

## Peer Review File

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### Reviewer A

Comment 1: For surrogate subtypes of invasive carcinoma, WHO recognized consensus of 13th St. Gallen International Breast Cancer Conference (2013).

Reply 1: Considering the Reviewer's suggestion, we have modified our text as advised.  
Changes in the text: Page 6, line 150, 155-162.

Comment 2: Surrogate molecular subtype is used for invasive breast carcinoma only, but in the table 3 and 4, it includes all non-invasive carcinomas.

Reply 2: We are very sorry for our negligence of molecular subtype and we have made correction.

Changes in the text: ①Page 23, line 549 (Table 3). ②Page 25, line 557 (Table 4). ③Page 2, line 53 and 56. ④Page 9, line 246 and 248.

Comment 3: Have any patients received neoadjuvant hormonal and HER2 targeted therapy?

Reply 3: No patient in our study received neoadjuvant hormonal and HER2 targeted therapy.

Changes in the text: None.

Comment 4: How's the rate of pathological complete response for those patients received neoadjuvant therapy?

Reply 4: A total of 39 patients received neoadjuvant chemotherapy and 9 of them (23.1%) achieved complete pathological responses.

Changes in the text: Page 7, line 199-200.

Comment 5: "lymphovascular invasion" is recommended to replace "carcinovascular invasion".

Reply 5: It is really true as Reviewer suggested. We have modified this terminology.

Changes in the text: ①Page 3, line 66. ②Page 11, line 293, 295 and 305. ③Page 14, line 389. ④Page 23, line 549 (Table 3) ⑤Page 25, line 557 (Table 4). ⑥Page 26, line 568 (Table 7). ⑦Page 27, line 571 (Table 8). ⑧Page 31, line 597 (Figure 6). ⑨Page 32, line 598 (Figure 6).

### Reviewer B

Comment 1: The article is not written in readable English.

Reply 1: We are very sorry for our incorrect writing and we have made some adjustments. We have modified terminology, for example, "lymphovascular invasion" was replaced by "carcinovascular invasion". We have adjusted the surrogate subtypes of invasive carcinoma based on consensus of 13th St. Gallen International Breast cancer Conference (2013).

Changes in the text: ①Page 3, line 66. ②Page 11, line 293, 295 and 305. ③Page 14, line

389. ④Page 23, line 549 (Table 3)⑤Page 25, line 557 (Table 4). ⑥Page 26, line 568 (Table 7). ⑦Page 27, line 571(Table 8).⑧Page 31, line 597 (Figure 6). ⑨Page 32, line 598 (Figure 6). ⑩Page 6, line 150, 155-162.

Comment 2: Using the first tumor as the index tumor to categorize metachronous breast cancer may not be appropriate

Reply 2: To compare the characteristics of unilateral breast cancer, we focused on the first tumors of bilateral breast cancer. Considering the Reviewer's suggestion, Index tumor was replaced by the first tumor.

Changes in the text: ①Page 2, line 53 and 56. ②Page 3, line 64 and 66. ③Page 6, line 148. ④Page 8, line 204, 218, 220, 227-229. ⑤Page 9, line 232, 235, 238-239, 245, 247, 255. ⑥Page 10, line 279, 285. ⑦Page 11, line 294, 296, 302, 306. ⑧Page 13, line 351, 357, 366. ⑨Page 14, line 388, 390, 400. ⑩Page 15, line 420-421. Page 31, line 595.

Comment 3: Table 4 is not indicating the characteristic of "the same" patient.

Reply 3: It's true that Table 4 compared 1st and 2nd tumor characteristic in BBC patients. We have made correction according to the Reviewer's comments.

Changes in the text: ①Page 2, line 57-58. ②Page 9, line 242, 251-252. ③Page 13, line 348-349. ④Page 24, line 556.

Comment 4: Try to avoid coining words such as "carcinovascular" as is not a universal term publically used.

Reply 4: "Carcinovascular invasion" was replaced by "lymphovascular invasion".

Changes in the text: ①Page 3, line 66. ②Page 11, line 293, 295 and 305. ③Page 14, line 389. ④Page 23, line 549 (Table 3)⑤Page 25, line 557 (Table 4). ⑥Page 26, line 568 (Table 7). ⑦Page 27, line 571(Table 8).⑧Page 31, line 597 (Figure 6). ⑨Page 32, line 598 (Figure 6).

Comment 5: The female surgeons only contributes to less than 10% of the cases and their contribution to poor disease-free survival is questionable.

Reply 5: We added "Gender of surgeron" as a categorical variable into Multivariate Cox proportional hazards model for DFS, but it showed  $P > 0.05$ , which was not considered statistically significant.

Changes in the text: None.

Other changes:

1. Page 23, line 549 and Page 25, line 557, " Tripple " was corrected as "Triple"

### **Reviewer C**

Comment 1: The data must be compared to the overall Chinese breast cancer patients data whether that have difference with this single institution data.

Reply 1: At present, there are few articles based on the data of Chinese bilateral breast cancer patients. But we still compared our results with those studies. For example, Page 12, line 326-327; Page 13, line 358-359,363-366; Page 14, Line 390-395. And we added

other comparisons, see Page 12, line 318-321,337-342; Page 13, line 355-358; 371-374. Changes in the text: ①Page 12, line 318-321. ②Page 12, line 337-342. ③Page 13, line 355-358. ④Page 13, line 371-374.

Comment 2: For survival analysis, it would be helpful to show univariate analysis results first then show multivariate analysis.

Reply 2: Univariate COX regression analysis was performed on the all clinicopathological features of the patients. Considering that this paper already has 9 tables and 6 figures, it would be too long if we add another table. We have presented the main results of univariate COX regression analysis in the form of words, see Page 10, line 279-283. So we didn't add extra tables in the article.

Changes in the text: Page 10, line 279.

Comment 3: It should be adjusted for matched control of treatment choice when they showed same stage or molecular characteristics.

Reply 3: It is really true as Reviewer suggested that matching is very important. We plan to write another article to elaborate on the characteristics of Bilateral Breast Cancer patients after matching.

Changes in the text: None.