Peer Review File

<mark>Reviewer A</mark>

Comment 1: The title needs to indicate the accuracy of combination of CEUS parameters and clinic-pathological characteristics to predict DCISM and the clinical research design of this study, i.e., a diagnostic test.

Reply 1: Thank you for your advice. We have changed the title to "The Diagnostic Value of Contrast-enhanced Ultrasound Combined with Clinicopathological Features in Microinvasive Ductal Carcinoma in Situ".

Changes in the text: See Page 1, line 3-4

Comment 2: In the abstract, the background did not explain why the authors adopted the combination of CEUS parameters and clinic-pathological characteristics to predict DCISM and what the current knowledge gap is, the authors did not describe the measurements of CEUS parameters and clinic-pathological characteristics, golden diagnosis of DCISM and how the diagnostic accuracy was measured in the methods, the results did not briefly describe the clinical characteristics of the patient sample, and the current conclusion needs to be tone down due to the small sample size of this study and no external validation of the predictive model.

Reply 2: Thank you for your advice. We have made changes in the abstract section based on the comments of the reviewer.

Changes in the text: See Page 2-3, line 29-81.

Comment 3: In the introduction of the main text, the authors need to review what has been known on the methods for the early diagnosis or noninvasive diagnosis of DCISM, why the authors need to combine both CEUS parameters and clinic-pathological characteristics, and what the clinical needs for this research focus are.

Reply 3: Thank you for your careful examination. We have made changes in the introduction section based on the comments of the reviewer.

Changes in the text: See Page 4-5, line 113-143.

Comment 4: In the methodology, the authors need to describe the clinical research design, sample size estimation, and how the CEUS parameters and clinic-pathological characteristics were measured. In statistics, please describe how the diagnostic accuracy was measured and what the threshold value of a good prediction model was. Please ensure P<0.05 is two-sided.

Reply 4: We agree with the reviewer's assessment. We have made corresponding changes throughout the methods section of the manuscript. Regarding the sample size assessment, we used pass software to use the AUC of US combined with pathological features derived from previous literature to diagnose DCISM with an AUC of 0.873(MA Ling, CHENG Ye, TANG Rong, et al. Pathologic and ultrasonographic characteristics of breast microinvasive ductal carcinoma in situ and analysis of its influencing factors[J]. Journal of the PLA Medical College,2022,43(09):949-953.) and an Alpha of 0.05 for bilateral testing, and

concluded that when the sample size of 6 cases of DCISM in the positive group and 66 cases of DCIS in the negative group was satisfied, the test efficiency could reach more than 90%, so the sample size of this study was sufficient.

Changes in the text: See Page 6, line 146-147; Page 7, line 190-191; Page 8, line 206-214.

Comment 5: Finally, please consider to cite several related papers: 1. Zhu M, Pi Y, Jiang Z, Wu Y, Bu H, Bao J, Chen Y, Zhao L, Peng Y. Application of deep learning to identify ductal carcinoma in situ and microinvasion of the breast using ultrasound imaging. Quant Imaging Med Surg 2022;12(9):4633-4646. doi: 10.21037/qims-22-46. 2. O'Keefe TJ, Harismendy O, Wallace AM. Histopathological growth distribution of ductal carcinoma in situ: tumor size is not "one size fits all". Gland Surg 2022;11(2):307-318. doi: 10.21037/gs-21-599. 3. Bonev VV. Ductal carcinoma in situ: a comprehensive review on current and future management for the surgeon and non-surgeon. AME Surg J 2021;1:27. 4. Zhao MR, Ma WJ, Song XC, Li ZJ, Shao ZZ, Lu H, Zhao R, Guo YJ, Ye ZX, Liu PF. Feasibility analysis of magnetic resonance imaging-based radiomics features for preoperative prediction of nuclear grading of ductal carcinoma in situ. Gland Surg 2023;12(9):1209-1223. doi: 10.21037/gs-23-132.

Reply 5: Thank you for your suggestions, we have cited recommended articles in the article.

Changes in the text: See Ref. 9, Ref. 19, Ref. 18, Ref. 20.

Reviewer B

1. If available, please update your reference list by including related literatures published within a year. Some of the references are outdated.

   Reply 1: We have updated as much as possible references to some of the literature published in recent years.

2. Please include the aim of the study in Background section of Abstract.

3. The author's name cited in text should be consistent with the reference.

4. If it is a "(A)(B)(C)(D)....." combined picture, the beginning of the Figure Caption needs an overview, followed by a caption of each subfigure.

5. Abbreviation should be spelled out the first time it is used in the Abstract/Highlight Box/Body Text/Figure/Table.

6. Numbers do not match Table 1.

   In terms of calcification, the presence of calcification was more frequent in the DCISM (60.9%, 14/23) than in the DCIS (59.1%, 39/66). The cases of DCIS and

7. Indicate which hospital it is.

   June 30, 2022 in our hospital. The inclusion criteria were as follows:(a) patients

Reply 2-7: Thank you very much for the review. We have made the necessary modifications based on the feedback.