Peer Review File
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Reviewer A

• The statement on page 1, sentence 9-10 ‘Most early cancers are classified as BI-RADS 4A….’ is misleading (no reference provided either). Is this on Screening mammography? Or ultrasound?
Reply 1: We appreciate the reviewer’s comment. The statement has been revised to clarify that BI-RADS 4A classification applies to ultrasound-based assessments. A reference to the ACR BI-RADS Atlas (5th edition) has been added to support this clarification.
Changes in the text:Page 1, lines 32–33:Original: "Most early lesions are classified as 4A or lower under the BI-RADS." Revised: "Most early lesions identified via ultrasound are classified as BI-RADS 4A or lower."

• Few criteria for BI-RADSA lesions have been mentioned in the ACR BIRADS atlas – such as lesions having circumscribed margins (which could appear to be atypical fibroadenoma to the radiologist); or lesions which could represent probable abscess. The likelihood of malignancy in BI-RADS 4A lesions is >2-10 %; biopsy is recommended and the ‘low-risk’ assessment is helpful to guide radiology-pathology concordance decisions.
Reply 2: Thank you for highlighting this. We have expanded the description of BI-RADS 4A criteria in the Methods section, including references to the ACR BI-RADS Atlas and additional studies. We also emphasized that biopsy remains the guideline recommendation despite the low malignancy risk.
Changes in the text: Page 4, lines 112–115: Revised:: "According to the ACR BI-RADS Atlas (11), BI-RADS 4A lesions typically exhibit one suspicious feature, such as circumscribed margins suggestive of atypical fibroadenoma or probable abscess. The malignancy likelihood for BI-RADS 4A is 2–10%, necessitating biopsy for confirmation (11,17,18)."

• According to a landmark study by Sickles et al 0.5%- 2% of circumscribed masses were found to be malignant. In several other studies it was found that irregular shape has ~ 70-73% association with malignancy, spiculated margins ~ 81-83% association with malignancy.
Reply 3:We appreciate the reviewer’s comment. This landmark study is very helpful to us.

• The definitions used for classifying lesions as BI-RADS 4a in this study are not clear- because the authors have said that ‘one suspicious’ feature if present was used to classify the lesion as BI-RADS 4A (sentence 103-106). The worst morphological feature is generally used to classify lesions, in which case it would be evident that most of the lesions which turned out to be malignant would have been classified as BIRADS 4 B or 4C based on morphology alone (without the need of CUES).
Reply 4: We acknowledge this concern. The classification criteria have been clarified to specify that lesions were classified as BI-RADS 4A based on the presence of only one suspicious feature (e.g.,

mixed echoes, posterior shadowing). This aligns with prior studies cited in the revised text.
Changes in the text:Page 4, lines 127–130: Revised: "Lesions with one suspicious ultrasound feature (e.g., mixed echoes, posterior shadowing) were classified as BI-RADS 4A, consistent with the ACR BI-RADS guidelines and prior studies (17,18). Lesions with multiple suspicious features were excluded to avoid overlap with BI-RADS 4B/C categories."

• Furthermore, in this study 25/52 BIRADS 4A lesions were malignant (51.9%)- this also casts a doubt on the categorization method and the expertise of the observer.
Reply 5: We agree that the high malignancy rate in our cohort is unusual. This may reflect stricter inclusion criteria (e.g., lesions confirmed by surgery) and regional epidemiological factors. A discussion of this limitation has been added to the Discussion section.
Changes in the text:Page 11, lines 343–346: Added: "The higher malignancy rate (48.1%) in our BI-RADS 4A cohort compared to the general population may reflect selection bias, as all lesions underwent surgical confirmation. Additionally, regional variations in breast cancer prevalence and diagnostic thresholds could contribute to this discrepancy."

• Also, it is known that magnification mammographic views are the gold-standard for evaluation of morphology of calcifications (high resolution ultrasound can detect calcification but cannot evaluate morphology)- we do not understand how micro-calcifications were classified as BIRADS 4A based on ultrasound. Lesion sizes also varied a lot- which may affect the evaluation and results.
Reply 6: We clarified that microcalcifications were assessed via high-resolution ultrasound, with suspicious morphology (e.g., clustered, irregular) prompting BI-RADS 4A classification. However, we acknowledge the limitations of ultrasound in evaluating calcifications compared to mammography, as noted in the revised text.
Changes in the text:Page 4, lines 130–133: Added: "Microcalcifications detected via ultrasound were classified as suspicious if clustered or irregular, following established protocols (12). However, ultrasound's inferior resolution compared to mammography for calcification morphology remains a limitation."

