ANSWERING REVIEWERS

October 23, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (5864_Review).

Title: Nuclear Imaging for Functional Evaluation and Theragnosis in Liver Malignancy and Transplantation

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Name of Journal: *World Journal of Gastroenterology*

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First of all, we deeply appreciate the reviewers' helpful comments. The manuscript has been revised according to the reviewers' comments.
The reviewers' comments are in *italics*, and our responses are in regular text, with changes to the manuscript in red color.

For Reviewer 1 (ID 00054102)

1. *Could you specify the real clinical application of each technique. For example, when do you suggest to perform PET when evaluating a patient with colorectal liver metastasis? Always? Only when extrahepatic disease is suspected....?*
   The appropriateness of an imaging modality depends on the cost-effectiveness as well as the efficacy of the modality. Thus, a suggestion on the use of an imaging modality requires extensive studies with regard to the efficacy and cost-effectiveness. In colorectal cancer, however, there are several guidelines that recommend FDG PET as an appropriate or necessary imaging method in initial staging of most conditions (unless the primary lesion is too small or superficial). We added a sentence with these guideline references. Now it reads:
   (Page 8, line 10) Thus, FDG PET/CT is recommended by several guidelines as an appropriate and necessary imaging tool for initial staging of colorectal cancers [42,43].

2. *In the same sense, When do you suggest to perform PET before LT for hepatocellular carcinoma? Is it useful to assess vascular invasion? And similarly in all clinical settings.*
   In liver transplantation for hepatocellular carcinoma, FDG PET is recommended as a preoperative work-up in almost all cases. FDG PET is the most sensitive imaging method for detection of extrahepatic metastasis. In addition, FDG PET can also be used for prognosis prediction. Therefore, FDG PET is recommended as a preoperative imaging in almost every case of liver transplantation. We added a sentence and now it reads:
   (Page 11, line 26) Thus, FDG PET can be recommended as an essential imaging modality for preoperative evaluation of liver transplantation.

For Reviewer 2 (ID 00054993)

1. *As the scope of this review is clinical practice, it seems desirable to also address the prerequisites of these methods (f.i. availability of nucleotides, preparation on site, necessity of zyclotron on site and the costs). Can these methods be offered countrywide or how many centers are needed to cover the needs of the population in question?*
   We agree that these questions are very important in the practical point of view. However, the availability, approval status, and cost of a certain radiopharmaceutical depend on the condition of each country. For example, FLT is approved for clinical use by the government in EU, but only for clinical investigation in USA. The cost of FDG also varies between different countries. Thus, we added simple comments on general availability of some widely used radiopharmaceuticals. Now, it reads:
   (Page 5, line 11) Because of the relatively long half-life of ^{18}F, FDG can be delivered to an imaging center without an on-site cyclotron, within 1 or 2-hour distance.
   (Page 9, line 9) ^{11}C-acetate PET is approved for human use in many countries including USA, EU, and Korea

2. *On page 5 the biological decay (renal excretory system, etc.) of FDG is mentioned and should be referenced.*
   We added a reference.
   (Page 5, line 6) FDG that is not taken up by cells is rapidly removed by renal excretory system [4].

3. *On page 6 three studies (RefNr.10,12,13) are cited and then a statement follows, that in one of these studies detection rates are specified, but a reference is lacking to indicate which one of these 3 studies is meant.*
   We added the specific reference number
   (Page 6, line 3) In one of these studies, detection rate was as low as 27.2% for 1 to 2 cm and 47.8% for 2 to 5 cm tumors [13].

Thank you again for consideration of publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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