

Format for ANSWERING REVIEWERS

August 25, 2012



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12456-edited revied by ZJ.doc).

Title: Cross-modality fusion of PET/CT and CECT for Pancreatic cancers

Author: Jian Zhang, Chang-jing Zuo, Ning-yang Jia, Jian-hua Wang, Sheng-ping Hu, Zhong-fei Yu, Yuan Zheng, An-yu Zhang, Xiao-Yuan Feng

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 12456

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

Thank you very much for your advice of our manuscript, and for the helpful comments by the expert referees. Amendments are highlighted in the revised manuscript. Point by point responses to the comments are listed below.

Reviewed by 00503608

(1) "Reference source not found" in the manuscript.

Thank you for your advice! We have re-checked the references and made some changes.

(2) The abstract is simply too long. Please summarize the data more succinctly. The reader can refer to the text/tables if they need more detail. In the conclusion, please state exactly where statistically significant differences were found and where they were not.

Thank you for your advice! We have summarized the abstract and highlighted the significant differences.

(3) Most guidelines (such as the NCCN pancreatic cancer guidelines) do not recommend PET/CT for the evaluation of pancreatic cancer. I think that this is notable and should be discussed along with some comments regarding why they are not recommended at the current time.

Thank you for your advice! We have added some discussion about the NCCN pancreatic cancer guidelines, and they are not recommended at the current time because the role of PET/CT scan in PC remains unclear.

(4) Perhaps there should be at least some discussion regarding cost.

Thank you for your advice! We have added some discussion about cost. Compared to conventional PET/CT, there was no increase in medical costs of patients.

(5) There should definitely be some discussion about EUS and the role of PET/CECT now that most patients are getting EUS as part of their workup.

Thank you for your advice! We have added some discussion about EUS. In diagnosing small pancreatic cancer and focal mass-forming pancreatitis, EUS may be of avail.

(6) Is PET/CT routinely used for pancreatic cancer evaluation at your institution? Since it is not currently recommended, most insurance companies will not reimburse for PET/CT. Is this not a problem in China?

In our hospital, PET/CT is not routinely used for pancreatic cancer, and insurance companies will not reimburse for PET/CT. PET/CT was recommended, when the lesion was difficult to

diagnose, or patients had “high-risk” to detect extra pancreatic metastases.

(7) Please comment specifically on the utility of PET/CECT for cystic lesions. Should this study be in the algorithm at all?

Thank you for your advice! We have added some comments specifically on the utility of PET/CECT for cystic lesions: PET/CECT correctly diagnosed all 11 of the patients with cystic lesions.

(8) All of the text on page 9 and the top of page 10 should probably be in the discussion section rather than the results section.

Thank you for your advice, and these contents have been moved to the section of discussion.

(9) Table III should probably look a little more like table II.

Thank you for your advice! We revised the table III, making it look like table II.

Reviewed by 00069105

(1) Abstract is too long and confusing. Too much numbers

Thank you for your advice! We have summarized the abstract and highlighted the significant differences.

(2) If you search in the paper the information exists but is difficult to find. Tables. a comparing table more resumed would be interesting.

Thank you for your advice! We have revised the results and table III, making them easier to be understood.

(3) Discussion: some information is confusing

Thank you for your advice! We have revised the discussion, making it easier to be understood

(4) Images in docx are of low quality

Thank you for your advice! We have re-offered the high-quality images.

Reviewed by 02454257

(1) Demographic data of the patients are supposed to be shown in the results section and not in the methods part.

Thank you for your advice, and these contents have been moved to the section of results.

(2) The presentation of the parameter in the results is difficult to read and unclear; the percent values should be more connected to the procedure. Taken together the results section as the abstract itself is too long and should be tightened.

Thank you for your advice! We have summarized the abstract and highlighted the significant differences, and revised the results and table III, making them easier to be understood.

(3) Introduction: Abbreviations should be introduced in general, i. e. CECT.

Thank you for your advice! We have introduced every abbreviations in the introduction.

(4) The listed reference #5 is kind of an unlucky choice since it reports an animal experiment and the response of a special form of therapy.

