Differentiation of Hepatic Adenoma versus Focal Nodular Hyperplasia using Gadoxetic Acid

Kiyarash Mohajer[1,2], Jessica Robbins[1], Agnes Loeffler[3], Richard Bruce[1], and Scott Reeder[1]

[1]*Radiology, University of Wisconsin, Madison, WI, United States,* [2]*Radiology, UCLA, Los Angeles, CA, United States,* [3]*Pathology, University of Wisconsin, Madison, WI*

Introduction: Hepatic adenoma (HA) and focal nodular hyperplasia (FNH) are benign hepatic lesions found predominantly in women of child-bearing age. Differentiation of the two is important because HA's are often resected due to risk of hemorrhage and possible malignant transformation, while FNH require no intervention. Characterization of HA vs. FNH with extracellular gadolinium based contrast agents is often challenging because imaging characteristics during dynamic contrast imaging can be very similar, and these lesions both occur in the same patient demographic. The advent of hepatobiliary gadolinium based contrast agents offers new opportunities for characterization of HA versus FNH. Extensive experience with delayed imaging with gadobenate dimeglumine at 1-2 hours has demonstrated a general behavior of hyper-intense or iso-intense enhancement of FNH and hypo-intense behavior of HA[1]. Gadoxetic acid (Eovist, Bayer Health Care Pharmaceuticals Inc, Wayne, NJ) is an alternative hepatobiliary gadolinium based agent which has more rapid uptake and excretion of contrast with 50% hepatic uptake and peak enhancement at approximately 20 minutes. To date, there has been a paucity of pathological-imaging correlation of HA and FNH using gadoxetic acid with a total of 6 reported cases of HA and 16 cases of FNH[2,3,4]. The purpose of this retrospective study is to perform pathological-imaging correlation of HA and FNH using gadoxetic acid-enhanced imaging at a dose of 0.05mmol/kg.

Methods: A retrospective study was performed after IRB approval by searching on the keywords "adenoma", "FNH", "focal nodular hyperplasia" on all MRI studies from July 2008 (when gadoxetic acid was first used at our institution) until 10/5/2010. A total of 6 HA's with histological correlation and 34 FNH's (2 with histological correlation) were identified. Delayed hepatobiliary imaging used an investigational version of a 3D-SPGR T1-weighted acquisition with intermittent spectrally selective fat suppression (LAVA, GE Healthcare) that allowed the use of higher flip angles (30-45^{o}) to maximize SNR and CNR performance[5]. All patients were administered 0.05 mmol/kg of gadoxetic acid at 2.0 ml/s and delayed phase imaging was performed at approximately 20 minutes. All imaging was re-reviewed by 2 board certified radiologists with 10 and 5 years of experience. Signal intensity ratios (SIR) were also measured as the ratio of the signal within the lesion compared to the adjacent liver that was free of vessels or large bile ducts. Lesions were characterized as hypo-intense if the SIR was <0.95, iso-intense if the lesion had a SIR from 0.95 – 1.05, and hyper-intense if the SIR>1.05. All pathological preparations were re-reviewed by a board certified pathologist with 9 years of experience.

Results: Figure 1 shows an example of HA on selected imaging sequences including delayed hepatobiliary imaging at approximately 20 minutes following administration of 0.05 mmol/kg of gadoxetic acid. Figure 2 shows an example of FNH with the same imaging protocols and selected sequences including delayed hepatobiliary imaging. Table 1 tabulates the important imaging characteristics of all adenomas and histologically proven FNHs identified as part of this study. These results demonstrate that all adenomas were hypo-intense relative to the adjacent liver parenchyma on delayed hepatobiliary phase imaging, while FNH lesions were hyper-intense or iso-intense on delayed imaging.

Table 1: Signal Characteristics of HA and FNH on Gadoxetic Acid-Enhanced MRI

Age/Sex	Dx	OOP/ IP	T2w	T1w arterial	T1w portal venous	T1w delayed (20min)
22 y/o F	HA	Iso	Hyper	Hyper	Hyper	Hypo [0.93]
34 y/o F	HA	Hypo	Hyper	Hyper	Hypo	Hypo [0.35]
21 y/o F	HA	Iso	Hyper	Hyper	Hypo	Hypo [0.29]
50 y/o F	HA	Hypo	Hyper	Hyper	Hyper	Hypo [0.48]
51 y/o F	HA*	Iso Hyper	Iso Hyper	Hyper Hyper	Hyper Hypo	Hypo [0.43] Hypo [0.41]
34 y/o F	FNH	Iso	Hyper	Hyper	Hyper	Hyper [1.07]
25 y/o F	FNH	Hyper	Iso	Hyper	Iso	Iso [1.01]

