Author's response to reviews

Title: Diagnostic assessment by dynamic contrast-enhanced and diffusion-weighted MR in differentiation of breast lesions under different imaging protocols

Authors:

Hongmin Cao (hmcai@scut.edu.cn)
Lizhi Liu (liulizhidoc@163.com)
Yanxia Peng (pengyanxia1226@126.com)
Yaopan Wu (wuyp@sysucc.org.cn)
Li Li (li2@mail.sysu.edu.cn)

Version: 5 Date: 13 February 2014

Author's response to reviews: see over
Dear Prof. Beatriz Adrada:

On behalf of the coauthors of Manuscript ID MS: 3281082791112323, we appreciate you very much for your decision to revise our manuscript above. We are also grateful to the reviewers for their helpful comments on our manuscript, which prompt us to examine our manuscript thoroughly. Authors of the manuscript have been required to look through the manuscript to avoid any errors. Following the suggestion from Editorial Office, we have also copyedited the paper to improve its style of written English by the help of Edanz. The paper was also reformatted to follow strictly the Instructions for authors by BMC Cancer.

Our manuscript has gone through third strict peer-reviews and revisions. We have also revised the title into: Diagnostic assessment by dynamic contrast-enhanced and diffusion-weighted magnetic resonance in differentiation of breast lesions under different imaging protocols. We hope our manuscript could meet the requirements of your Journal. Now we resubmit the revised manuscript and look forward to its acceptance by BMC Cancer!

Very best regards

Sincerely Yours,

Li Li, PhD, MD
Sun Yat-sen University Cancer Center

The following are our point-by-point response to the comments of reviewers and the Editorial request:

1) Reformat the current section labeled as Results to that of Results and Discussion, or include a separate "Discussion" section.

We have reformatted the Conclusion section into two sections of Conclusion and Discussion at Page 19-20.

2) Move the discussion of the study limitations (that is currently in the Conclusion section) to the Results and Discussion or "Discussion" section, rather than introducing this for the first time in the Conclusion section. Likewise, the Conclusion section is very lengthy, and some of the contents of the current Conclusion section should be moved to the Results and Discussion or "Discussion" section.

We have revised the paper accordingly by adding a new section of Discussion.

(3) Reformat the paper to being DOUBLE-spaced and not single-spaced.

The paper has been formatted to being double-spaced.

(4) Re-check all of their reference formatting, as many references have an ‘et al.’ reference formatting styles in their reference section that do not comply with the BMC Cancer Instructions for authors that clearly states ‘Citations in the reference list should include all named authors, up to the first 30 before adding ’et al.‘.
The reference list has been revised carefully to follow the guideline of BMC Cancer.

Referee: 1

This study investigated the prognostic capabilities of image characteristics, estimated from two image modalities, DWI MRI and DCE-MRI for breast masses. Similar researches have been reported early. One of the main contributions of this paper is that the medical data was evaluated in the second patient group, though the later one was not obtained under the same imaging protocol to the first one. The author also suggested three critical questions related to the discrimination power of the data and analyzed them individually. The paper are well formatted and clearly presented. The experimental results are nice in that the false positive is largely decreased. The main findings are important to those with closely related research interests. Therefore, I recommend accepting it after minor essential revisions, listed in bellow:

1. **The title did not accurately in defining the two patients group datasets**
   We appreciate the reviewer 1 for his/her careful comments. We have revised the title as: Diagnostic assessment by dynamic contrast-enhanced and diffusion-weighted MR in differentiation of breast lesions under different imaging protocols.

