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April 2, 2019

Dr. Jia-Ping Yan

Science Editor, Editorial Office

Baishideng Publishing Group Inc.

E-mail: j.p.yan@wjgnet.com

Dear Doctor and Editor Yan:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects" (ID: 47459). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied the comments carefully and have made corrections which we hope are met with approval. Revised portions are marked in red in the paper. The main corrections in the paper and the responses to the reviewer's comments are as flowing:

Thank you again, and I am looking forward to hearing from you soon.

Sincerely,

Dr. Shao-Bo Wang

PET-CT Center, the First People's Hospital of Yunnan Province

E-mail: wshbo_98@126.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 03724099

Reviewer's country: United States

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-12 16:49

Reviewer performed review: 2019-04-12 17:04

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a comprehensive, well written review on the role of PET in HCC. Few minor comments. 1. Page 3 - please explain multidrug resistance (MDR) to what? 2. Page 3 - change instable to unstable 3. page 2 - consider including hepatologist to the team of



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multidisciplinary team for managing HCC.

Response:

Thank you so much for your positive remarks. That's a very good suggestion for us and we have made detailed modifications as follows:

1. Section 1, paragraph 1: Multidrug resistance (MDR) is the ability of tumor cells to become resistant to different drugs and represents a major barrier to successful treatments. The overexpression of MDR proteins is thought to be a major obstacle to successful chemotherapy in various cancer types, including HCC. Studies have shown that cells that present increased MDR protein expression exhibit low ¹⁸F-FDG accumulation
2. We changed instable to unstable in paragraph 2 of section 1.
3. Hepatologists were included into the multidisciplinary teams in our revised manuscript.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 00504119

Reviewer's country: Brazil

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-12 14:51

Reviewer performed review: 2019-04-12 17:07

Review time: 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This novel radiotracers and immuno-PET have showed great potential value for PET imaging and become the focus of current research, which may enhance the ability of PET for HCC. An overview of the advantages and disadvantages for the current PET

diagnostic status of HCC will be reviewed, and this paper can be very important to this.

Response:

Thank you so much for your positive remarks. Although PET-CT is an effective diagnostic method for HCC, the low sensitivity limits its use. Novel radiotracers and protocols enhance the utility of PET for HCC, and the advantages and disadvantages are mentioned in the corresponding paragraphs as follows:

- a. Section 1, the advantage of ^{18}F -labeled amino acids and peptides is that it has good tumor-to-background contrast and is stable in vitro, while the disadvantage is that it is unstable in plasma, tumor tissue, and urine.
- b. ^{11}C -labeled acetate and choline have a high uptake in tumor cells, but the use of ^{11}C -labeled tracers is limited based on the access to an on-site cyclotron due to the short half-life (20 min).
- c. ^{68}Ga -DOTA has an appropriate physical half-life (68 min) and good blood clearance, and there was a higher uptake in low-grade neuroendocrine tumors. ^{68}Ga -NGR (asparagine-glycine-arginine) uptake was higher than ^{18}F -FDG for imaging of well differentiated HCC xenografts. However, limited data using ^{68}Ga for HCC are just now emerging, and its potential clinical utility is unclear.
- d. $^{64}\text{CuCl}_2$ PET-CT for the early detection of HCC intracranial metastasis is significant but the abundant physiologic uptake in liver limits its use.

Thanks for your suggestions. We appreciate it very much.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No



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BPG Search:

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 03477256

Reviewer's country: Germany

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-15 07:50

Reviewer performed review: 2019-04-15 08:07

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1. Can PET differentiate between HCC and intrahepatic cholangiocarcinoma (CCC) ? 2. Which significant value does contrast-enhanced ultrasound imaging still have in daily clinical practice? 3. What about digital angiography ? With this technique even small



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HCC's can be detected. 4. The authors should discuss about the significance of PET-MRI. Might this device be of interest and significance in future ?

