

Dear Dr. Yu,

thank you for the opportunity to resubmit our paper entitled "MR Imaging of the cirrhotic liver in the era of Gd-EOB-DTPA" for consideration for publication in World Journal of Gastroenterology.

We acknowledge the kind and constructive comments by the second Reviewer that have contributed to improve significantly the quality of our manuscript. An answer for each specific comment follows:

- Reviewer comment 1: As requested, we have described the literature data supporting the clinical usefulness of Gd-EOB in cirrhotic patients, adding a paragraph entitled "Why Gd-EOB-DTPA in the cirrhotic liver";

-Reviewer comment 2: *"Instead of "hepatobiliary", it would be better to use the term "hepatospecific" to describe contrast media as BOPTA or EOB-DTPA, which is more widely used in radiological literature and better describes the most relevant distinctive characteristic of these agents"*. We respectfully disagree with this comment: in the most recent consensus article on gadoteric acid (see below) the term hepatobiliary is the one utilized all over the article, while the term hepatospecific is never used (Merkle EM, Zech CJ, Bartolozzi C, Bashir MR, Ba-Ssalamah A, Huppertz A, Lee JM, Ricke J, Sakamoto M, Sirlin CB, Ye SL, Zeng M. Consensus report from the 7th International Forum for Liver Magnetic Resonance Imaging. Eur Radiol. 2015 Jun 13. DOI 10.1007/s00330-015-3873-2); same applies for the most prestigious Journal in our field, RADIOLOGY. Whenever an article is referring to Gadoteric acid, the term used is hepatobiliary and not hepatospecific.

- Reviewer comment 3: as requested, we have defined all abbreviations;

- Reviewer comment 4: as requested, we have described economic reasons for the preference of Gd-EOB-DTPA over Gd-BOPTA;

-Reviewer comment 5: *"Be careful: "among" is different from "between" (see, for example, Introduction, line 15)." We have modified the text;*

-Reviewer comment 6: As requested, we have put the "Differences in phases of enhancement between Gd-EOB-DTPA and extra-cellular contrast materials" section immediately after the "Optimal study protocol for the liver" section, and we have merged the section "Transitional phase" with the "Optimal study protocol for the liver" section;

-Reviewer comment 7: as requested, minor language errors have been corrected;

-Reviewer comment 8: as requested, we have modified the abstract;

- Reviewer comments 9-13*: as requested, we have modified the text;
- Reviewer comment 14*: we have modified the paragraph entitled “Optimal study protocol for the liver” according to reviewer suggestion, except for the description of “conventional” MR protocol for liver examination. As “conventional” phases of enhancement were otherwise described in the text (e.g., “Differences in phases of enhancement between Gd-EOB-DTPA and extra-cellular contrast materials” section), description of conventional MR protocol should be a redundancy;
- Reviewer comment 15*: as requested, we have defined more precisely the enhancement phases of EOB-enhanced MRI;
- Reviewer comment 16*: “All specific technical considerations (flow rate injection, timing, etc) on EOB should be moved to the end of this section.” We respectfully disagree with this comment because such modifications could decrease reader’s interest;
- Reviewer comment 17*: “the time necessary to the contrast material to get from the suprarenal abdominal aorta into the liver”: try to be more precise (when the aortic threshold has been reached, the “head” of the contrast medium bolus is probably already into the hepatic artery).” We have modified the text as follows: “The optimal scan delay for late hepatic arterial phase is 15-20 seconds after the peak aortic enhancement, which corresponds to the time necessary to synchronize the arrival of contrast material in the main portal vein with central k-space filling.”;
- Reviewer comment 18*: “portal venous phase should be obtained as soon as possible after the end of the arterial phase”: it depends on the scan duration of your arterial phase. Portal venous phase should be obtained with the correct timing”. We have modified the text as follows: “Portal venous phase is acquired 50-70 seconds after Gd-EOB-DTPA injection”;
- Reviewer comment 19*: “moreover, the adjunction of diffusion-weighted images does not significantly improve...”: if so, why did you suggest to perform DWI at the beginning of this section?”. We have reported the utility of DW images in the differentiation of hypovascular HCC from high-grade dysplastic nodules, and the prediction of the progression of hypovascular hypointense nodules on hepatobiliary phase into hypervascular HCC;
- Reviewer comment 20*: As requested, we have modified the paragraph “Differences in phases of enhancement between cirrhotic and normal liver with Gd-EOB-DTPA”;

-Reviewer comment 21: “Then, “oftentimes at 20 minutes the vessels will not be “dark” enough, resulting in a suboptimal hepatobiliary phase”: in which patients? Cirrhotics or healthy patients?”.

We have added “in patients with Child-Pugh class C cirrhosis” in the text;

-Reviewer comment 22: “Differences in phases of enhancement between Gd-EOB-DTPA and extra-cellular contrast materials. Last sentence should be expanded: provide more details regarding the suboptimal evaluation of portal and hepatic veins, particularly how this could affect local staging of focal liver lesions and how to overcome this drawback.” We have described the importance of evaluation of portal and hepatic veins in cirrhotic patients;

-Reviewer comment 23: “You correctly put “hepatic fibrosis” among the causes of reduced hepatobiliary phase enhancement; afterwards, you conclude that “these patients should be evaluated with alternative modalities as contrast-enhanced CT”. Nevertheless, this paper deals with the use Gd-EOB in patients with cirrhosis, so this conclusion should be clarified.” We have modified the sentence as follows: “These patients should be evaluated with alternative modalities such as contrast-enhanced CT and contrast-enhanced ultrasound in order to avoid misdiagnosis”.

We are submitting a copy of our revised manuscript.

We can see how our manuscript is improved after modifying it according to yours and the reviewer suggestion, and we very much hope we can anticipate a favorable editorial decision.

Sincerely,

Giuseppe Brancatelli