Author’s response to reviews

Title: A pilot evaluation of magnetic resonance imaging characteristics seen with solid papillary carcinomas of the breast in 4 patients

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Version: 2 Date: 28 Jul 2016

Author’s response to reviews:

Dear Editor and Reviewers:

We are deeply grateful to the insightful comments and suggestions made by the reviewers on our manuscript. We have made revisions accordingly by taking account of each and every comment and suggestion by all reviewers. The revised portions (or portions we’d like to draw attention to from our responses) in the manuscript have been highlighted in yellow. After revising as suggested, we believe that the description of MRI findings in this manuscript have been improved significantly to present the rare type of breast cancer. Detailed point-by-point responses to each comment by the reviewers (in blue font) are provided below.
Response to editor

Comment 1: Were all of the 4 included SPCs considered in situ disease, or did any of them exhibit invasion? Were they differentiated in situ versus invasive?

Author: All of the 4 included SPC cases are considered in situ disease based on pathology. We added this description in the revised manuscript and please see line 61-63: “All patients were diagnosed as SPC in situ by pathology after breast conserving therapy (case 2) or modified radical mastectomy (case 1, 3, and 4).”

Comment 2: Were any or all of them associated with a mucinous component on pathology?

Author: Yes, There were 2 cases associated with a mucinous component on pathology.

We added this description in the revised manuscript and please see Line 105-106: “Case 2 and 4 were associated with a mucinous component on pathology.”

Comment 3: Can authors provide explanation of why choline peak is absent? Could this be a limitation of lesion size (at least for 2 tumors measuring only 8 mm)? Would be nice to see imaging for all 4 cases, and include the choline peak for the larger 2 tumors. pg 8, line 143 states that lack of Cho peak is not a typical characteristic of invasive breast cancer - what about in situ cancers?

Author: Thank you for the comment.

We had explained the reason of absent of choline peak in the revised manuscript and please see Line 156-161: “ Although Malignant lesions are more likely to show high levels of choline-containing compounds compared to benign or normal breast tissues [10], it has been reported that low-grade tumor may contains low level of choline-containing compounds [10,17,18]. We speculated the failure to detect choline in these four lesions might be related to their low grade nature that tumor cells grow with intervening stromal cells [18,19].”

We provide another larger 2 tumors MRS imaging as suggested.

Comment 4: All figures should have arrows clearly labeling what the legend is describing
Author: Thank you for the comment. We added arrows as recommended.

Response to Reviewer 1

Comment: This article is written very nicely on the MRI findings of a rare type of breast tumor. The number of cases that have been presented in this article is low; however, this can be explained by the rare nature of this type of tumor. Even with this limited number of cases, the description of MRI findings are useful for other investigators and clinicians who work in breast cancer imaging.

Author: Thank you so much for the comment. It is the goal of this pilot study to evaluate the magnetic resonance imaging characteristics of solid papillary carcinomas of the breast.

Response to Reviewer 2

Comment 1: Descriptions on how the patients were diagnosed and included in the study as well as why breast MRI performed for these patients would give a better understanding for the patient selection. Also, what were the findings in other imaging modalities (mammography and sonography)?

Author: Thank you for the comment. In this study, we focused on the MRI characteristics of SPC partially due to lack of findings in other image modalities. In the revised manuscript, we added on descriptions of the diagnosis, please see Line 68-69: “All patients had a unilateral lesion that cannot be identified by either mammography or ultrasound, where MRIs were used for diagnosis instead.”

Comment 2: Some background information regarding MR spectroscopy would be beneficial for reader's understanding of the significance in application of MRS as it is not routine protocol in breast MRI in the U.S.
Author: Thank you for the comment. 1H MRS has shown promising results for evaluating breast cancer, Choline-containing compounds are the major components of cell membrane required for structural stability and cell proliferation.

We added as recommended in the revised manuscript and please see Line 87-89:

“As 1H MRS has become an adjunct to dynamic contrast enhanced MRI (DCE-MRI) in the clinical evaluation of breast lesions [10], MRS is added to our protocol to investigate the performance of MRS in SPC diagnosis.”

Comment 3: The authors briefly mentions lymph node status. Since there are only four patients, it could be helpful to include staging of the patients and discuss surgical management (i.e. lumpectomy versus mastectomy, surgical margins, axillary lymph node dissection versus sentinel lymph node dissection, etc.). Also how were these patients followed post treatment when the authors commented that there was no metastasis or recurrence at the one year follow up. Were they only followed up to a year or was that at the time of the termination of the study?

Author: We added the staging of the patients and surgical management as recommended in the revised manuscript and please see Line 61-64: “All patients were diagnosed as SPC in situ through pathology after breast conserving therapy (case 2) or modified radical mastectomy (case 1, 3, and 4). Stage of the patients were PT1N0M0 (Case 1 and 3) and PT2N0M0 (Case 2 and 4) indicating no lymph nodes involvement.”

Unfortunately, the following up data of these patients such as metastasis or recurrence are not available up to date yet.

Comment 4: Some of the MRI BI-RADS descriptors need to be corrected.

We changed as recommended in the revised manuscript and please see Line 120: heterogeneous in cases 2.

Legend Line 306, 313: iso-hyper
Comment 5: If the authors are speculating why the ADC value is relatively higher in SPC, then it needs to be supported with why they think so, perhaps with an illustration. Also, in literature, the normal breast parenchyma and benign lesions are shown to have higher ADC values.

Author: Thank you for the comment. We added illustration in the revised manuscript and please see Line 148-152:

“Higher ADC values are associated with well-differentiated tumors, normal breast parenchyma or benign conditions [14,15]. Woodhams [16] found ADC values in Mucinous Cancer to be higher than those of benign tumors such as fibrous adenomas and attribute the high ADC values to relatively free motion of water molecules in mucin pool than in the interstitium of fibrous adenomas.”

Comment 6: Ranges of radiologists experience may be appropriate. Also are they dedicated breast radiologists?

Author: LN Z, AL L, and ZJ L are all dedicated breast radiologists who has 10 years, 20 years and 25 years of clinical experience respectively.

Comment 7: Figures would benefit from having arrows pointing towards the findings. Also there is a typo (figure 2A). Also, for figure 2, the mass may be seen as irregular mass than oval. If this is due to imaging slice selection, a better image selection would be helpful.

Author: Thank you for the comment. We changed the imaging slice as suggested on Figure 2.