Response:

Thank you so much for your kind suggestions and we have made detailed modification according to your suggestions:

1. It seems to be difficult to differentiate between HCC and ICC based on FDG PET alone and there is a lack of literature on this issue. However, other modalities (CECT and MRI) may help to differentiate them, and developing new specific radiotracers can be a desirable alternative for enhancing the ability of differential diagnosis. We added this detail in section 2.2.
2. Contrast-enhanced ultrasound (CEUS) imaging is useful for HCC diagnosis only when the tumor sites are identified with B-mode US. This has been added to the introduction.
3. We added the sentence "Digital angiography is another examination method that can diagnose HCC, but it is invasive and is usually only performed when transarterial treatment is necessary" to the introduction, which shows the value of digital angiography.
4. It is really true as the reviewer suggested that PET-MRI may be of interest and significance in the future, hence we wrote a separate paragraph to illustrate the values and limits of PET-MRI, as shown in section 6.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
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- ☐ Plagiarism
- ☐ No



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BPG Search:

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- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 02530754

Reviewer's country: Spain

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-12 08:44

Reviewer performed review: 2019-04-16 08:41

Review time: 3 Days and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The present review by L. Ren-Cai and cols. summarize the role of PET-scan in patients with hepatocellular carcinoma and discuss the potential advantages of recently developed radiotracers. The authors provide a nice background including a description

of the available radiotracers. Although the topic is of great interest, there is a very recent review published in WJG which overlaps widely with the present manuscript and therefore the authors should consider redirecting the focus as detailed below. - As outlined above, a recent manuscript addressing this topic was recently published in WJG: "Lee et al. Emerging role of 18F-fluorodeoxyglucose positron emission tomography for guiding management of hepatocellular carcinoma. World J Gastroenterol. 2019 Mar 21;25(11):1289-1306". I would recommend the authors to remove most of the information regarding 18-FDG while expanding the potential applications of newly developed radiotracers. - The review is too optimistic and does not provide a complete viewpoint in some sections. PET scan has well known limitations in HCC assessment. A significant proportion of HCCs does not show increased radiotracer uptake. In these patients, the PET scan may have no role at all. In patients with HCC and positive PET, there is a risk of over-staging which needs to be further discussed. The use of PET as screening may not be cost-effective and its systematic implementation in tumor staging is a matter of debate. Maybe these caveats could be joined in a section of "Limitations of 18-FDG PET-scan in HCC" to be included immediately after the background in order to reinforce the need to develop specific radiotracers (which should be the main focus of the review). - Is there any cost-effectiveness analysis of PET in HCC patients undergoing potentially curative therapies? As far as I know, this is a literature gap that requires further investigations. Please comment. - In page 5, it can be read: "PET scanning has a high sensitivity for detecting metastases but a low sensitivity for HCC". I guess that the authors meant that the sensitivity to detect the primary tumor is reduced but this requires clarification. - I would recommend a summary table including all radiotracers with their supporting evidence in HCC (if available), either to detect intrahepatic or extrahepatic lesions: sensitivity, specificity, predictive values, validation in independent cohorts... It would ease the reading while providing an overview of the strength of the

evidence. - In most scenarios, sensitivity and specificity provides an incomplete evaluation of the precision of a diagnostic technique. Whenever available, predictive values and population of study (BCLC stage, screening vs staging vs evaluation of recurrence) needs to be described. - Figure 3 should be enlarged. In the final version of the manuscript, the image quality should be optimized. - In the conclusion the authors should emphasize the potential clinical role of PET-scan in HCC and more precisely to describe the clinical scenarios where PET-scan should be mandatory vs strongly recommended vs potentially considered vs not useful. This could be also summarized in a table. This information, if based in solid evidence, would be of great interest for the readership. - Pages should be numbered

Response:

Special thanks to you for your good comments and we made detailed modification according to your suggestions:

1. We removed most of the information regarding ^{18}F -FDG and the utility of novel radiotracers are fully discussed.
2. The limitation of ^{18}F -FDG PET-CT for HCC should not be neglected and we highlighted the limitations in section 2.3. EASL Clinical Practice Guidelines for HCC was cited to show its low detection rate of 40%. Section 2.1, paragraph 3, due to its limitations and expensive cost, we changed the original sentence to "Overall, ^{18}F -FDG PET-CT has an additional value for HCC staging".
3. As far as we know, there was no literature regarding cost-effectiveness analysis of PET in HCC, perhaps this is worth exploring in future research.
4. We changed "PET scanning has a high sensitivity for detecting metastases but a low sensitivity for HCC" to "PET scanning has a high sensitivity for detecting extrahepatic metastases but a low sensitivity for primary HCC" in section 2.1, paragraph 2.
5. We summarized a table to interpret the utility of all radiotracers. However, most



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studies concerning novel radiotracers are animal experiments, we summarized its advantages and disadvantages in another table. Positive and negative predictive values were not available in most literature and these values could not be listed in the table.

