Response to Letter: Intrapatient Comparison of the Hepatobiliary Phase of Gd-BOPTA and Gd-EOB-DTPA in the Differentiation of HCA From FNH

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To the Editor:

We thank Edouard Reizine et al for their interest in our work and for their thoughtful comments. As mentioned in our article, and in accordance with the current literature, the hepatobiliary phase (HBP) of Gd-BOPTA does not appear to be reliable to differentiate between hepatocellular adenoma (HCA) and focal nodular hyperplasia (FNH).1 Several remarks mentioned in the letter will be addressed.

T1-Weighted Hyperintensity Before Contrast Injection

As suggested by our findings, difficulties concerning HBP may be partially due to precontrast hyperintensity of the lesion. The letter’s authors argue that this is probably due to underlying steatosis, which will reveal the lesion as hyperintense on fat-saturated images. We agree with this and have previously highlighted this potential diagnostic dilemma, particularly in inflammatory HCAs after injection of Gd-BOPTA.2 However, in contrast to previously published data from Reizine et al, we found that surrounding steatosis is not the only cause of hyperintensity on precontrast images.3 Intrinsic hyperintensity is demonstrably an additional source of false-positive iso/hyperintensity in HBP. This can easily be appreciated on in-phase T1-weighted images and is probably due to residue from microscopic bleeds. Upon reanalysis of our data, we found that hyperintensity on precontrast images was due to steatosis in 29/41 cases (71%), intrinsic hyperintensity in 7/41 cases (17%), and was attributable to both causes in 5/41 cases (12%). More important, intrinsic hyperintensity is a very reliable sign for HCA, as it is never seen in FNH (because FNHs simply do not bleed).4

Enhancement vs. Pseudoenhancement

We agree with the authors that real uptake versus pseudoenhancement (due to surrounding steatosis or intrinsic hyperintensity) is an important issue when relying on the HBP alone; even more so since uptake is related to glutamine synthetase expression and b-catenin positivity.5 Tumors that show noticeable uptake in HBP include FNH, inflammatory HCAs, b-catenin HCAs, and some well-differentiated hepatocellular carcinomas (HCCs).6 It should also be noted that in most cases FNH can be easily differentiated from other lesions (which may require closer observation) based on additional radiological and clinical parameters.

LLCER Method

The LLCER (lesion-to-liver contrast enhancement ratio) method, as proposed by Roux et al7 and mentioned by the authors of the letter, is an elegant approach to objectify whether iso/hyperintensity in HBP is due to uptake of contrast. This method takes into account the intensity of the lesion before contrast injection. Theoretically, if the LLCER is above a certain threshold the uptake is real, thus favoring FNH, or in some rare cases, inflammatory HCA, b-catenin HCA, or HCC. Unfortunately, the benefits of LLCER currently remain within the confines of theory, as we have shown that the method is poorly reproducible, and most important, does not provide reliable cutoffs.8 These problems are due to the fact that the patient is removed from the bore after the dynamic phase, to return only after around 1 hour. In contrast to computed tomography (CT), absolute values cannot be determined in magnetic resonance imaging (MRI) and repositioning of the patient has a very disruptive effect on absolute measurements. One way to potentially overcome this problem is by comparing relative measurements before and 1 hour after contrast injection. However, this approach also appears to have limited reliability, based on our previous validation study.8 At the present time we are forced to conclude that this method needs further refinement and is therefore not yet suitable for use in daily clinical practice.

Inflammatory HCA

The final remarks of Reizine et al relate to the fact that the subtyping of inflammatory HCA is less feasible when using Gd-EOB-DTPA. This is indeed correct and is due to the poorer reliability of the venous phase when using this contrast agent. However, clinical practice has taught us that the most important role of MRI is to differentiate HCA from FNH in young females using oral contraceptives. Whether a lesion is in fact an inflammatory HCA can provide useful additional information to predict b-catenin positivity (ie, b-catenin-positive inflammatory HCAs), and malignant potential.9 Once radiological diagnosis confirms an inflammatory HCA, one could opt for biopsy to exclude b-catenin positivity, although current guidelines do not discuss this option at the present time.10

In conclusion, measuring lesion contrast uptake would be an attractive tool for differentiating HCAs and FNHs; however, we think the current status does not allow us to use this method in daily clinical practice.

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References


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