Thank you for your advice! We have deleted the reference #5, and added the reference (Lee JW, Kang CM, Choi HJ, Lee WJ, Song SY, Lee JH, Lee JD. Prognostic Value of Metabolic Tumor Volume and Total Lesion Glycolysis on Preoperative 18F-FDG PET/CT in Patients with Pancreatic Cancer. J Nucl Med 2014;55:898-904 [PMID:24711649 DOI:10.2967/jnumed.113.131847])

(5) Argumentation of iodine allergy after application of contrast material is insufficient. According to i. e. Wysowski et al 2008 and Kim MH et al 2014 there is an incidence of an anaphylactic shock of 1 in one million. Given the extremely bad prognosis of a pancreatic carcinoma this incidence is negligible.

Thank you for your advice! Although there is a low incidence of an anaphylactic shock of 1 in one million, it has a greater chance to cause adverse reactions such as nausea, vomiting, rash, and so on.

(6) It is not necessary to mention the vote of the ethics committee in the introduction.

Thank you for your advice! We have moved it to the section of materials and methods.

(7) It is not necessary to mention the vote of the ethics committee in the introduction. Materials and Methods: As mentioned earlier abbreviations should be introduced. Most readers know for sure what ERCP or FNA biopsy means but a high quality manuscript should bother with the introduction of abbreviations, even those which are common.

Thank you for your advice! We have introduced every abbreviations in section of the Materials and Methods.

(8) Has oral contrast medium been applied in the CECT group as well?

Yes, water was used as negative contrast medium.

(9) How was "experienced physician" defined?

Thank you for your advice! We have added some description of these experienced physicians: CECT was retrospectively evaluated using consensus of two experienced radiologists (readers A and B with 12 and 25 years of experience in CT, respectively) ; The PET/CTs were retrospectively interpreted using consensus of two experienced nuclear medicine physicians (readers C and D with 6 and 4 years of experience in PET/CT, respectively); The PET/CECT fusion images were prospectively interpreted in consensus by a experienced radiologists and a experienced nuclear medicine physicians (reader E with 6 years of experience in PET/CT, and reader F with 15 years of experience in CT).

(10) Material and methods does not provide information on the reconciliation of intra-/postoperative findings. How was made sure that lymph nodes classified under imaging as tumor infested were really infested? How was controlled that there were for sure no distant metastases? For 19 patients the diagnosis was made by FNA biopsy; were there lymph nodes aspirates to correlate with the imaging? How was the clinical follow up (mentioned on page #8) performed? Were all patients followed up or individuals only? How many died?

Thank you for your advice! In present study, we only have explored the lymphatic and distant metastases based on patient analysis, and lesion-based study has to be furtherly explored. Clinical follow up was performed more than 6 months for not died patients, mainly including the tumor marks , imaging examinations and histopathology to confirm the nature of the lesion, so there was not enough information of patients survival.

(11) Statistical analysis: Power analysis would be useful even for a retrospective analysis to show that the sample size is sufficient to significantly present the differences.

Thank you for your advice! We would do some furtherly study about this in the future.

(12) Why are IPMNs listed as benign lesions in table 1 (see Backer MS et al 2014)?

Thank you for your advice! In latest WHO classification of Tumours of the Digestive System(2010), IPMN included noninvasive IPMNs and invasive IPMNs. Noninvasive IPMNs are classified into three categories on the basis of the highest degree of cytoarchitectural atypia: low-grade dysplasia, intermediate-grade dysplasia and high-grade dysplasia. The presence of a component of invasive carcinoma leads to the designation "IPMN with an associated invasive carcinoma". In our study, we used WHO classification for IPMN.

(13) Table II and III: Table legends should provide an explanation of the abbreviations. It remains unclear why under table II "TP, FN, TN and FP" are mentioned but not presented in the table. In table III the columns CECT:NP and PET-CT:S show obscurities.

Thank you for your advice! We have revised Table II and III and provided the explanations of the abbreviations.

(14) Discussion: The discussion is held very common. It does not become obvious what is really new in the study the authors present. There is no independent message provided by the authors, only a hint that the study of Wakabayashi et al showed similar results. In my opinion the comparison with multidetector computed tomographic angiography (MDCTA) (see Kaneko OF et al 2010) should be discussed as well. This method shows similar good predictive values and may be more cost efficient. With relation to the prediction of peritoneal tumor infiltration the comparison with a staging

laparoscopy should be made to avoid a laparotomy (page 10, 2nd paragraph).

Thank you for your advice! We have revised the section of discussion. Because a staging laparoscopy is rarely done for pancreatic cancer patients in our hospital, it was difficult to compare with it.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Zhang Jian' in Chinese characters, written in a cursive style.

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