Addressing Clinical Challenges in the Body with MRI
- Update on Contrast Agents –

Utaroh Motosugi, MD.PhD   utaroh-motosugi@nifty.com

Highlights

- Gadoxetic acid and gadobenate dimeglumine are available as Gd-based hepatobiliary contrast agents. Gadoxetic acid has advantage in hepatobiliary phase imaging, whereas gadobenate dimeglumine is superior in arterial phase imaging.
- Hepatobiliary phase of these agents has two roles; detection and characterization of focal liver lesions.
- Signal intensities in hepatobiliary phase can be associated with a function of the tissue, which can be another advantage over conventional Gd-based contrast agents (GBCA).

Title: **Hepatobiliary contrast agents**

Target audience: radiologists, imaging scientists, or MR technologists who wish to learn about clinical use of hepatobiliary contrast agents as well as implementation of protocols for assessment of diseases in the liver with these agents.

Outcome/Objective: Audience will be able to understand the basic roles of Gd-based hepatobiliary contrast agents in clinical practice and become familiar with the protocols which maximize the ability of these agents (1). Also, they will be aware with limitations of these agents.

Purpose: Standard healthcare for focal liver diseases include dynamic contrast-enhanced CT/MRI as problem solving tools. For MRI, conventional GBCA have been adopted as established diagnostic tool for over a decade (2). However, from the clinical point of view, the sensitivity and specificity of standard CT/MRI are not sufficiently high (3). For the sake of improving the outcomes of patients with focal liver disease, higher contrast between lesion and liver is required so that we can find small lesions and make the diagnosis at early clinical stage. Also, it is desired to make contrast between benign and malignant lesions, as well as between lesions which require treatment and lesions which do not.

Methods: Quite a few researches were performed to confirm the diagnostic ability of hepatobiliary contrast agents (4), compared with standard CT/MRI in patients with focal liver disease. Reviewing the available evidences, I will try to reveal common sense about the use of hepatobiliary contrast agents in clinical practice. Also, I will try to elucidate the additional use of these agents (use as a functional tool), which is interesting for clinicians. Limitation of these agents described in the literatures will be also reminded.

Results:

- Hepatobiliary contrast agents offer significantly higher sensitivity to detect focal liver lesions, either for metastases (5, 6) and hepatocellular carcinoma (7-12), especially if they are small (**Fig.1**); hepatobiliary phase image plays the major role for this improvement. However, the specificity does not necessarily increase by adding hepatobiliary phase images.
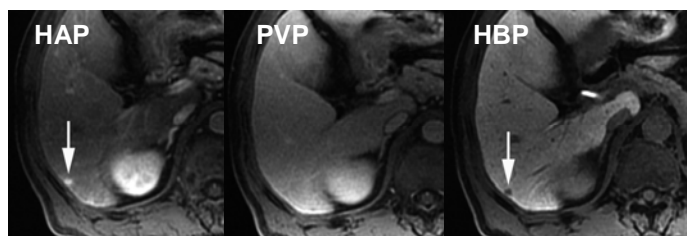

Fig.1.*A small hepatocellular carcinoma (HCC) shows high signal intensity in arterial phase, but not seen in portal venous phase. The nodule is clearly dark in hepatobiliary phase (HBP). Considering the cirrhosis and non-bright signal on T2WI (not shown), the diagnosis of small hypervascular HCC can be made.*

- Significant role for tissue characterization with hepatobiliary contrast agents include distinguishing hepatocellular adenoma from focal nodular hyperplasia (FNH) (13, 14): adenoma shows decreased uptake, whereas FNH has at least some uptake of gadoxetic acid. (*Fig.2*)   Also, gadoxetic acid enables to distinguish non-hypervascular hepatocellular carcinoma (15) from pre-malignant hepatocellular lesions which also show non-hypervacularity (16).
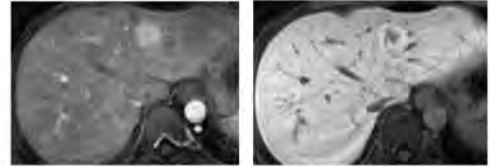

Fig.2. *A focal nodular hyperplasia (FNH) typically uptake gadoxetic acid because of hyperplastic nature, not neoplastic. Hepatobiliary phase has important role to distinguish FNH from hepatic adenoma, a neoplasia which requires surgical removal.*

- A nodule in cirrhotic liver that shows hypovascularity in arterial phase and hypointensity in hepatobiliary phase is of interest. It is most likely early stage (hypovascular) hepatocellular carcinoma (17) and has high prevalence to become hypervascular hepatocellular in a few years (18, 19). (*Fig.3*) Further, the presence of these nodules suggests that the underlying liver is at high risk of developing separate hepatocellular carcinoma in a future (20, 21).
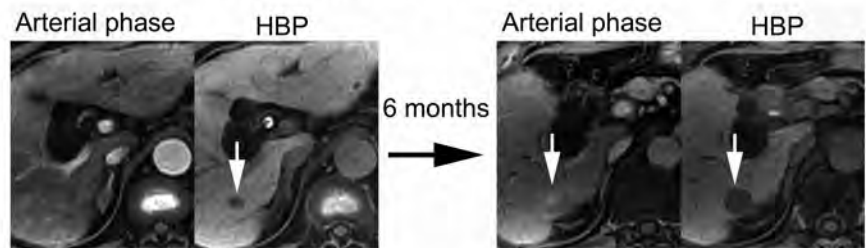

Fig.3.*A nodule showing hypovascularity in arterial phase and hypointensity in hepatobiliary phase (HBP), which became hypervascular hepatocellular carcinoma in 6 months. The nodule was supposed to be hypovascular (early stage) hepatocellular carcinoma even at the initial MRI.*

- Signal intensity or a degree of uptake of gadoxetic acid in hepatobiliary phase can be a biomarker for an outcome of hepatocellular carcinoma; preserved uptake in the tumor may suggest low grade tumor behavior and favorable outcome (22). (*Fig.4*)
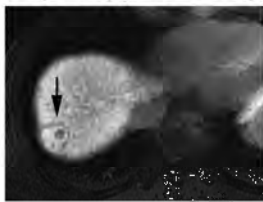

Fig.4.*A hepatocellular carcinoma sometimes uptakes gadoxetic acid, which results in high SI in hepatobiliary phase. That suggests the tumor cells preserve their function as hepatocytes, meaning well differentiated (= low grade malignancy). This finding is known as a biomarker predicting preferable outcome after treatment.*

- Recently potential adverse effect of gadoxetic acid, transient dyspnea also known as transient severe motion was described (23-25). When using gadoxetic acid, patients are supposed to fail their breath-holding during the arterial phase acquisition more frequently than other contrast agents, probably due to transient dyspnea. That leads image deterioration. (*Fig.5*)   We can think of dealing with this limitation by letting patients know it in advance and using oxygen mask to let them hold their breath with ease.

Fig.5. *Deteriorated arterial phase image due to breath hold failure during scan.*

Conclusion: Hepatobiliary contrast agents are useful and should be used for detecting small focal liver lesions including metastases and hepatocellular carcinoma.

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