Author's response to reviews

Title: Identification of Apoptosis-related Biomarkers of Ductal Carcinoma in situ with Microinvasion of the Breast

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The attached paper titled “Identification of Apoptosis-related Biomarkers of Ductal Carcinoma in situ with Microinvasion of the Breast” has been carefully reviewed by an experienced medical editor whose first language is English and who is specialized in the editing of papers written by physicians and scientists whose native language is not English.

Answers to the reviewer 1

Thank you for your comments and we are pleased that you are interested in our paper. We have replied to your questions, one by one, below; we hope that you will find our responses adequate. Within the manuscript we have used blue font to distinguish those parts that apply to your queries.

1. The title has been changed to: Identification of Apoptosis-related Biomarkers of Ductal Carcinoma in situ with Microinvasion of the Breast. Additionally, the short title has also been changed to: Apoptosis-related biomarkers in DCIS-Mi.

2. The detection rate of DCIS, including DCIS-Mi, is increasing rapidly via the use of mammography screening. We think this fact is very important for the clinical background concerning DCIS and DCIS-Mi.

3. We have changed the sentence as follows: Identification of any differences in the biological parameters between DCIS to DCIS-Mi is very important for improving our understanding of the nature of the progression from DCIS to invasive ductal carcinoma.

4. Because of word limitations, in the Abstract we were unable to mention all the methods used in our study. Instead, we used the following phrase to get around this: “mainly through the use of immunohistochemistry”.

5. Page 5: In this first paragraph we only mention about the increasing detection rate of DCIS, including DCIS-Mi, through the use of mammography screening. We maintain that this fact is very important for the clinical setting of DCIS and
DCIS-Mi.

6. P5, L 16; Thank you. We have changed ‘variation’ to ‘morphology’.

7. P6, last 3 lines; This last sentence is integral to our hypothesis and therefore we have left this sentence in the Introduction.

8. P7; Thank you. We have now presented the information in this section in a more logical order.

9. We have changed it to: The histological diagnosis was made by 2 specialized pathologists.

10. Page8; Thank you for these helpful suggestions.
    We have changed ‘prepared’ to ‘mounted’.
    We have changed ‘adhesive-coated slides’.
    We have changed “Sections were” to “The sections were”.
    Retrieval buffer at pH 9 was used for survivin; the buffers used for the other antigens are mentioned in Table 1.
    The “previously published” has been changed to “previously described”.
    We have changed ‘Netherland’ to ‘Netherlands’.
    All of the immunohistochemical details are presented in Table 1, and therefore we do not feel that any change is necessary.

11. Page 9, Line 2; we have specified the type of alcohol used in the dehydration.
    Line 16-17, we have changed to: To quantitate apoptosis, the mean number of……

12. Page 10;
    Paragraph 2 has been moved to the beginning of the Discussion.
    We have changed ‘Exam’ to ‘examine’.

13. Page11; we have changed ‘previous’ to ‘previously’.

14. Page 12; Lines 3-5: We feel that it is best to leave this statement here. If we move it to the Discussion and it will make the discussion more complicated.
15. Page 13: Line 3: we have changed ‘Therefore’ to ‘Hence’.

16. Page 14: end of second paragraph: we have changed ‘balance’ to ‘specific interaction’.

17. Reference 24: We have used Endnote to edit the references and we have checked all references again very carefully. We apologize for misspelling the authors’ name and have corrected it.

We hope we have addressed all of the issues satisfactorily. Thank you for your consideration.

Sincerely,

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Thank you for your comments and we are pleased that you are interested in our paper. In reply to your two specific points:

1. Any differences in expression levels of survivin and other biomarkers might help predict the presence of microinvasion in the ductal component of the lesion. This was the basic hypothesis on which we designed our study and is therefore explained at the end of the Introduction and also reiterated in the Discussion.

2. Cytoplasmic and nuclear staining were both visible in the tumor cells. However, we did not mention the membrane staining in our paper. Thank you for your comment; we realize that this intracellular localization of survivin is important and reflects the future direction of our interests.

We hope we have addressed these issues satisfactorily. Thank you for your consideration.

Sincerely,

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