** Hepatic adenomatosis: two representative biopsied lesions; OOP: out of phase image, IP: in phase, Hyper=hyper-intense, Iso=iso-intense, Hypo=hypo-intense. SIR in brackets.*

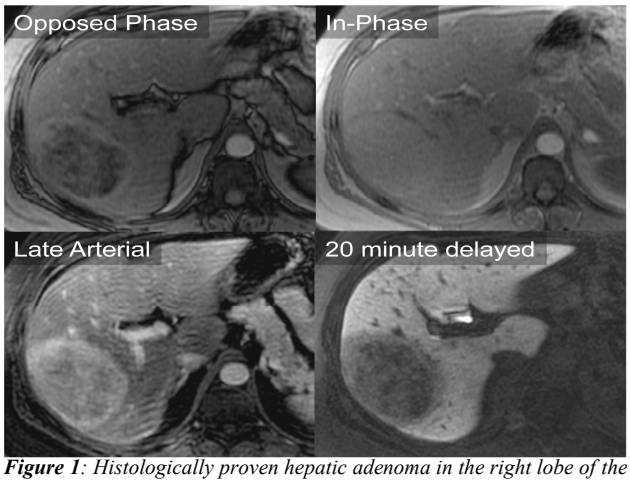

***Figure 1**: Histologically proven hepatic adenoma in the right lobe of the liver of a 34 year-old woman, demonstrates hypo-intensity on delayed 20 minute gadoxetic acid-enhanced images (bottom right). Signal drop-out is seen on opposed phase images indicating s intracellular fat (top row), while arterial phase enhancement (bottom left), washout on portal venous phase (not shown), and iso-intensity on T2 weighted imaging (not shown) are also noted. These imaging features are all characteristic of hepatic adenoma.*

Discussion: In this study we have described the imaging characteristics of 6 hisotlogically proven HA's and 34 FNHs, 2 with pathological correlation. This doubles the number of gadoxetic acid-enhanced adenoma cases described in the literature. Further, at our institution we use twice the package insert dose of gadoxetic acid (0.05mmol/kg), and to our knowledge these are the first pathologically proven reported cases with this dose. Our findings confirm the behavior of HA and FNH reported by other investigators[3,4] at lower doses (0.025mmol/kg). Since HA is a rare lesion[6], continued studies are needed to increase the number of reported cases for improved confidence in these findings.

References: 1. Grazioli L, et al. Radiology. 2005; 236(1): 166-77 **2.** Huppertz A, et al. Radiology. 2005; 234(2):468-78 **3.** Giovanoli O, et al. Am J Roentgenol. 2008 190(5):W290-3 **4.** Zech CJ, et al. Invest Radiol. 2008; 43(7):504-11 **5.** Frydrychowicz, A, et al. JMRI 2011 [Epub ahead of print] **6.** Hussain SM. Heidelberg: Springer Verlag; 2007. P. 132-133.

Acknowledgements: This work was supported by GE HealthCare, the NIH (R01-DK083380, R01-DK088925, RC1-EB010384), and the Coulter Foundation

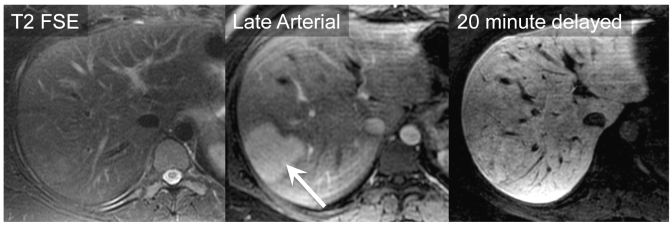

***Figure 2**: Histologically proven FNH in the right lobe of the liver of a 25 year old woman demonstrates isointensity on delayed 20 minute gadoxetic-acid enhanced images (right). The lesion is iso-intense on T2 weighted imaging (left), very hyper-intense on arterial phase (middle), and iso-intense on portal venous phase (not shown). Imaging appearance was compatible with FNH on all sequences, but lack of central scar, commonly seen with FNH, raised some question of whether the lesion might be an adenoma.*