Format for ANSWERING REVIEWERS

October 31, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14013-Review.doc).

Title: Endoscopic Ultrasound in the Evaluation of Pancreas Neoplasms-Solid and Cystic: Review

Author: Eric M Nelsen, Darya Buehler, Anurag V Soni, Deepak V Gopal

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

ESPS Manuscript NO: 14013

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) Reviewer's comments: "The paper is well organized. The character of Review should be reported also in the title. The content is updated with a review of a very recent literature. Also the illustrations added are appropriate and valuable. The actual diagnostic procedures for pancreatic lesions (solid, cystic and atypical) are correctly evaluated and illustrated."

Response to reviewer:
Thank you for your kind words. We have added Review to the title of the manuscript. We have edited our manuscript to better answer questions raised by other reviewers; we hope that you find it is still well organized. Thanks for taking the time to review our manuscript.

(2) Reviewer's comments: "Authors Since firstly introduced in 1990s, EUS-FNA has quickly become a common and reliable way of obtaining tissue in the diagnosis of pancreatic lesions. This review summarizes our current knowledge on this topic, especially on the evaluation of cystic lesions. The manuscript is generally well written, however, the author should pay more attention on how this technique brings benefits to disease management when comparing with other techniques but not only listed out how many diseases that can by diagnosed by this technique. Page 2 last paragraph line 3: "with sensitivities as high 80-95% for pancreatic masses" should be "with sensitivities as high as 80-95% for pancreatic masses". Page 5 paragraph 1. According to the context, the term "primary non-adenocarcinoma of the pancreas" is more accurate than the term "non-primary pancreatic adenocarcinoma". Page 6, last paragraph. The most common metastatic tumors of pancreas have been reported to be from kidney, I suggest the author should give more information on this point.

Response to reviewer:
Thank you so much for reviewing out manuscript we hope that we have addressed all of your comments and made the necessary changes.
--In regards to the first comment, we have made edits and tried to highlight how the technique of EUS-FNA compares to other techniques. For the atypical/rare lesions of the pancreas, our aim

was to describe lesions that are less commonly seen in hopes of highlighting the importance of tissue diagnosis. As EUS-FNA is the best method for obtaining tissue from the pancreas, it would be difficult to describe other techniques in diagnosing these lesions. CT and ERCP are discussed and their limitations are highlighted in the manuscript.
--In regards to the second comment, we changed the sentence "with sensitivities as high 80-95% for pancreatic masses" to "with sensitivities as high as 80-95% for pancreatic masses" as suggested.
--We agree that the term "primary non-adenocarcinoma of the pancreas" is more accurate than the term "non-primary pancreatic adenocarcinoma" and have made the appropriate changes.
--Lastly, we added more information on metastatic tumors to include the kidney, which is indeed the most common metastatic tumor.

(3) Reviewers comments: "Major comments 1) Pancreatic adenocarcinoma: Para 1: It is unclear what the authors imply when they say that "Despite advances in diagnosis, pancreatic adenocarcinoma remains a rising and leading cause of cancer death in the United States". It is unclear as to how advances in diagnosis impact outcomes? The fact that Pancreatic cancer has poor outcomes is because patients present late and not because we can better diagnose pancreatic cancer! – which is the fact that the authors allude to in their next sentence. Please delete the first sentence. Moreover, in the last sentence of this paragraph the authors suggest that EUS-FNA offers a chance for early diagnosis. I am uncertain about any screening programmes in pancreatic cancer that are underway and comprise EUS-FNA to permit early diagnosis. The authors should bear in mind that current surgical practice indicates that whipples / pancreatic surgery may be undertaken even without pathological proof. The only need for a pretreatment diagnosis in pancreatic adenocarcinoma is prior to commencing neoadjuvant chemo- / radiotherapy (for a disease that is locally advanced or borderline resectable). Please rephrase the paragraphs in line of current management of pancreatic adenocarcinoma as the current paragraphs are very misleading to the reader. 2) Optimizing EUS-FNA on pancreatic masses – this section needs to have a more smooth flow as the current state is staccato and haphazard with the authors moving from cytopathologists on site to needles to suction. 3) Non adenocarcinoma masses: - the authors appear to have summarized the conclusions of other manuscripts in under each pathological sub-heading. This is not informative to the reader as he/she could easily get this information from trawling the PUBMED/ EMbase, etc. Minor comments: 1) Introduction: In the introduction, the authors make a number of broad statements that are unreferenced. These should be avoided and appropriate references provided. The Introduction reads like the conclusion of the manuscript. The authors should preferably put EUS into context in light of the pre-existing investigative tools for pancreatic lesions being not so useful and save their opinions for the discussion after the intervening paragraphs have provided the objective evidence. The authors should refrain from using superlatives – eg – 'dramatic impact'. Being a scientific journal, the authors should contain themselves in their descriptions. 2) Pancreatic adenocarcinoma: Para 2: The sentence of 1990s introduction of EUS is repeated within the same page. Please avoid this."

Response to reviewer:
Thank you so much for reviewing out manuscript we hope that we have addressed all of your changes.
In regards to the reviewers Major comments:

1) We agree that the original paragraph was misleading and have made the changes as suggested. EUS indeed has not changed the treatment management or survival statistics of adenocarcinoma. We have made the necessary edits so that it is not to be misleading.
2) In regards to the section on optimizing EUS-FNA, we agree the original format was lacking transitions. We hope you find the updated version flows more smoothly and has a logical progression.

3) In regards to the Non-adenocarcinoma section, our hope was to highlight some of the rare cancers of the pancreas and specifically give examples of some rare lesions that providers may not get exposure to. It would be difficult to provide a thorough review of each lesion but hope our review highlights key aspects that readers should know about rare pancreatic tumors and their appearance on EUS and cytology. We have updated the manuscript to reflect our intentions and clarify EUS-FNA role in diagnosing these lesions.

In regards to the reviewers Minor comments:

1) The introduction has been changed as recommended. It should now read more like an introduction and less like a conclusion. We highlighted what the review would discuss.
2) The repeated sentence has been changed. Superlatives have been removed as recommended.

Thank you for taking the time to review our manuscript.

3. References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal Gastrointestinal Endoscopy*

Sincerely yours,

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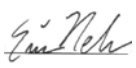

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