Combined Gadoxetic Acid and Gadofosveset enhanced Liver MRI: Detection and Characterization of Focal Liver Lesions

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Target Audience: Physicists and clinicians interested in contrast enhanced imaging of the liver for detection of metastatic disease.

Purpose: On gadoxetic acid enhanced hepatobiliary-phase MRI it can be challenging to detect small and/or perivascular focal liver lesions and to distinguish metastases from hemangiomas [1,2]. The ***purpose of this work*** is to improve the diagnostic accuracy of the hepatobiliary phase for *detection* and *characterization* of small metastatic lesions by using gadofosveset trisodium addition to gadoxetic acid. We hypothesized that the enhancement of blood vessels from gadofosveset will improve the detection of small lesions, while the enhancement of hemangiomas will improve lesion characterization. Metastases will appear dark with very little or no enhancement, while hemangiomas will appear bright, isointense to blood vessels.

Methods: In this retrospective IRB-approved study, 78 patients (age 58±14 years; range, 18-90, 44:34 M:F) with a total of 124 metastases and 21 hemangiomas underwent gadoxetic acid-enhanced MR imaging at 1.5 or 3T (Signa HDx, and Discovery 450w and MR750, GE Healthcare, Waukesha, WI). Twenty minutes after injection of gadoxetic acid (0.025 mmol/kg; Eovist, Bayer Healthcare) hepatobiliary phase T1-weighted (T1WI) imaging was performed. Thereafter, T1WI was repeated 5min after the additional injection of gadofosveset trisodium (0.05 mmol/kg; Ablavar, Lantheus Medical Imaging). Imaging parameters of the breath-held 3D spoiled gradient echo sequence at 1.5 T included: TR/TE/ 3.6/1.7 msec, flip angle 12º, FOV 38 x27 cm, matrix 256 x 192, slice thickness 5 mm and at 3T: TR/TE/ 4.2/1.9 msec, flip angle 15º, FOV 40 x 32 cm, matrix 288 x 192, slice thickness 3.6 mm.

One radiologist was first presented only the gadoxetic acid-alone enhanced images and asked to record the presence and localization of all hypointense liver lesions on blinded examinations and to grade the conspicuity of each lesion (1=almost missed to 4=excellent conspicuity). The observer was then presented the combined gadoxetic/gadofosveset enhanced images and asked to reassess the conspicuity of each lesion as well as to record all additionally detected lesions and their conspicuity grade. Alternative free-response receiver operating characteristics (AFROC) curves were calculated for comparison of lesion detection performance. Signal intensities (SI) were also measured in all lesions (metastases and hemangiomas) and the adjacent liver parenchyma to calculate lesion/liver signal ratios. SI-ratios were compared using *t-tests*.

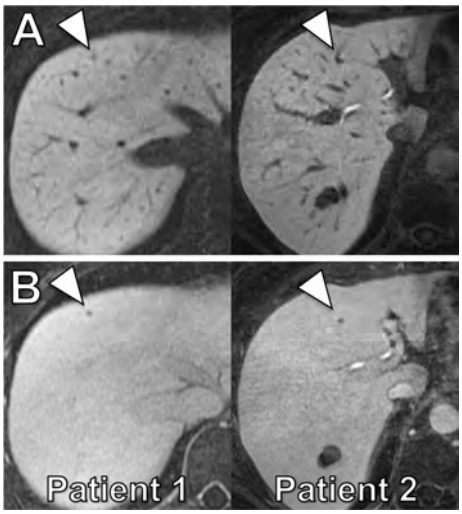

Figure 1: Improved conspicuity of non-enhancing small liver lesions. (A) *T1 weighted images with gadoxetic acid alone and* ***(B)*** *in combination with gadofosveset in patients with melanoma (left) and esophageal cancer (right). Note the improved conspicuity of the histopathologically confirmed metastases (arrow heads).*

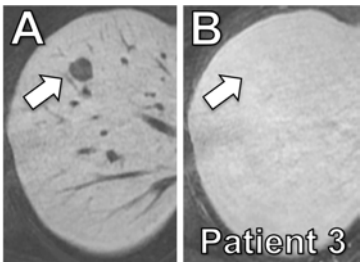

Figure 2: The additional injection of gadofosveset in the hepatobiliary phase of gadoxetic acid renders hemangiomas isointense to liver tissue. (A) *T1 weighted images with gadoxetic acid alone and* ***(B)*** *in combination with gadofosveset show enhancement of the hemangioma (arrow) similar to the vessels, i.e. following the signal of the blood pool.*

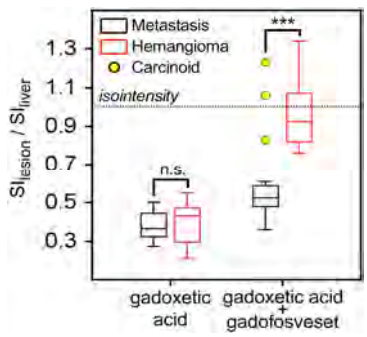

Figure 3: Improved differentiation of metastases vs. hemangiomas. *Using gadoxetic acid alone does not allow differentiation of metastases from hemangiomas by signal intensity; both appear dark and have low SI-ratios relative to the liver. Enhancement with gadofosveset significantly increases the hemangioma/liver-ratio, whereas the liver/metastasis ratio is only slightly increased, allowing differentiation. Outliers represent metastases in a patient with carcinoid metastases*

Results: Gadoxetic acid alone enabled correct localization of 92/124 metastases (74.2%) compared to 110/124 metastases (88.7%) when using combined gadoxetic acid/gadofosveset. ***Figure 1*** demonstrates the increased conspicuity of small non-enhancing lesions of the combined approach. The AFROC area under the curve (AUC) was higher for combined gadoxetic acid/gadofosveset (0.93; CI: 0.90-0.98) than for gadoxetic acid alone (0.89; CI: 0.83-0.95). There was a statistically significant difference in the AUC of 0.05 (CI: 0.02-0.09, P = .004) between the methods, demonstrating a higher performance for the detection of metastatic disease using gadoxetic acid and gadofosveset. ***Figure 2*** illustrates that after injection of gadofosveset the contrast characteristics of hemangiomas follow the blood pool. ***Figure 3*** shows that there was no significant difference between the SI-ratio of metastases and hemangiomas on gadoxetic alone-enhanced images (P = .51). Enhancement with gadofosveset increases the hemangioma/liver-ratio, while the metastasis/liver-ratio only slightly increases, rendering significantly different SI-ratios (P < .0001).

Discussion: The addition of gadofosveset to gadoxetic enhanced MRI significantly increases the conspicuity and lesion detection of hepatic metastases. Moreover, the different contrast behaviors of metastases and hemangiomas after injection of gadofosveset may improve the diagnostic accuracy to distinguish metastases from hemangiomas.

Conclusion: Combined gadoxetic acid and gadofosveset enhanced liver MRI improves lesion detection and characterization compared to gadoxetic acid alone and should be evaluated further in prospective studies to identify the patient populations that may benefit most from this approach.

References: [1] Motosugi et al InvestRadiol 2011; [2] Gupta et al EJR 2011

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