Reviewer B

Interesting idea of combining both CEUS and elastography
Clear and concise writing
Enjoyable read

Suggest
Make a specific note that this is strain elastography
Reply 1: Thank you for the suggestion. We have specified the use of strain elastography in the

Methods section.

Changes in the text: Page 5, line 161: Revised: "UE examination: Strain elastography was performed using the LOGIQ E9 system"

- include doppler vascularity data if available (if doppler is comparable to CEUS, then there may be an argument for combined doppler plus elastography)

Reply 2: Doppler data were collected but not analyzed in the original manuscript. We have added a supplementary table comparing Doppler findings with CEUS results to the Supplementary Materials.

Changes in the text:Page 8, lines 237–238: Added: "Doppler vascularity patterns were analyzed and compared to CEUS findings.

- outline a practical workflow for radiologists who want to combine CEUS with UE, and how they will practically manage lesions based on these features e.g. if CEUS suggests benignity and UE is suspicious, how does this affect eventual assessment?

Reply 3: A proposed workflow has been added to the Discussion section to guide clinicians in integrating UE and CEUS.

Changes in the text: Page 11, lines 356–360: Added: *"Practical Workflow: For BI-RADS 4A lesions, we recommend:Perform strain elastography (UE) to assess stiffness.If UE score ≥4, proceed to CEUS for microvascular evaluation. Upgrade to BI-RADS 4B if both UE and CEUS suggest malignancy; downgrade to BI-RADS 3 if either is benign.Biopsy lesions upgraded to 4B. This approach balances diagnostic accuracy and reduces unnecessary procedures."*

Reviewer C

I am deeply grateful for reviewing your excellent manuscript.

1) Conclusion “UE and CEUS technologies demonstrate significant diagnostic value for breast lesions, particularly for BI-RADS 4A lesions. Their combined application enhances diagnostic accuracy, helping clinicians better assess breast cancer and reduce unnecessary biopsies.”

→I completely agree with the author's argument.

The subject and method are adequate, and the results are robust. The high specificity of EU and the good sensitivity of CEUS are consistent with previous reports and are reasonable results. The analysis of the results is also spot on.

Here are some suggestions to improve this research paper:

2) The authors have created their own diagnostic criteria for UE. They cite a paper by Ito et al., but the criteria seem to be slightly different from the elasticity score proposed by Ito et al. If the diagnostic criteria are based on the elasticity score, please revise them. If they are original diagnostic criteria, please attach a diagram or typical images.

Reply: Thank you for the suggestion. Our diagnosis was mainly based on previous studies combined with our own clinical experience. We have made revisions. Thank you again for your review comments.

Changes in the text: Page 6, lines 179–180: Revised: " The diagnostic criteria for UE adopted the 5-point scoring system and improved based on clinical experience on…"

3) Please also attach a schematic or representative image of the CEUS diagnostic criteria.

Reply: Thank you for the suggestion. Our diagnosis was mainly based on previous studies combined with our own clinical experience. We have made revisions. Thank you again for your review comments.

Changes in the text: Page 6, lines 199–200: Revised: "The CEUS 5-point method was employed and improved based on clinical experience to…"

Let me further explain my thoughts.

4) I believe that needle biopsy for BI-RADS 4A lesions is overly invasive. However, contrast-enhanced ultrasound also requires venipuncture and administration of contrast agent, and I would think that performing it on all patients with BI-RADS 4A lesions is overly invasive.

Reply: Thank you for the suggestion. It is true that angiography puncture can also cause invasive damage, and further research is needed to explore the necessary timing of angiography.

Reviewer D

The manuscript titles diagnostic value of elastography and CEUS in characterising BIRADS 4a lesions. The concept is intriguing; however there has not been single figure of USG/ mammography/ Elastography/ CEUS in the manuscript.

The novelty of the study has not been adequately discussed.

The quantitative parameters of neither shear-wave elastography nor CEUS have been described

Results should be revised after combining the three modalities as USG+SWE vs USG+CEUS vs

SWE+CEUS vs USG.

That will enhance the value of the study.

Reply: Thank you very much for your comments. Thank you for providing us with the direction of research. We will also carry out forward-looking research in this area in the future to improve the value of these studies.