6. Figures have been reprocessed and the image quality was further optimized.

7. Thank you so much for your kind suggestions. We think the clinical recommendation is of great interest for the readership but should be developed by multidisciplinary experts to ensure its reliability. We will conduct more clinical studies in the future to provide certain evidence for developing the clinical recommendation.

8. Pages numbers have been added.

Thanks for your suggestions. We appreciate it very much.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 03004570

Reviewer's country: Turkey

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-12 08:53

Reviewer performed review: 2019-04-19 11:03

Review time: 7 Days and 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript is a comprehensive, informative review about the current use of PET in HCC. Title, abstract and key words are adequate. Authors benefited from 82 references. Background information, current situation and future prospects about the use of



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18F-FDG PET and new tracers are sufficiently documented. Discussion is highly informative and helpful for clinicians. Figures are perfect. I recommend for publication.

Response:

Special thanks to you for your good comments.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 00039518

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-14 16:45

Reviewer performed review: 2019-04-21 21:12

Review time: 7 Days and 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The paper "Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects" is a well written review about the present role of PET-CT in the diagnosis, staging and prognosis of HCC. Generally speaking, the Authors should

better highlight the limited role of this technique in the present guidelines for the HCC management. The strength of the paper is the excellent overview of the promising perspectives of the new PET-CT applications (dual tracers, immune-PET). I have some concerns that must be addressed by the Authors:

- Abstract: write as follows:has improved the ability to detect lesions and has made it possible to achieve great progress
- Introduction, lines 3-4: What does it mean comprehensive treatment? Do the Authors mean multimodal treatments? Please specify
- Introduction, lines 5-6: The Authors write that “partial liver resection and liver transplantation remain the only realistic treatment options for HCC”. Does realistic means curative? In this case , even ablative treatments are included among the curative treatments for HCC.
- Radiotracers: The Authors claim that CuCl₂ PET-CT is useful for the early detection of HCC intracranial metastasis. However, the occurrence of intracranial metastasis in HCC is anecdotal; then, this tracer could be clinically useful only if it is able to early detect extrahepatic HCC metastases independently from intracranial localization. This must be explained
- Section 2. Generally speaking and according to the present EASL guidelines (J Hepatol 2018) , HCC is not a very avid tumour for 18F-FDG PET as uptake is observed in less than 40% of the cases and most well differentiated HCCs are 18F-FDG PET negative. This should be better highlighted in this section.
- Section 2, Paragraph 2.1 : It is not clear to me why 18F-FDG PET-CT has a better sensitivity for extrahepatic metastasis than for intrahepatic HCC. The Authors should comment on this point, even considering that poorly differentiated HCC is largely less frequent than well/moderately differentiated HCC
- Section 2, Paragraph 2.1 The statement “Overall, the staging capacity of 18F-FDG PET-CT is incontestable” must be attenuated as the current guidelines for HCC management do not include PET-CT among the diagnostic and staging techniques for HCC
- Section 2, Paragraph 2.2: All the statements contained in this paragraph (Differential diagnosis) are based on small case series or case reports and

should be changed. Indeed, in my opinion the role of 18F-FDG PET-CT in the differential diagnosis of HCC from other neoplasms and in the extrahepatic staging of HCC remains limited due to the fact that no more than 40% of HCC show an increased uptake of the tracer. Furthermore, it is not clear how this technique can help in the differentiation of malignant from bland portal thrombosis that is usually achieved using CEUS, CECT or even fine needle biopsy of the thrombus - Section 2, Paragraph 2.4: In some of the cited papers the Authors should specify which is the treatment applied (external beam radiotherapy ref. 60, liver transplantation ref 61) - Section 4: The Authors should specify that the role of Dual-phase imaging of 11C-acetate PET in the differential diagnosis of FNH and hemangioma from malignant liver lesions is obviously limited given that this differential diagnosis is easily achieved in most cases using CECT, MRI and even CEUS

