Comparison of 1.5T and 3T MRI for R2* measurement of iron burden in transfusion-dependent anemias

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Introduction: Patients with certain hereditary anemias such as thalassemia major require regular blood transfusions to maintain adequate hemoglobin levels. The body however has limited capacity to excrete iron, so frequent transfusions cause iron accumulation, primarily in the liver, spleen, endocrine organs and heart. To avoid endocrine and cardiac dysfunction, transfusion-dependent patients must undergo life-long chelation therapy and regular monitoring of iron burden. Liver biopsy is the conventional means used to estimate total body iron, but measurements of R2 and R2* by MRI are gaining acceptance as a non-invasive alternative. Not only does MRI reduce the need for liver biopsy, but it can also be used to detect iron overload in the heart, which is not readily accessible to biopsy. Large studies have shown an approximately linear relationship between R2* at 1.5T and hepatic iron concentration as measured by biopsy [1], with R2* increasing by about 37.4 s^{-1} per mg/g dry weight. As 3T scanners become more widespread there is a growing need to assess the practicality of evaluating iron burden at 3T, and to relate the relaxation rates at 3T to tissue iron concentration, either directly by means of biopsy, or indirectly through calibration against 1.5T values. The goal of this study was to determine normative R2* values in the liver and heart at 3T, and to establish the relationship between R2* values at 3T and 1.5T over a range of tissue iron concentrations.

Methods: The study included 20 control subjects (26.1 ± 6.6 years) and 6 transfusion-dependent patients (27.3 ± 7.0 years), 5 with thalassemia major and 1 with dyserythropoietic anemia. Each person was scanned at 1.5T and 3T, with an intervening break of less than 15 minutes. The scans were performed on GE Healthcare Twinspeed systems, using a cardiac phased-array coil at 1.5T and a torso phased-array coil at 3T. A multiple-gradient-echo (MGRE) sequence was used to measure R2* in the liver and heart at both field strengths. All acquisitions were performed during breath holding and used the following parameters: BW = ±83.3 kHz, slice thickness = 8 mm, flip angle = 20º. The liver was imaged in a single axial slice using 6 NEX, 16 echoes and a matrix size of 128x128, giving min TE ≈ 1.3 ms, echo spacing ≈ 1.0 ms and TR ≈ 20 ms. The heart was scanned in 4 mid-ventricular short axis slices using pulse gating, 1 NEX, 8 echoes and a matrix size of 192x160, giving min TE ≈ 1.6 ms, echo spacing ≈ 1.4 ms and TR ≈ 13 ms. Images were analyzed offline using customized routines in MATLAB (Natick, MA). About 10 regions of interest (ROIs) were chosen in the liver, avoiding all visible vessels. In the heart up to 3 ROIs were chosen per slice. For each ROI, the mean intensities of all images in the echo train were calculated and plotted as a function of TE. In cases of rapid signal decay, the data were truncated at the point where the intensity fell below about twice its asymptotic value. R2* was estimated by fitting the data to a monoexponential decay using a nonlinear Levenberg-Marquardt algorithm.

Results: Figure 1a shows the 3T-versus-1.5T R2* values in the liver for both control subjects (blue dots) and patients (red check marks). Note that the y-axis covers twice the range of the x-axis. The coordinates and error bars indicate the means and standard deviations over all the ROIs. Over the control group the liver R2* values were 39.2 ± 9.0 s^{-1} at 1.5T and 69.1 ± 21.9 s^{-1} at 3T (mean ± std). Three of the control subjects exhibited R2* values that were notably higher than the means, but in each case the 1.5T and 3T values were correlated, suggesting that the cause was physiological rather than artifactual. The patients all had significantly higher liver R2* than the controls, and their 3T values were approximately double their 1.5T values. In one patient (not shown) the 1.5T value was 870 s^{-1}, and the 3T value was out of range for our MGRE technique (>1000s^{-1}). Excluding this one person, the line of best fit for all the subjects (controls and patients) had a slope of 1.93 ± 0.08 and an intercept of –9 ± 4 s^{-1}. The chi-squared value for the fit was χ^2=19.6, which is less than the number of degrees of freedom (df = 23), indicating that the relationship between the 3T and 1.5T liver R2* values is appropriately described by a linear model.

