ANSWER LETTER

Reviewer: 1

Major concerns:

1. **There are many types of contrast medium available in an MRI study for hepatocellular carcinoma. Especially gadoxetic acid, which chelates a gadolinium ion with the moiety of ethoxybenzyl diethylenetriaminepentaacetic acid, reveals not only flow dynamics in the liver but also function of hepatocytes in a hepatobiliary phase. It is helpful to summarize characteristics of contrast agents available in an MRI study for hepatocellular carcinoma.**

Authors: The new paragraph regarding contrast media used for MRI study in the detection and characterization of hepatocellular carcinoma was added in the revised manuscript, Pg 6, ln 3-19. The corresponding references (21-24) were added in the Reference section, Pg 17, ln 15-23.

2. It is important to keep it in mind that the iso or hyper intensities in hepatobiliary phase indicates that the tumor is consisting of the hepatocytes. It is precious information for differential diagnosis of a tumor in the liver.

Authors: Added in the revised manuscript, Pg 6, ln 19-21.

3. The hypervascularity in arterial phase is one of the key determinants for the diagnostic imaging of hepatocellular carcinoma and should not be determined only by CT/MRI study, because in CT/MRI study the images in arterial phase are taken at a certain time point through the time course of a contrast study. That time point may not be always the best moment to evaluate hypervascularity of hepatocellular carcinoma. It is quite important to evaluate hypervascularity by observing flow dynamics throughout the entire time course of a contrast study using ultrasound.

Authors: The advantages of contrast enhanced ultrasound (CEUS) are added in the revised manuscript, Pg 4, ln 15-20. The corresponding references were added in the revised manuscript, Pg 16, ln 3-17.

4. MRI including the subtraction technique is useful for determining contrast enhancement for the lesion with high precontrast T1 signal intensity.

Authors: Added in the revised manuscript, Pg 5, ln 32, and Pg 6, ln 1-2.

Minor concerns:

1. Although the authors stated that hepatocellular carcinoma predominantly arises in a

cirrhotic liver with estimated 5 years incidence of 25%, the incidence is quite different among different background liver diseases.

Authors: Added in the revised manuscript, Pg 4, ln 4.

2. Ancillary, a typo in TYPICAL MRI FEATURES OF HEPATOCELLULAR CARCINOMA section, 2nd paragraph, 4th line from the bottom.

Authors: Corrected in the revised manuscript, Pg 6, ln 30.

3. In terms of organic anion-transporting polypeptide, there are several subtypes. Please specify the subtypes, which are involved in the uptake of gadoxetic acid in hepatocytes.

Authors: Added in the revised manuscript, Pg 6, ln 11-17.

4. In the Figure 1, it is better to show a T1-weighted image before an injection of contrast medium to show the vascularity.

Authors: Corrected in the revised manuscript, precontrast T1-weighted image was added in the Figure 1, Pg 28.

5. Hypervascular, a typo in the Figure 5D.

Authors: Corrected in the revised manuscript, Pg 32, ln 6.

6. In the Figure 6, it is better to indicate portal vein thrombosis by arrows or something.

Authors: Corrected in the revised manuscript, Pg 33.

7. In the Figure 7, it is better to indicate the area that shows hypervascularity and washout.

Authors: The arrows in the Figure 7C already show area of hypervascularity which is ill-defined and displays washout (Figure 7D) in portal-venous phase.

8. In Scirrhous HCC section, the authors referred the report suggesting that T2-weighted central darkness and the presence of capsule are significant and independent MRI predictors for scirrhous HCC. If these characteristic features are shown in the Figure 11, it is better to indicate them.

Authors: Corrected in the revised manuscript, Pg 38.

9. I am wondering that the arrows may indicate incorrect points in the Figure 14A.

Authors: Corrected in the revised manuscript, Pg 41.