

Comparison of serum liver function tests and liver R2* measurements before and after gadoxetic acid

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Target Audience: Researchers and clinicians interested in liver imaging, fat quantification and hepatobiliary gadolinium based contrast agents.

Purpose: To investigate the relationship between demographics, biometrics and serum markers of liver disease and changes in R2* as measured by a confounder-corrected liver R2* quantification method, performed before and after administration of gadoxetic acid.

Methods: With IRB approval and informed written consent, 24 patients (M/F=12/12, 51.8 years (range 18-84)) were studied prospectively at 1.5T (Signa HDxt and Optima MR450w, GE Healthcare, Waukesha, WI). The patients' clinical records were retrospectively reviewed. If available, BMI and serum lab values obtained within 3 months before or after imaging were recorded. Recorded serum measurements included total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatases, creatinine, international normalized ratio (INR), and albumin. The model for end-stage liver disease (MELD) score was calculated for patients not taking coumadin, using same-day recorded values of serum bilirubin, serum creatinine and INR¹.

Imaging was performed before and after the IV administration of 0.05 mmol/kg of gadoxetic acid (Eovist, Bayer Health Care Pharmaceuticals Inc., Wayne NJ). To obtain whole-liver R2* maps², we used a 3D multi-echo gradient-echo sequence: axial slab, flip = 15°, TR/TE1/ΔTE=13.5/1.2/2.0ms, ETL=6, matrix=224-256x160x32, FOV=36x32cm, slice=8mm, BW=±83-125kHz with ARC parallel imaging (R=3.2) for 21s scan time. R2* maps were calculated using a complex-based fat-corrected R2* estimation algorithm³. R2* was measured pre- and post-contrast from regions-of-interest in all 9 Couinaud segments. Values were averaged across segments for each subject.

Imaging measurements were compared with the patients' clinical data: R2* (pre-contrast) and ΔR2* = R2* (post-contrast)-R2* (pre-contrast) were each compared to the BMI and blood analysis measurements described above. Also, R2* and ΔR2* were compared with each other. Comparisons were performed using linear regression analysis on the logarithms of the measurements (excluding negative measurements) to create a uniform spread of data in the regression. For each of the 25 linear regressions, the p-value for the null hypothesis that slope=0 was calculated. To account for the large number of regressions, the sequential Holm-Šidák procedure was used⁴, after which p-values <0.05 were considered statistically significant.

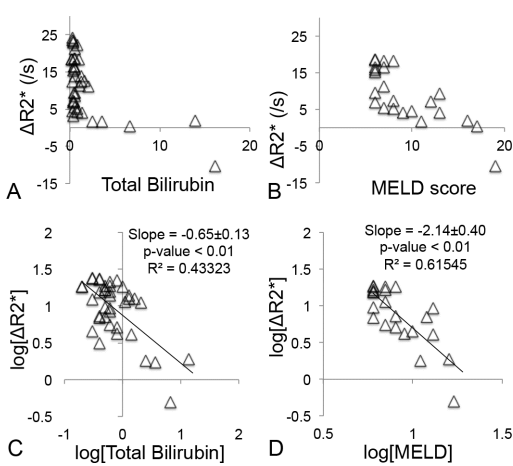


Figure 2: Comparison between imaging and blood analysis measurements, including scatterplots of (a) ΔR2* vs total bilirubin, and (b) ΔR2* vs MELD score. Also shown are logarithm-domain linear regressions for the same comparisons (excluding the one value ΔR2* < 0): (c) ΔR2* vs total bilirubin, and (d) ΔR2* vs MELD score.

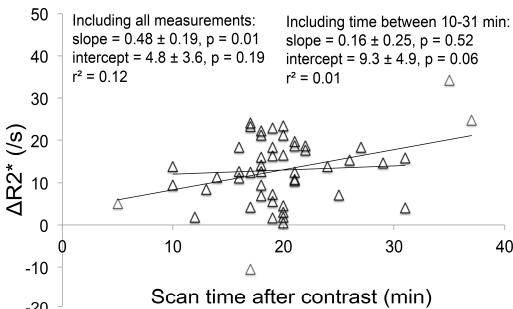


Figure 3: Comparison between the delay time after contrast (in minutes) and ΔR2* (in s⁻¹).

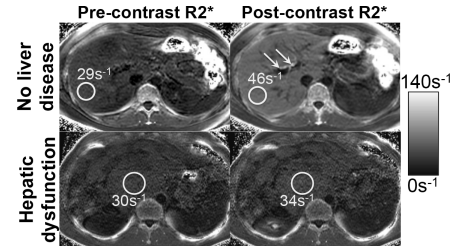


Figure 1: Gadoxetic acid increases the R2* in normal liver, including severe increases in the bile ducts (arrow). However, little increase is often found in cases of hepatic dysfunction.

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Additionally, Bland-Altman analysis of R2* (pre- and post-contrast) was performed separately among patients with total bilirubin < 2.5 mg/dL, and those with total bilirubin ≥ 2.5mg/dL. Finally, ΔR2* was compared using linear correlation to the time after contrast administration (in minutes) after which the post-contrast R2* maps were acquired.

Results: Fig 1 shows example R2* maps in subjects without and with liver disease. Upon retrospective review of the patients' clinical data, BMI was available from 43 patients, bilirubin from 39 patients, AST from 40 patients, ALT from 41 patients, GGT from 14 patients, alkaline phosphatase from 37 patients, creatinine from 40 patients, INR from 27 patients, albumin from 31 patients, platelets from 37 patients, and MELD scores from 24 patients. After performing the Holm procedure, only two pairwise comparisons resulted in slopes significantly different from zero: total bilirubin vs ΔR2* and MELD vs ΔR2* (**Figure 2**): ΔR2* had a negative correlation with both total bilirubin and MELD scores.

Bland-Altman analysis of R2* pre- and post-contrast revealed a significant R2* increase among patients with total bilirubin < 2.5 mg/dL (95% CI= 13.4 ± 12.7s⁻¹), but no increase among patients with total bilirubin ≥ 2.5mg/dL (95% CI= -0.9 ± 10.5s⁻¹). Finally, a comparison between the delay time after contrast (in minutes) and ΔR2* (in s⁻¹) is shown in **Figure 3**. Including very short (<10 min) and very long (>34 min) times results in a significant increase in ΔR2* with time after contrast, but excluding these extreme values results in little correlation between ΔR2* and delay after contrast.

Discussion and conclusion: A lack of increase of R2* after administration of gadoxetic acid correlated with elevated values of both total bilirubin and MELD scores, which are measures of liver dysfunction and severity of chronic liver disease. Future work will be needed to further characterize whether changes in R2* with gadoxetic acid administration could be used as a quantitative biomarker of hepatic function.

References: ¹Malinchoc, Hepatology 2000;31:864-871. ²Yu, MRM 2008;60:1122-1134. ³Hernando, MRM; 2013;70:1319-1331 ⁴Holm, Scand J of Statistics 1979;6:65-70.

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