Response:

Special thanks to you for your good comments. We have made corrections according to the Reviewer's comments:

1. We highlighted the limited role of PET for its low sensitivity at 40%, and cited the current guidelines: *European Association for the Study of the L. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol 2018*. Which may be important for the understanding of the value of PET for HCC.
2. Comprehensive treatment means radiotherapy, chemotherapy, immunotherapy, interventional therapy or combined. We added this to the introduction.
3. We are very sorry for our incorrect writing "the only realistic treatment options for HCC", in this statement, ablation was added and "Liver transplantation (LT), partial liver resection and ablation remain the main therapeutic tools for HCC and have a high rate of complete response".
4. Due to the abundant physiological distribution of ^{64}Cu in the liver, there was limited value for the evaluation of HCC but there is potential value for detecting intracranial

and other extrahepatic metastasis located in areas with low physiological uptake such as musculoskeletal tissues. We reinterpreted it in section 1, paragraph 7.

5. We cited the EASL guidelines in this part to highlight the limitation of PET for HCC according to the reviewer.

6. The reasons why ^{18}F -FDG PET-CT has a better sensitivity for extrahepatic metastasis than for intrahepatic HCC were as follows: Normal liver tissue has a relatively high FDG uptake, which reduces the tumor-to-liver standardized uptake value ratio (TLR) and makes it difficult to distinguish tumor lesions. But the metastasis usually has a better contrast to surround tissues. We reinterpreted it in section 2.1, paragraph 3.

7. According to the reviewer, in Section 2, Paragraph 2.1, The statement “Overall, the staging capacity of ^{18}F -FDG PET-CT is incontestable” was attenuated. We used “Overall, ^{18}F -FDG PET-CT has an additional value for HCC staging” to replace the original sentence.

8. It is really true as the reviewer suggested that the statements contained in differential diagnosis are based on small case series or case reports. In fact, PET has limited value for differential diagnosis and the literature was rare. We emphasized this drawback in the revised manuscript.

9. Section 2, Paragraph 2.4: The treatment methods were specified according to the reviewer.

10. Section 4, Paragraph 4: “But ^{11}C -acetate PET, compared to CT, MRI or ultrasound, is not easy to acquire due to ^{11}C has a short half-life (20 min), this will limit its utility in clinical work” was added to show its limited value.

Special thanks to you for your good comments. We appreciate it very much.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:



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- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47459

Title: Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects

Reviewer's code: 03742333

Reviewer's country: United Kingdom

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-15 01:28

Reviewer performed review: 2019-04-21 22:13

Review time: 6 Days and 20 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have read with great interest the manuscript entitled "Positron-Emission Tomography for Hepatocellular Carcinoma: Current Status and Future Prospects", submitted to the World Journal of Gastroenterology. In this narrative review, the role of PET for the



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diagnosis and follow-up of hepatocellular carcinoma is explored. The manuscript is well written and the topic of clinical interest. The major criticism is the study design's selection (a narrative review) because the high risk of selection bias; however, the limitations of the studies included are fairly discussed throughout the manuscript. In addition, the manuscript is quite long and the suggestion is to shorten it slightly to improve readability.

Response:

Special thanks to you for your good comments. Our manuscript was shortened. Hence, we deleted or rewrote the following contents, but is not limited to, to improve the readability:

Section2.1, paragraph 3, the sentence "PET-CT scans are a feasible tool for detecting extrahepatic metastasis in patients with HCC" was erased.

Section2.2, paragraph 3, we rewrote and simplified the whole paragraph was.

Section2.3, paragraph 2, we adjusted the position and simplified the sentence "Studies have indicated the ... has an incremental prognostic value".

We adapted and shortened the whole manuscript to improve its quality. Special thanks to you for your good comments. We appreciate it very much.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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- ☐ No

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