Combined Gadoxetic Acid and Gadofosveset Enhanced Liver MRI: A Feasibility and Parameter Optimization Study

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Target Audience: Physicists and clinicians interested in contrast enhanced liver imaging.

Purpose: Metastases, vessels and benign cavernous hemangiomas all appear hypointense on delayed hepatobiliary phase gadoxetic acid enhanced MRI and are difficult to distinguish from one another. The purpose of this work was to improve the diagnostic accuracy of the hepatobiliary phase for detection and characterization of small metastatic lesions by using an intravascular gadolinium based contrast agent, gadofosveset trisodium, in addition to gadoxetic acid. We hypothesize that the enhancement of blood vessels and hemangiomas from gadofosveset after the injection of gadoxetic acid will improve detection and characterization of small focal liver lesions – metastases will appear dark with no or very little contrast enhancement, while blood vessels and hemangiomas will be appear very bright.

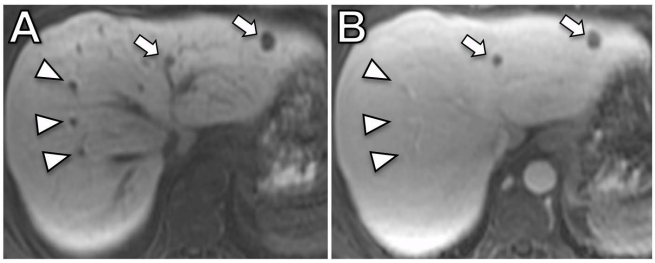

Figure 1: *Improved conspicuity of small liver lesions.* ***(A)*** *Breathhold T1 weighted images with gadoxetic acid alone and* ***(B)*** *in combination with gadofosveset trisodium. Note the improved conspicuity of the cyst adjacent to the left hepatic vein (arrow), similar appearance would be seen for metastases, whereas vessels (arrowheads) have similar intensity as liver.*

Methods: Nine healthy subjects underwent two back-to-back MR protocols of the liver at 3 Tesla (MR750, GE Healthcare, Waukesha, WI). The first MR protocol was performed in the gadoxetic acid enhanced hepatobiliary phase (0.025 mmol/kg; Eovist, Bayer Healthcare) 20min after injection. The second MR protocol was performed 5min after the additional injection of gadofosveset trisodium (0.05 mmol/kg; Ablavar, Lantheus Medical Imaging). We used a 3D spoiled gradient echo with dual-echo chemical shift encoded water-fat separation sequence. Scan parameters were: slab volume = 35(R/L)x26(A/P)×48(S/I) cm^3, matrix = 224×140×44, bandwidth = ±63kHz, partial k_z (0.75) acquisition, $TR/TE_1/TE_2$ = 5.5/1.8/3.6 ms, scan time 23sec. No parallel imaging was used to allow SNR measurements. We performed multiple breath-held acquisitions with a fixed TR and varying flip angles (10º-50º) to determine the optimal flip angle. Region of interests (ROIs) were placed to measure signal intensity (SI) of liver, portal vein, muscle (surrogate for metastases)[1], and standard deviation (SD) in the air. The SNR of the organs was calculated by the following equation[2]; $SNR = (SI_{organ}/SD_{air}) \times 0.7049$. Statistical comparison of SNR and SNR ratios were performed using paired two-sided t-tests.

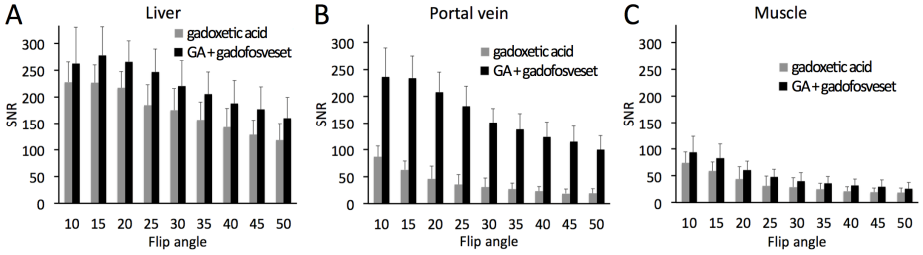

Figure 2: *Adding gadofosveset to gadoxetic acid alone enhanced MRI significantly increases the signal of* ***(A)*** *liver,* ***(B)*** *portal vein and* ***(C)*** *muscle. The most notable difference is observed for the portal vein, which has only low signal (appears dark) on gadoxetic acid enhanced images in the hepatobiliary phase. Adding gadofosveset increases the intravascular signal to levels comparable to that of the liver. Higher flip angles lead to decreased signal for all three tissues.*

Results: *Figure 1* demonstrates the utility of combined use of gadofosveset and gadoxetic acid. The cross-section of several portal vein branches (arrowheads) and cysts (arrows) both appear as hypointense lesions with gadoxetic acid alone. After injection of gadofosveset, the vessels enhance with SNR very similar to liver, while the cysts remain clearly visible and distinct from vessels. The conspicuity of the cyst adjacent to the left hepatic vein is particularly notable. The mean SNR was significantly increased for all organs when combining gadofosveset with gadoxetic acid (liver, $p < 0.029$; portal vein, $p < 0.00001$; muscle, $p < 0.007$). The most dramatic effect was observed for the portal vein where the SNR increases from levels similar to muscle (*Figure 2B vs. 2C*) to SNR comparable to the liver (*Figure 2A vs. 2B*). As seen in *figure 3*, after the addition of gadofosveset, there was a dramatic increase in signal in the portal vein, which lead to a reduction in the liver/ portal vein signal ratio. The liver/ muscle ratio was only slightly reduced, impacting the contrast of the liver with potential metastases, minimally. All SNR ratios showed increases as a function of flip angle, reaching a plateau at 35º - 40º.

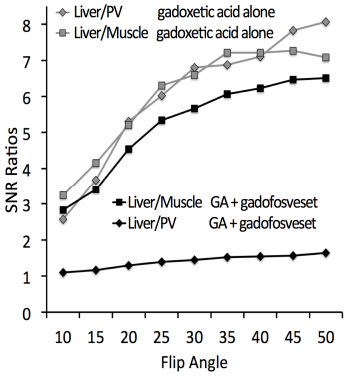

Figure 3: *Using gadoxetic acid alone does not allow differentiation of vessels from muscle by signal intensity; both appear dark and have a high signal ratio relative to the liver. Enhancing the vessels with gadofosveset dramatically reduces the liver/ PV ratio, whereas the liver / muscle ratio is only slightly reduced, allowing clear differentiation. Both, liver / PV and liver/ muscle ratios increase with increasing flip angles.*

Discussion: The addition of gadofosveset to gadoxetic enhanced MRI dramatically increased the signal of the vessels, with only a minimal increase in signal in the liver and muscle. In this way, the conspicuity of small focal liver lesions can be significantly improved, particularly at higher flip angles, compared to gadoxetic acid alone.

Conclusion: Combining gadofosveset to gadoxetic acid enhanced liver imaging is feasible and may facilitate improved detection and characterization of small focal liver lesions.

References: 1. Nagle SK. J Magn Reson Imaging 2012; 36:890–899; 2. Dietrich O. Magn Reson Imaging 2008; 26: 754-762

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