Dynamic Contrast Enhanced MRI Grading of Liver Fibrosis using the Elimination Rate of Gd-EOB-DTPA

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Introduction: Liver fibrosis is a form of liver injury that can progress to organ failure. Assessment of the degree of fibrosis over time is essential to determining the effectiveness of therapy. The current gold-standard for the determination of liver fibrosis severity is biopsy, which is an invasive procedure prone to sampling error and risk of patient injury.Dynamic contrast enhanced (DCE) MRI of the whole liver using a liver specific contrast agent Gd-EOB-DTPA (Eovist) provides a unique opportunity to assess intracellular uptake of the agent in the functioning liver as well as elimination through both hepatic and renal routes.[1] We hypothesize that evaluation of liver uptake and elimination of this agent will correlate with the degree of liver fibrosis, and thereby provide a non-invasive technique for monitoring progression of this disease.

Methods: Under approval of our institutional review board, seventeen DCE-MRI data sets were prospectively acquired from 2 normal controls and 15 hepatitis-C subjects [54.1±8.1yrs, 10M/5F] on a 1.5T General Electric Excite HDx MRI scanner with an 8-channel phased array coil. Eovist was injected at a standard dose of 0.025 mmol/kg at a rate of 1cc/s followed by a 30 cc saline flush. A 3D spiral sequence was reconstructed to yield 2 seconds/frames for the first 90 seconds and sampled every 1 minute out to 20 minutes post-contrast for a total of between 35-55 frames. Acquisition parameters included: TR/TE = 5.6ms/0.4ms, 256x256x24 matrix, 40cm FOV, 8mm slice thickness. A rigid 6 parameter temporal realignment was performed on the raw DCE-MRI data set using SPM5.The liver was segmented using a voxel wise Pearson's R^2 correlation with a slice specific normal liver reference time intensity curve (TIC). The Brix 2C model was used to fit uptake parameters to the TIC and correlate with fibrosis grade derived from CT guided liver biopsy samples.[2] The model contains the parameters: A(signal amplitude),k_{ep}(exchange rate between plasma and extravascular extracellular space (EES) in min^{-1}), and k_{el}(elimination rate in min^{-1}). Analysis software was written in-house using IDL 8.1 (Boulder, CO).

Results: Figures 1 and 2 show the TICs from a normal control subject and a subject with fibrosis grade 4, respectively. The Pearson's R^2 correlation coefficient between the elimination rate (k_{el}) and fibrosis grade was 0.37 (p=0.01). If a cutoff of k_{el} = -0.0015/min is defined, the accuracy of EOB DCE-MRI in predicting whether a subject has fibrosis grade 3 or above is 88.2%. Likewise, the sensitivity of this method was 75% and the specificity 100%. The peak enhancement value at 20 minutes post-injection inversely correlated with the fibrosis grade at R^2 = 0.27, p=0.032.

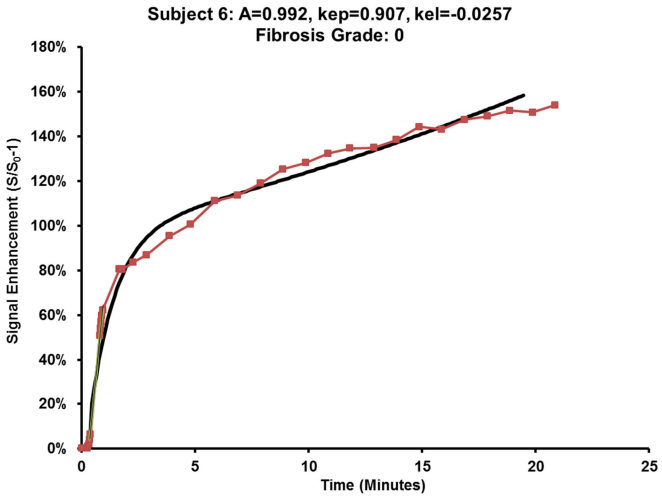

Figure 1

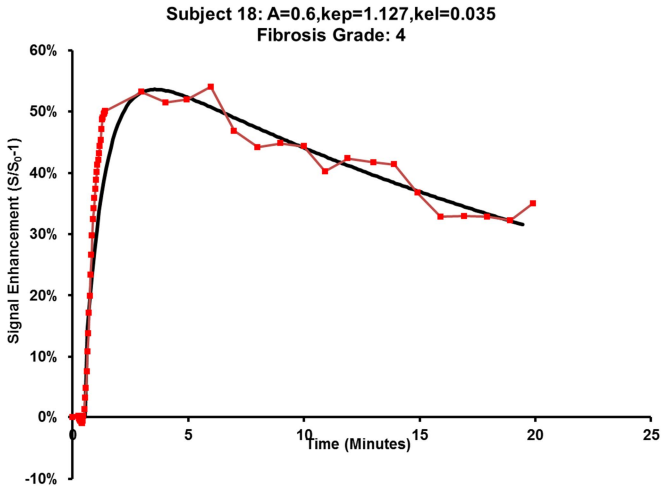

Figure2

Discussion: The difference in elimination rates between fibrosis grades of <3 and ≥3 is hypothesized to be related to changes in liver function associated with fibrosis-related liver injury. Healthy livers continue to accumulate Eovist intracellularly over 20 minutes, while diseased liver cells are unable to process this agent; subsequent renal excretion leads to a decline in liver signal over 20 minutes, as shown in Figure 2. Although there is overlap in the whole liver elimination rates for fibrosis grades 0-<3, only 2 false negatives were found in subjects with fibrosis grade 3 or above. Future work will perform region specific analysis at the CT defined biopsy site as well as in specific lobes of the liver which may yield additional utility for this technique.

References: 1) Nilsson H, Blomqvist L, Douglas L, et.al. HPB 2010;12:567–576. 2) Brix G, Semmler W, Port R, et.al. JCAT 1991;15:621-628.