**Author’s response to reviews**

**Title:** Differential diagnosis between hepatic alveolar echinococciosis and intrahepatic cholangiocarcinoma with conventional ultrasound and contrast-enhanced ultrasound

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**Author’s response to reviews:**

Dear Editor and Reviewers,

Thank you very much for your comments and suggestions for our manuscript BMIM-D-19-00296: “Differential diagnosis between hepatic alveolar echinococciosis and intrahepatic cholangiocarcinoma with conventional ultrasound and contrast-enhanced ultrasound”, which are very valuable and have helped us revise and improve our manuscript. We appreciate all of your work on our manuscript.

We have carefully studied your comments and corrected our manuscript accordingly. We hope this version of the manuscript meets your approval. All changes have been marked using the 'track changes' option in Microsoft Word. The main corrections in the paper and the response to the editor and reviewers are as follows:

**Response to the editor:**

- Please include the full name of the ethics committee (and the institute to which it belongs to) that approved the study and the committee’s reference number if appropriate in the "Ethics
Approval and Consent to Participate" subsection of the Declarations. To establish this declaration subsection, please merge the current sections for ethical approval and consent.

Response: Thank you very much. We have included the full name of the ethics committee that approved the study in the "Ethics Approval and Consent to Participate" subsection of the Declarations, and merged the current sections for ethical approval and consent.

- Please move all declarations (titled revised to match those indicated at the end of this email) between the Abbreviations list and the references. Please then remove relevant sections from the title page.

Response: Thank you very much. We have revised all declarations between the Abbreviations list and the references, and removed relevant sections from the title page.

Response to Reviewer 1:

1. the authors must provide the value of US (1, 2 or 3 main features), CEUS (1, 2 or maybe 3 features) and a simple combined US+CEUS score. This approach is much easier and more practical.

Response: Thank you very much. We have revised our results according to your instruction. In table 3, the simple combined US+CEUS score is given based on the coefficient of selected features. Diagnostic performance of US or CEUS alone for differentiating between HAE and ICC are shown in table 4. (Page 11-12 in the revised manuscript)

2. the US score designed and calculated is more difficult to calculate and may not be reproducible among other groups. So it's practical value is quite limited.

Response: Thank you very much. According to your instructions, we have revised our scoring system. New simplified scores are given based on the coefficient of selected features. New results are listed in table 4 (Page 11-12 in the revised manuscript).

3. the authors did not mentioned other imaging methods which could be also useful in the differential diagnosis.

Response: Thank you very much. We have mentioned in background section that a study by Mueller et al found that no or septal enhancement and matrix calcifications on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) offered the strongest discriminating potential between HAE and ICC with a high sensitivity and specificity (line 83-87 in the revised manuscript). However, we did not compare the differential diagnosis between CEUS and CT/MRI. We have mentioned this in the limitations of the discussion section, and indicated that future research about comparing the diagnostic performance of CEUS and CT/MRI will be needed (line 306-307 in the revised manuscript).

4. in most of the cases both diseases need pathological evaluation but no data about it was included in the paper.

Response: Thank you very much. We have clarified that all HAE and ICC lesions were confirmed by pathologic evaluation after surgery. (line 189 in the revised manuscript)

5. the reference list is not properly written (the title of the journal is missing)

Response: Thank you very much. We have revised the reference styles referred to the journal's Submission Guidelines.
Response to Reviewer 2:

- The following sentence (statistical analysis) is unnecessary for the abstract: "The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and receiver operating characteristic (ROC) curves were calculated". It can be replaced by primary or secondary outcome measures.
  Response: Thank you very much. We have revised the sentence in the abstract as “diagnostic performance was evaluated”. (line 50 in the revised manuscript)

- There is no background information or description of the problem to support the study rationale in your abstract. You have only mentioned the study objectives in your abstract. I would add one or two sentences as the lead of the abstract to provide an introduction to the main study topic, to highlight the gap in knowledge and the motivation or rationale for the study.
  Response: Thank you very much. We have added background information as the lead of the abstract as “Misclassifications of hepatic alveolar echinococcosis (HAE) as intrahepatic cholangiocarcinoma (ICC) may lead to inappropriate treatment strategies. The aim of this study was to explore the differential diagnosis with conventional ultrasound and contrast-enhanced ultrasound (CEUS)”. (line 40-43 in the revised manuscript)

- More relevant key words are needed.
  Response: Thank you very much. We have added a key word: “Contrast-enhanced ultrasound”. (line 64 in the revised manuscript)

- This abbreviation is not previously defined in full in the text. Please note that all abbreviations (such as FLL) need to be defined in full at their first appearance in the text.
  Response: Thank you very much. We have revised the manuscript and checked that all abbreviations were defined in full at their first appearance in the text.

- Instead of "Materials and methods", please use "Patients and methods".
  Response: Thank you very much. We have revised the title as "Patients and methods". (line 98 in the revised manuscript)

- Please be more specific about "bileduct dilatation". Intra-hepatic or extra-hepatic biliary ducts? How did you define biliary ductal dilatation? Did you match for the patient's age?
  Response: Thank you very much. We have defined bile duct dilatation as “intra-hepatic bile duct &gt;3mm, or extra-hepatic bile duct &gt;8mm” (line 150-151 in the revised manuscript). We are sorry for the mistake that we did not match for the patient's age. We have revised the sentence in the revised manuscript (line 115 in the revised manuscript).

- Although you briefly mention the need for further studies, the statement is rather general. I suggest elaborating on this statement with a few directions for future research that are supported by your current results and would benefit the field.
  Response: Thank you very much. We have mentioned that “further prospective studies are necessary, especially to explore if prognosis correlates with the different enhancement patterns of HAE” in the manuscript, and added additional directions for future research as “Future research
about comparing the diagnostic performance of CEUS and CT/MRI will be also needed” in the revised manuscript. (line 304-307 in the revised manuscript)

- The quality of the provided is suboptimal with low signal to noise ratio.
Response: Thank you very much. We have improved the quality of images with the pixel of 300dpi.