iron deposition on fat-only images.