Peer Review File

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Comment 1 ： The paper is easy to read and clearly structured. The topic is in some way interesting, but the additional new information is limited to the already published papers. Some sentences contain poor English and should therefore be corrected by a native English speaker.

Reply 1: Thank you for your recognition and comments. First of all, compared with previous studies, our study has the following innovations ： (1) three imaging modes were combined; (2) the features of background parenchyma except the tumor itself were analyzed; and (3) factors influencing the upgrade of HR-I and HR-II were further analyzed. We will explain the innovation of this paper in detail in the Discussion section. Second, our article has been corrected by a native English speaker, here is the editorial certificate:

EDITORIAL CERTIFICATE

This document certifies that the manuscript listed below was edited for proper English language,grammar,punctuation,spelling,and overall style by one or more highly qualified native English speaking Editors at Yiji-to-Edit

MANUSCRIPT TITLE:

The value of imaging combined with clinicopathological features in the diagnosis of high-risk breast lesions

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*This certificate can be verified on www.uegesci.com.cn Documents receiving this certification should be Englisherady for publication .The authors should accept our suggestions and changes.

Comment 2: Abstract-Line 43: What do you mean with single?

Reply 2: Thank you very much for your question. We want to express that this study included a total of 230 HRLs in 230 women, there is only one lesion per patient.

Changes in the text: We have modified our text as 'We included 230 HRLs in 230 women in the study' (see Page 1, line 12).

Comment 3: Abstract-Line 43 to 44: sentence suggestion, The upgrade rate was higher in HR-I compared to HR-II (38.5% vs 4.1%, P<0.01).

Reply 3: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article.

Changes in the text: We have changed 'The upgrade rate (8.5% vs 4.1%) was higher in HR-I compared to HR-II (P < 0.01)' to 'The upgrade rate was higher in HR-I compared to HR-II (38.5% vs 4.1%, P<0.01)' (see Page 1, line 13).

Comment 4: Background-Line 78, You state that there are some limitations in other studies, but provide only one example, can you mention one more?

Reply 4: We are glad to mention one more limitation. In addition to the limitation we have mentioned, the current study also only focused on the imaging characteristics of the tumor without analyzing the background parenchyma.

Changes in the text: We added another example in the article as 'For example, the imaging characteristics used in the studies were limited to a single mode, and only the tumor's imaging features were analyzed, whereas the background parenchyma features were ignored' (see Page 3, line 48-50).

Comment 5: Background-There is already a lot of information about the different predictive characteristics. Which predictive characteristics were new in this study?

Reply 5: Thank you very much for your question. As I mentioned above, although previous studies have found many features for predicting upgrading, the features included were not comprehensive enough, especially in the image aspect, only the features of the tumor itself in one image mode were analyzed. Our study combined three

image modes for analysis and compared prediction efficiency of different modes. We also analyzed the features of BPE in addition to the tumor itself.

Changes in the text: We have modified our text as 'Our study included clinicopathological features and imaging features of three modes (breast ultrasound, mammography, and MRI), comparing the value of different features in predicting the upgrade of HRLs to better stratify the risk of upgrade and assist in clinical decisions. Furthermore, we analyzed the BPE of MRI to study the effect of breast parenchymal features on the upgrade' (see Page 3, line 50-53).

Comment 6: Material and Methods-Line 92, not necessary to mention number of patients here, this belongs to the results section.

Reply 6: We were aware of this problem and deleted the sentence from the article.

Changes in the text: We have modified our text as advised (see Page 3-4, line 65-66).

Comment 7: Material and Methods-Line 114: sentence suggestion, Immunohistochemical methods were used to determine the expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2), and the Ki-67 antigen.

Reply 7: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article.

Changes in the text: We have modified the sentence as 'Immunohistochemical methods were used to determine the expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2), and the Ki-67 antigen' (see Page 4, line 75-76).

Comment 8: Material and Methods-Line 118: sentence suggestion, High-risk lesion upgrade was defined as the presence of DCIS or invasive ductal carcinoma components at subsequent surgery based on histopathology (17).

Reply 8: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article.

Changes in the text: We have modified the sentence as ‘High-risk lesion upgrade was defined as the presence of DCIS or invasive ductal carcinoma components at subsequent surgery based on histopathology (16)’ (see Page 4, line 78-79).

Comment 9: Results-How many patients were excluded based on the exclusion criteria?

Reply 9: Thank you for your question. According to your request, we have modified the inclusion and exclusion criteria, and supplemented the number of excluded cases and the reasons for their exclusion.

