ANSWERING REVIEWERS

March 24, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16726-review.doc).

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
(1) *Regarding the title and subtitle, authors need to correct some expressions. First of all, the term of prognostication should be reconsidered. Authors wrote this article in several paragraphs. One of the paragraph title is 'prognostic stratification'. They infered that classification of differentiation or accurate staging play an important role for prognostic stratification. Therefore they titled in that way. However, there is only one article which dealt with the recurrence (Nakanishi et al.). Generally the study associated with prognosis might include some survival analysis or recurrence data. If the study mentioned mainly the evaluation of cancer differentiation, it will be better to change the title in these way, for example histologic classification or pathologic classification.*
I agree that studies dealing with prognostication should include survival analysis or present data on diseases recurrence. It must be otherwise noted that most studies that have been evaluated in the present paper provided correlations between parameters derived from functional imaging techniques (diffusion-weighted imaging, dynamic contrast-enhanced MRI and perfusion CT) and pathological findings (as the histological grade) or clinical outcome (as recurrence after resection or response to therapy). Both these features are important prognostic factors for patients with hepatic or pancreatic malignancies. In this view, I do not agree with the reviewer and I think that the term "prognostication" is neither wrong nor misleading. Nevertheless, according to reviewer's suggestions, the title of paragraph 2 has been changed into "**CORRELATION WITH PATHOLOGICAL FINDINGS AND PROGNOSTIC STRATIFICATION**".

(2) *Secondly, they just considered that they wrote about functional imaging in*

hepato-bilio-pancreatic disease. But, I think they mainly talk about the functional imagings of MRI, CT, not whole functional imagings. Therefore I recommended the term of functional imaging into the functional imagings of MRI, CT. There are only limited number of study regarding nuclear medicine in this article and no study was mentioned regarding ultrasound. I suggested a review article titled 'Functional imaging techniques in hepatocellular carcinoma' for reference (Goh V, Sarker D, Osmany S, Cook GJ. Functional imaging techniques in hepatocellular carcinoma. Eur J Nucl Med Mol Imaging. 2012;39(6):1070-9.). In this review article, authhours mentioned diverse radiotracers and various modalities

Functional imaging techniques include different modalities that can detect or measure changes in metabolism, blood flow, regional chemical composition. This group includes nuclear medicine techniques, as PET or SPECT, but also techniques derived from conventional imaging methods, as perfusion CT, diffusion weighted imaging, arterial spin labeling MRI, dynamic contrast-enhanced MRI, BOLD imaging. For example, functional MRI (fMRI) is a functional neuroimaging procedure that is independent from the use of radiotracers and can measure brain activity by detecting associated changes in blood flow [Huettel, S. A.; Song, A. W.; McCarthy, G. (2009), *Functional Magnetic Resonance Imaging* (2 ed.), Massachusetts: Sinauer, ISBN 978-0-87893-286-3].

As clearly stated in the abstract and in the introduction, this paper focuses on functional imaging techniques apart from nuclear medicine; we did not aim to describe applications of molecular imaging techniques. Specific sentences have been added throughout the text; see highlighted text. The term "imagings" has no meaning.

(3) *Additionally, there are some differences of structes between 'prognostic stratification' and 'response to treatments'. It might be better to organize the sub-paragraph. In the part of prognostic stratification, that part is composed of HCC, CCC, PDAC, PanNET. With respect to response to Tx, that parts is composed of primary liver tumors, liver metastases, pancreatic tumors. I recommend them to match as it possible.*

Please note that sub-paragraphs have been organized according to reviewer's suggestions.

(4) *format; Generally, the Ktrans is expressed into superscript, not subscript.*
Ok, changed.

(5) *p9: check grammar (prognostic stratification associate with)*
Ok, changed ("prognostic stratification associated with").

(6) *p10: 18FDG PET-CT -> 18F-FDG PET-CT*
Ok, changed.

(7) *p15: specific uptake values (SUVs) -> standardized uptake values (SUVs)*
Ok, changed.

(8) *p18, 1st line: need to specify the DCE MRI parameters.*
DCE-MRI parameters were already specified (Arterial fraction and portal venous hepatic blood flow).

(9) *p19, 8th line: Y-90, need to specify, probably Y-90 TARE*

Ok, changed.

(10) *p20, 21th line: need to specify the pCT parameters.*
Ok, pCT parameters have been specified.

(11) *p21, 27th line: it appears not accurate. need to check. (non-responding patients (<10% viable tumor).)*
Ok, changed.

(12) *conclusion: the expression of "should be always considered" is too strong. need to modify.*
Ok, changed.

(13) *Table4: need to add TARE, and it is inappropriate to abbreviate Y-90 into Y-90 TARE, because there is another Y-90.*
Ok, changed.

(12) *Also, I added some candidate references. Horger M, Lauer UM, Schraml C, Berg CP, Koppenhofer U, Claussen CD et al. Early MRI response monitoring of patients with advanced hepatocellular carcinoma under treatment with the multikinase inhibitor sorafenib. BMC Cancer. 2009;9:208. doi:1471-2407-9-208*
This paper does not fit with the aims of this paper, as it does not deal with functional imaging techniques.

[pii] Sacco R, Faggioni L, Bargellini I, Romano A, Bertini M, Ginanni B et al. Treatment Response After Unusual Low Dose Sorafenib: Diagnosis with Perfusion CT and Follow-up in a Patient with Recurrent Hepatocellular Carcinoma. J Gastrointest Cancer. 2012. doi:10.1007/s12029-012-9403-4
This paper is not retrievable from PubMed.

Schraml C, Schwenzer NF, Martirosian P, Bitzer M, L
Reviewer's suggestion is incomplete; probably he was suggesting AJR Am J Roentgenol. 2009 Oct;193(4):W301-7. doi: 10.2214/AJR.08.2289. **Diffusion-weighted MRI of advanced hepatocellular carcinoma during sorafenib treatment: initial results.** Schraml C[1], Schwenzer NF, Martirosian P, Bitzer M, Lauer U, Claussen CD, Horger M. If so, this article should not be included because it does not fit with the aims of this paper.

3 Further language editing was performed.

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

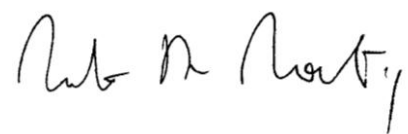Sincerely yours,
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