Figure 1b shows the results for the heart. Note that the scale is different from that used for the liver data. 15 of the 20 control subjects exhibited cardiac R2* values that were tightly clustered at both 1.5T and 3T; over this group R2* = 23.4 ± 2.2 s^{-1} at 1.5T and 30.0 ± 3.7 s^{-1} at 3T. In 4 of the remaining control subjects the 3T values were much higher than average while the 1.5T values were within the normal range; in 1 subject the 1.5T result was much higher than average while the 3T result was within normal range. These outlying points probably reflect bulk susceptibility artifacts due to air in the lung or bowel, and were excluded from the analysis. Of the patients, one had cardiac R2* values within normal range, but the remaining 5 had significantly higher R2* values. The line of best fit to the cardiac data for all subjects (excluding the 5 outliers) had a slope of 1.90 ± 0.19 and an intercept of –15 ± 5 s^{-1}. The chi-squared value for the fit was χ^2=8.6, which is less than the number of degrees of freedom (df = 19), indicating that the relationship between the 3T and 1.5T cardiac R2* values is appropriately described by a linear model.

Discussion: In the control group the cardiac R2* values were fairly tightly clustered at both field strengths, with the exception of a few outlying points, which were probably due to bulk susceptibility artifacts. The liver data showed a slightly greater spread among the control subjects than the cardiac data, with 3 people (all male) having liver R2* values that were significantly higher than the mean at both field strengths. Two of those subjects were substantially older than the other men in the cohort, so their higher R2* values may be attributable to age-related iron accumulation. Other possible explanations include a prior history of transfusions or heterozygosity for hemachromatosis.

In both the liver and heart, the 3T R2* values in the control group were higher than, but not double, the 1.5T values. In patients with substantial iron burden, however, the R2* values were approximately twice as high at 3T as 1.5T. Over all subjects (patients and controls), the relationship between the 3T and 1.5T R2* values appeared to be linear. The lines of best fit to the 3T-versus-1.5T data in the heart and liver had slopes of about 2 (to within measurement error), but did not pass through the origin, suggesting that R2* may comprise a susceptibility component that is proportional to field strength, and a dipole-dipole component that is approximately independent of field strength.

The scaling of R2* with field strength limits the range of iron concentrations that can be quantified at 3T, since most conventional sequences cannot achieve echo times much below 1ms. A further disadvantage at 3T may be a higher incidence of bulk susceptibility artifacts, particularly in the heart, due to its proximity to the lung and bowel. It is possible that this problem can be alleviated with improved shimming techniques. While 3T may not be preferable to 1.5T for assessing iron burden in transfusion-dependent patients, it is nevertheless important to be able to relate 3T relaxation rates to iron concentration, particularly as some sites now have only 3T scanners. Further confirmation of the relationship between R2* values at 3T and 1.5T over a broader range of iron concentrations will help achieve this goal.

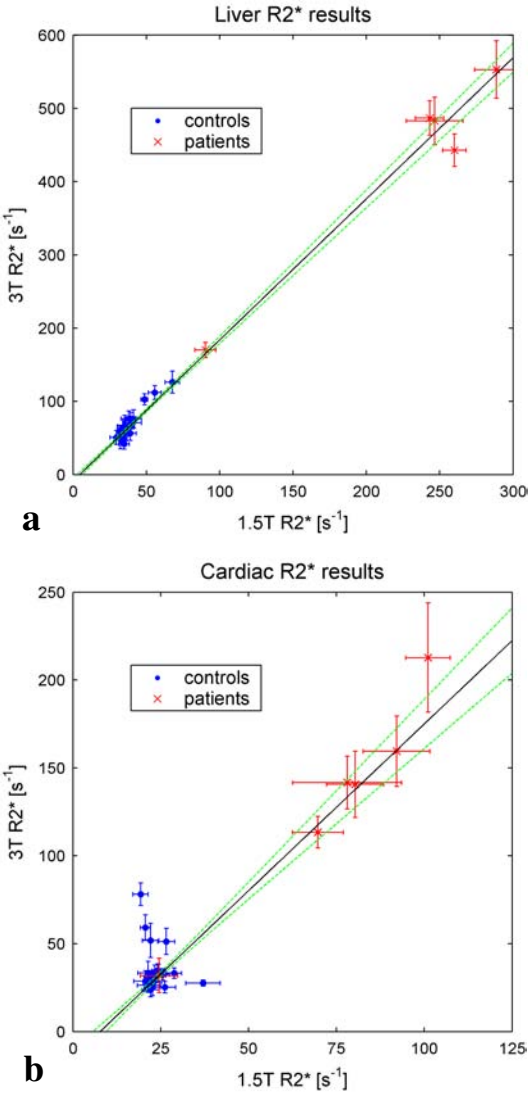

Figure 1: 3T-versus-1.5T R2* values in the liver (a) and heart (b) for control subjects (blue dots) and patients (red check marks). The line of best fit is shown in black, and its uncertainty bounds are indicated by the green curves. Note that the scales are different in the two graphs, but in each case the y-axis covers twice the range of the x-axis.

References: [1] Wood JC et al, Blood 2005; 106: 1460-5