

I'm very grateful for the comments, suggestions raised by the reviewers which I found to be insightful and very constructive. The followings are my responses to the reviewers' comments.

### **Response to the comments raised by the Reviewer #1**

1- Emphasizing on the degree of differentiation in HCCs must be done considering this fact that the less differentiation of HCC will lead to less signal drop or even no signal drop due to lack of kuppfer cells on SPIO agents which can help for better differentiation of HCC from the background liver.

Reply:

Thanks for pointing this out. In letter we noted that:

However, it has been shown that no significant difference in number of K  pffer cells between well-differentiated hepatocellular carcinoma (HCC) and the surrounding healthy liver tissue<sup>[8]</sup>.

Actually, SPIO has been phased out for liver imaging, particularly due to the scuesss of another agent ((Gd-EOB-DTPA, Primovist  ),

2- A sentence could be added about another SPIO product called Lumirem as a useful oral contrast agent for darkening of bowel loops in MRCP.

Reply: as Li et al's meta-analysis paper is SPIO-enhanced MRI for focal hepatic lesions, which deal with intravenously administered SPIO. This current letter also discusses injectable SPIO.

Lumirem is again rarely used clinically.

3- At the first line, "interested" should be replaced by "interest".

Reply: thanks for pointing this out, I realized this typo, and "interested" has been replaced by "**interest**"

### **Response to the comments raised by the Reviewer #2**

This letter introduces complementary and valuable data to the review article. Your letter is well written and it can be published as submitted.

Reply: Thank you for your comments!