Accurate differentiation of focal nodular hyperplasia from hepatic adenoma and liver adenomatosis with gadobenate dimeglumine (Gd-BOPTA)

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Synopsis: The ability of gadobenate dimeglumine (Gd-BOPTA, MultiHance®) to differentiate FNH from hepatic adenoma (HA) and liver adenomatosis (LA) was evaluated in 109 patients with confirmed lesions. Images were acquired before (T2wTSE and T1wGRE sequences) and during the dynamic and delayed phases after (T1wGRE sequences) the bolus injection of 0.1 mmol/kg Gd-BOPTA. Accurate differentiation was not possible on pre-contrast images or on post-contrast dynamic phase images. On delayed phase images 124/128 (97%) FNH appeared hyper- or isointense while 107/107 (100%) HA/LA appeared hypointense. The sensitivity, specificity, PPV, NPV and overall accuracy for differentiation was 96.9%, 100%, 100%, 96.4% and 98.3%, respectively.

Background/Purpose: Focal nodular hyperplasia (FNH) is a true benign tumor-like hepatic lesion that is the result of a hyperplastic response to abnormal vasculature. Histologically it is characterized by the presence of normal hepatocytes with a malformed biliary system which leads to a slowing of biliary excretion. Generally, FNH does not require treatment or surgical intervention. Hepatic adenoma (HA) is also a benign lesion in that it does not have any malignant potential. HA possesses functioning hepatocytes but lacks bile ducts and has altered hepatobiliary metabolism relative to normal hepatocytes. Unlike FNH, HA is often a candidate for resection because of its tendency for hemorrhage, particularly among larger lesions. Given the different management of these lesions, the clinical need is to accurately differentiate FNH from HA to prevent unnecessary interventions. Unfortunately, the enhancement patterns of FNH and HA on dynamic MR imaging with conventional contrast agents (e.g. Gd-DTPA) are frequently very similar making accurate differentiation difficult. The present study was aimed at evaluating gadobenate dimeglumine (Gd-BOPTA, MultiHance®; Bracco Imaging SpA, Milan, Italy) for the differentiation of FNH from HA. Gd-BOPTA differs from conventional gadolinium agents in possessing a two-fold greater T1 relaxivity *in vivo* (r1=9.7 $mmol \bullet L^{-1}s^{-1}$) and a dual route of elimination through both the renal and hepatobiliary pathways. The latter feature permits delayed (1–3 h post-injection) MR imaging of the liver which may be advantageous for differentiation of FNH from HA.

Methods and Materials: Seventy-three patients with FNH and 28 patients with HA were evaluated. An additional 8 patients with liver adenomatosis (LA) were also included since the pathological and radiological features of this lesion type are identical to those of HA. MR imaging was performed at 1.5 T before and after the intravenous bolus (≥ 2 ml/sec) injection of Gd-BOPTA at a dose of 0.1 mmol/kg BW. T2-weighted turbo spin echo images (T2wTSE; TR/TE = 3900-4100/90-108ms) and T1-weighted gradient echo images (T1wGRE; TR/TE/FA = 110-140/4.8ms/80°) were acquired pre-contrast followed by repetition of the T1wGRE sequence during the dynamic phase of contrast enhancement at 20-30 sec (arterial phase), 50-80 sec (portal-venous phase) and 3-5 min (equilibrium phase) after the injection of Gd-BOPTA. Finally, T1wGRE images were acquired during the delayed phase at 1-3 h post-injection. A total of 128 FNH, 32 HA and 75 LA were evaluated. Among patients with LA, only lesions bigger than 1 cm were considered. Lesions were characterized according to the observed enhancement behavior (homogenous or heterogenous hypointense, isointense, or hyperintense appearance relative to normal liver parenchyma) during the different phases of contrast enhancement.

Results: Unenhanced T2wTSE and T1wGRE images were unable to differentiate FNH from HA/LA (>75% of all lesion types hyper- or isointense on T2wTSE images and hypo- or isointense on T1wGRE images). Similarly, 100% of FNH and 96.3% of all HA/LA were either homogenously (FNH:122/128 lesions; HA/LA: 90/107 lesions) or heterogenously hyperintense to the normal parenchyma on post-contrast arterial phase images, with rapid contrast agent washout on subsequent portal-venous and equilibrium phase images. However, on delayed phase images 124/128 (96.9%) FNH were either hyper- or isointense to the normal liver parenchyma while 107/107 (100%) of HA/LA were hypointense (Fig. 1). The sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy for the differentiation of FNH from HA/LA was 96.9%, 100%, 100%, 96.4% and 98.3%, respectively, when considering hyper- or isointensity on delayed phase images as indicative of FNH and hypointensity as indicative of HA/LA.

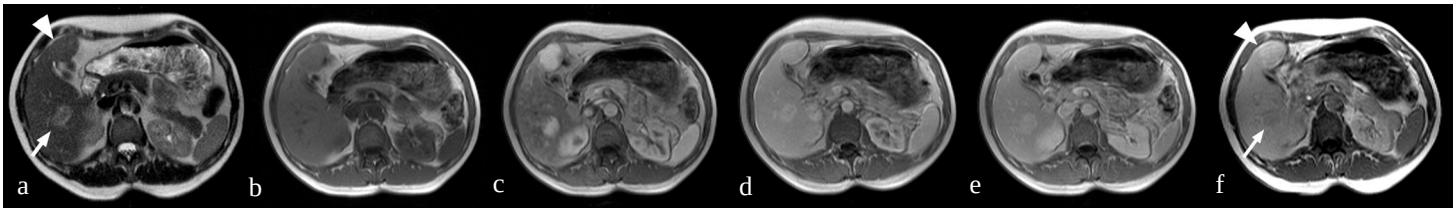

Fig. 1. The unenhanced T2wTSE image (a) reveals a hyperintense lesion (arrow) and an isointense lesion (arrowhead). The lesions are not evident on the pre-contrast T1wGRE image (b) but are both strongly hyperintense on the post-contrast arterial phase T1wGRE image (c). Contrast agent wshout from both lesions is evident on the subsequent portal-venous (d) and equilibrium (e) phase images. The lesions can only be differentiated on the delayed phase image (f) after Gd-BOPTA when the adenoma is seen as hypointense (arrow) and the FNH as hyperintense (arrowhead) to the normal liver parenchyma.

Discussion/Conclusion: Accurate differentiation of FNH from HA and LA is possible on T1wGRE images acquired during the delayed phase at 1-3 hours after injection of Gd-BOPTA. FNH appear hyper- or isointense on delayed images because the malformed biliary system in these lesions results in a slowing of the hepatobiliary elimination of Gd-BOPTA relative to that from normal hepatocytes. HA/LA, on the other hand, appear hypointense presumably because uptake and hepatobiliary elimination of Gd-BOPTA is reduced or prevented in these lesions as a result of altered hepatobiliary metabolism, as evidenced by the absence of bile ducts. Reliable differentiation of these lesions is not possible with conventional gadolinium contrast agents because of the purely extracellular distribution of these agents. The study confirms that delayed phase T1wGRE acquisitions are valuable not only for liver lesion detection (e.g. of metastases) but also for liver lesion characterization.