Changes in the text: In the Materials and Methods section, we have modified our text as ‘We continuously retrospectively analyzed patients who met the following inclusion criteria in the Fudan University Cancer Hospital from January 2017 to March 2018: (1) the pathology of the biopsies (including hollow-core needle biopsy, vacuum-assisted biopsy, and open biopsy) showed HRLs, including ADH, ALH, sclerosing adenosis (including radial scarring and complex sclerosing adenosis), intraductal papilloma, mucocele-like lesions, and FEA; (2) complete imaging data of the three modes—breast ultrasound, mammography, and MRI—are available; (3) all imaging examinations were performed before biopsy; and (4) short-term follow-up was performed for six months to one year. The exclusion criteria included (1) poor image quality, and (2) lack of follow-up’ (see Page 3-4, line 58-65).

In the Results section, we have modified our text as ‘During the study period, 274 HRLs in 274 patients were diagnosed by biopsy. Of these lesions, 10 were excluded for poor image quality, and 34 were excluded for lack of follow-up. Therefore, 230 HRLs in 230 women were included in the study’ (see Page 6, line 112-114).

Comment 10: Results-Line 137: What do you mean with single?

Reply 10: As mentioned above, we want to express that this study included a total of 230 HRLs in 230 women, there is only one lesion per patient.

Changes in the text: We have modified our text as ‘Therefore, 230 HRLs in 230 women were included in the study’ (see Page 6, line 113-114).

Comment 11: Results-Line 141: change ‘reoperation’ in ‘surgery’

Reply 11: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article.

Changes in the text: We have modified our text as advised (see Page 6, line 117).

Comment 12: Results-Line 143: change ‘reoperation’ in ‘surgery’

Reply 12: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article. In addition, we changed other ‘reoperation’ into ‘surgery’ in the paper.

Changes in the text: We have modified our text as advised (see Page 6, line 119; Page 9, line 177; and Page 11, line 322/336).

Comment 13: Results-Line 154: remove one dot.

Reply 13: Thank you for providing the professional suggestion. We have accepted your opinion and modified it in the article.

Changes in the text: We have modified our text as advised (see Page 6, line 130-131).

Comment 14: Results-Line 161-163: Part of the material and methods

Reply 14: Thank you for your thoughtful suggestion. We have realized the problem and moved the sentence to the right place. We have switched ‘Histopathologic Analysis’ and ‘Image Interpretation’ and modified adjacent context to make it logical.

Changes in the text: In the Materials and Methods section, we have modified our text as ‘Because of the significant difference in the upgrade rates between HR-I and HR-II lesions, we researched the relationship between the imaging features and the upgrade rates of all HRLs, HR-I, and HR-II lesions, respectively’ (see Page 4-5, line 85-88).

In the Results section, we have modified our text as ‘The correlation of imaging features in relation to the rate of upgrade among all HRLs, HR-I, and HR-II lesions is shown in Table 3’ (see Page 7, line 138-139).

Comment 15: Discussion-Overall, I miss the added value of this study in comparison with all other studies which were performed on this topic.

Reply 15: Thank you for your thoughtful suggestion. We have added the elaboration about innovation in this paper.

Changes in the text: In the Discussion section, we have added ‘Because the upgrade rates of HR-I and HR-II are very different, it is important to select the correct follow-up management. We further investigated the factors influencing the upgrade in the HR-I and HR-II groups and found that only BPE of MRI had predictive value in both groups, which can guide the clinical selection of surgery or follow-up’ (see Page 9, line 179-183) and ‘In brief, our study has the following three advantages compared with other studies. First, we combined three imaging modes of mammography, ultrasound, and MRI for analysis, comparing the prediction efficiency of each mode. We found that MRI had the highest predictive efficacy, suggesting the importance of MRI follow-up for patients with HRLs. Second, we added features of breast parenchyma and found that BPE was an independent factor in predicting upgrade. Third, previous studies have proved that HRLs with AH are more likely to upgrade. To better determine the need for surgery, we further analyzed the factors that predicted the upgrade of HR-I and HR-II. We found that BPE was the only predictor of both groups and the odds ratio of BPE was highest. Based on this, we can infer that HR-I lesions with moderate to marked BPE are more suitable for surgery, and HR-II lesions with minimal to mild BPE can be considered for regular follow-up’ (see Page 10-11, line 209-218).

Reply 16 :In addition, we have modified some of the sentences in order to fit the number of words in the abstract.

Changes in the text: We have modified our text as ‘AUCs for predicting upgrade in mammography, ultrasound, and MRI were 0.606, 0.590, and 0.913, respectively, indicating that MRI diagnosis was significantly better than mammography and ultrasound ($P < 0.001$)’ (see Page 1, line 20-22).