Author’s response to reviews

Title: Screening mammography for second breast cancers in women with history of early-stage breast cancer: Factors and causes associated with non-detection

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Dear Editor and reviewers,

We thank the Editor and reviewers for valuable comments. We have provided point-to-point responses to the comments below.

Please let me know if you require any additional changes or information.

Reviewer #1:

Robert E Lenkinski, Ph.D. (Reviewer 1): This is a solid manuscript that examined a large population of women who had undergone breast surgery for second breast cancers. Of 188 patients who met the inclusion criteria for the study of the 188 patients 74 showed a non-detectable lesion on mammography. The primary factors that caused non-detection were overlap with dense breast tissue and the characteristics of the primary cancer. The statistical analysis is solid and the conclusions presented are supported by the results reported.
Reviewer #2:
Takahito Nakajima, M.D., Ph.D (Reviewer 2): The authors reported the factors and causes associated with non-detection of second breast cancers on screening mammography in women with a personal history of early-stage breast cancer (PHBC). This manuscript includes a fatal statistical misunderstanding of their data. Some critical issues should be discussed with regard to the methods to have a final diagnosis of secondary in-breast cancer and the duration between final diagnosis of secondary in-breast cancer and MMG.

Major issues:

Reviewer comment #2-1) Tables

1) The presentation of the tables is strange, which may be related to an inaccuracy of statistical analyses. Table legends are needed for readers to understand these analyses.

2) Univariate logistic regression analysis was employed for the statistical analyses in Tables 1 and 2. However, I feel that Chi square test would be preferable since each analysis can be more simplified in Tables 1 and 2. For example, "Symptom of PBC" was divided into two groups, "No" and "Yes", while the MMG detection included "No" and "Yes". This 2 x 2 table can be analyzed by a Chi square test.

3) Please reconsider these analyses in the tables. This misunderstanding might derive from the table presentation itself. Please see an attached file that demonstrates the table presentation using Table 3 as an example. Other two tables have similar problems.

4) Calculation of the incidences presented by "%" appears improper. For example, in Table 3, although the number of fatty patients, "71" was divided by the total number of non-detection, the number of fatty patients, "71", should be divided by the total number of patients with fatty breast. In my opinion, this misunderstanding obscured the statistical errors.

--> Response to comment #2-1) Thank you for your valuable comment. As recommended, we re-analyzed the association between variables and non-detection using chi-square or Fisher’s exact test for categorical variables and t-test or Mann-Whitney test for continuous variables, instead of univariate logistic regression. The results from re-analysis were almost similar, and revised through Table 1-3. And we revised the calculation of the incidences presented by “%” in the Tables, according to your suggestion. We also revised the manuscript in accordance with these changes.

Reviewer comment #2-2) Clarification of the final diagnostic methods of secondary in-breast cancer
In this manuscript, the methods of final diagnosis could not be found. Please clarify the methods used for the final diagnosis.

--> Response to comment #2-2) As your recommendation, we added the following statement in the results: “The final diagnosis of the second breast cancers was based on surgery (n = 172), core needle biopsy (n = 13), or fine needle aspiration (n = 3).”
Reviewer comment #2-3) Investigation of the duration between final diagnosis of secondary in-breast cancer and MMG.

The short duration between final diagnosis and MMG acquisition would contribute to the high detectability of secondary in-breast cancer on MMG. The authors should investigate the correlation between the duration between the final diagnosis and the acquisition of MMG.

--> Response to comment #2-3) Thank you for comment. We further analyzed the correlation between the duration between the final diagnosis of second breast cancer and the acquisition of mammography. As a result, no significant difference was observed in the time interval between two groups (p=0.306). We added the following statement in the results: “There was no statistically significant difference in the time interval between the final diagnosis of second breast cancers and mammography.”