Review 1:

This is very interesting paper. Author concluded that large tumor size, corona enhancement, and peritumoral hypointensity in hepatobiliary phase were associated with high risk of microvascular invasion. Other paper saying that Histopathology confirmed that MVI were observed in 17 of 66 HCCs. Univariate analysis showed tumor size (p = 0.003), margin (p = 0.013), peritumor enhancement (p = 0.001), and hypointensity during hepatobiliary phase (p = 0.004) were associated with MVI. (Prediction of Microvascular Invasion in Hepatocellular Carcinoma: Preoperative Gd-EOB-DTPA-Dynamic Enhanced MRI and Histopathological Correlation. Contrast Media Mol Imaging. 2018) I think this paper is similar to author's opinion. I found the paper saying that Serum Alp was a simple, accurate and inexpensive alternative to predict MVI and an independent risk factor of prognosis for HCC patients. (A new laboratory-based algorithm to predict microvascular invasion and survival in patients with hepatocellular carcinoma International of surgery 2018) I ask question to author. Please comment Alp for the diagnosis of microvascular invasion of HCC.

Yes, our findings are somehow consistent with the conclusion of the published paper (**Contrast Media Mol Imaging**. 2018) you mentioned. In addition to findings that were similar to those in the paper you cite, we also found a 'protective' imaging feature that can even be observed in some patients with large HCCs. We have revised our manuscript to include this reference.

It is indeed very impressive that a simple laboratory test (alkaline phosphatase (ALP)-to-lymphocyte ratio (ALR)) can be used to predict microvascular invasion (MVI) (**International of surgery 2018**). We revised our 'introduction' section and cite this particular paper to document the use of a noninvasive test for MVI prediction. However, as mentioned in the paper's

conclusion, the false-positive and false-negative rates still exceed 30%. In addition, both alkaline phosphatase (ALP) level and lymphocyte count are affected by many confounding factors, such as infection, co-existing bile duct diseases, etc. It indeed needs further validation in different clinical settings. This also justifies implementing yet another non-invasive alternative, i.e., tumor diagnosis by analyzing pre-treatment MRI features. Such an approach would be particularly useful because of all the HCC patients who receive CT or MR imaging studies before treatment. Furthermore, imaging studies provide straightforward information about the tumor and its surrounding liver parenchyma.

Review 2:

This is a well-designed image and pathology study. This is interesting results for early prediction of hepatocellular carcinoma based on cirrhosis. The following questions need to clarify

1. What is the standard of pathological staging of hepatocellular carcinoma and its relationship with clinical stage?

HCC was staged according to the 7th version of Cancer Staging Manual of American Joint Committee on Cancer (AJCC). All the tumors in the study were obtained by surgical resection and their stages (pT1 or pT2) were confirmed by a pathologist. The HCCs included in the study were all single solitary tumors and therefore clinical stage cT1 (AJCC).

2.In this study, 70% of patients without cirrhosis, In fact, in patients without cirrhosis, early diagnosis of hepatocellular carcinoma is easy. How to distinguish cirrhotic nodules.

We completely agree that diagnosing HCC is easier in patients with non-cirrhotic liver than in those with cirrhotic liver. However, this is beyond the scope of this research. What we tried to achieve in this particular study was to predict pathological stage from tumor features discerned on MRI using Gd-EOB-DTPA as a contrast agent.
Cirrhotic nodules can be classified into regenerative nodules (RNs), low-grade dysplastic nodules (LGDNs), and high-grade dysplastic nodules (HGDNs). Only HCCs and HGDNs appear hypointense on hepatobiliary-phase T1W images. A recent publication reported that HCCs are hyperintense on high-b DWI, while HGDNs are isointense (**Gut** 2018;0:1–9. doi:10.1136/gutjnl-2017-315384). Therefore, according to this publication, using EOB MRI can achieve quite good sensitivity and specificity in terms of differentiating HCCs from cirrhotic nodules.

Review 3:

1.Explain what pathological changes associate with peritumoral hypointensity in hepatobiliary phase.

The cause of peritumoral hypointensity on hepatobiliary phase images is still not clear. One possibility is that tumor microinvasion into small portal branches results in hemodynamic and perfusion changes. Perfusion change may be associated with change in the levels of organic anion–transporting polypeptide (OATP) and multidrug-resistant protein (MPR) expressed on hepatocytes. We have already included this point in the "Discussion" section. This finding has also been reported by other researchers (**J Magn Reson Imaging** 2012;35: 629–634; **Radiology** 2010; 256: 817–826)

2.Why CA-19-9 of pT2 group were much higher than pT1? how many cases?

The CA-19-9 data varied among patients in our study. The difference between the two groups (pT1, pT2) was not significant (p value is about 0.3). Since elevated CA-19-9 is an independent predictor of poor prognosis in patients with HCC (**Clin Transl Gastroenterol**. 2015 Feb; 6(2): e74.), it would also seem to be reasonable that CA-19-9 was higher in our pT2 group.

3.Interval between the dates of imaging and surgery were too long.

The mean time interval between MRI and surgery was 18 days in both groups. In fact, this interval was less than 30 days in more than 80% of the enrolled cases in both groups. The majority of the HCC patients in our study underwent pre-operative EOB MRI less than 3 days before the operation. We agree that this is not perfect. However, these time intervals are common in real-world clinical settings. We would like to demonstrate that our research findings are applicable in most clinical settings. We also added this point

about time interval length and variability as a limitation in our revised manuscript. Thank you so much for your kind reminder.

4.Previous studies show that DWI and ADC can predict HCC stage, you can compare detail values of ADC, not just compare high or low.

We did not quantify ADC value of each HCC in this study. The reasons are

a. HCC can be small and therefore difficult to depict accurately on an ADC map
b. Diffusion has different components (true diffusion, incoherent motion of water molecules). Moreover, currently there is no universally-accepted standard protocol for DWI and ADC mapping
c. The reproducibility of ADC in HCC can be low (**J Magn Reson Imaging**. 2015 Jan;41(1):149-56)
d. Most of the practice guidelines and studies do not endorse using ADC quantification as a practical tool

To be more clinically applicable, we decided to use the conventional approach of describing tumor signal intensity relative to that of the background liver parenchyma. This approach has also been used in a recent publication regarding HCC (**Gut** 2018;0:1–9. doi:10.1136/gutjnl-2017-315384) and recommended by major practice guidelines of the American Association for the Study of Liver Diseases (AASLD), and the liver reporting and data system (LI-RADS) of the American College of Radiology (**Hepatology**, 2018, 68(2):723-750).

5.In method part, add detail parameters of MRI (TR/TE/slice thickness/NEX, et, al)

The "Materials and Methods" section in the revised manuscript now contains the parameters for T2-weighted FSE with fat suppression (repetition time [TR], 4175 ms; echo time [TE], 76 ms; acceleration factor, 2; number of excitations (NEX), 1; slice thickness, 5 mm); double-echo T1-weighted gradient-echo sequence (in-phase and opposed-phase images), (in-phase: TR,

164 ms; TE 4.76 ms; opposed-phase: TR, 164; TE 2.38 ms; acceleration factor, 2; NEX, 1; slice thickness, 5 mm); and T1-weighted volume-interpolated breath-hold examination (VIBE) sequence with fat suppression (TR, 4.45 ms; TE, 1.60 ms; flip angle, 10° for arterial to transitional phase, 30° for hepatobiliary phase; acceleration factor, 2; NEX, 1; slice thickness, 3 mm).