2. **The author should elaborate more on the medical implication and method advantages/disadvantages in Conclusion.**
   Our experiments developed a multi-parametric model combining ADC and other multi-sided characteristics. This model provided a high accuracy both in 1.5 T and 3.0 T for differentiation of benign and malignant breast lesion. This may be useful for building a CAD system combining of ADC value, morphological, and dynamic contrast-enhanced features to help radiologists in classifying breast lesions on MRI. Our study has some limitations. The databases of 3.0 T group with sample size of 95, is not sufficiently large enough to allow extracting a strict model statistically. In current study, we built the prediction models based on 1.5T patients and tested it on 3.0 T patients. In the next stage of our studies, it will be necessary to collect more data and build a model based on MRI at 3.0 T. We have added a short paragraph in conclusion to summarize the findings reported in this paper.

3. **Remove the vertical line in Tables unless necessary.**
   We have reformatted all the four Tables in the current version.

4. **The classification model used in paper should be described simply.**
   We have added a short introduction on the classification models in Appendix 2.

5. **The author should elaborate more on the Discussion Section to stress on the medical implications.**
   We have added a short paragraph in conclusion to summarize the findings reported in
this paper.

Referee: 2

1. Paper is mainly an application study of the existing algorithms, and lacks the sufficient comparison with other the previous work.
   We have added a short paragraph in Introduction to summarize previous works in breast lesion classification.

2. Minor Essential Revisions
   In the third paragraph of “Materials and Methods”, the word “exclusion” is used twice in the statement of “Patients were excluded from the trial for any of the following exclusion criteria.” It is advised to remove the word “exclusion” or replace it with its synonym.
   We appreciate the reviewer 2 for his careful comments. We have corrected the errors and finished proofreading of the draft thoroughly.

3. In the Figure1.Overview of System, the layout of charts is not very beautiful. A type of Tree layout from top to down may be better, which is more visual, clear and easy to read.
   We thank the Review for this nice suggestion. We have reproduced the Figure 1 according to the Reviewer 2’s suggestion.

4. The term of ADC is referred in the first paragraph of Abstract, which isn’t given a full explanation until Introduction. It may cause an understanding obstacle for a person who is unfamiliar with this field. It is advised to add its full name at the beginning.
   We have corrected this error by adding full word for the abbreviation.

5. The training group and testing group are based on different Tesla. Can you give a specific explanation of its reasons and significance for why we need to do experiments on ? What’s more, Is there a possibility collecting data(B) with training group 3.0 Tesla and testing group 1.5 Tesla? When (A) the training group is based on 1.5 Tesla and the testing group is based on 3.0 Tesla. If it is possible, are the results of (B) similar to (A)’s results?
   Although 1.5T MRI scanners are popular in clinical practice currently in China, 3.0T systems are becoming increasingly used for MR imaging of breast. The changing of magnetic power between 1.5T and 3T MR systems can influence the scanning time, image quality, contrast, and other imaging parameters, including signal-to-noise ratio, contrast-to-noise ratio, spatial resolution, sequence acquisition time and ADC value. The influence of imaging protocols on the diagnostic performance was rarely reported, and current study fill the gap. We have added explanation in revised manuscript.
   As 1.5 T group had more patients than 3.0 T group (234 patients vs. 95 patients), we selected 1.5 T group as a training group to build the prediction models. We very
thank the reviewer’s comments. We also redone the experiments by selected 3.0 T group as training group, and tested it by 1.5 T group. The results were show in the following Table 1.

**Table 1.** Diagnostic performances of classification model by Support Vector Machine on different feature subsets. The 3.0 T group was selected as training group, and tested it on 1.5 T group. Due to the limited sample size of 3.0T patients group, the biases are large and the prognostic performances were unsatisfactory. We are currently working on expanding the database.

<table>
<thead>
<tr>
<th>Classifier</th>
<th>Feature subset</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Accuracy</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVM</td>
<td>Morphology</td>
<td>0</td>
<td>1</td>
<td>62.19</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Morphology+Texture</td>
<td>0</td>
<td>1</td>
<td>62.19</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>ADC+SER</td>
<td>0.54</td>
<td>0.971</td>
<td>80.72</td>
<td>0.755</td>
</tr>
<tr>
<td></td>
<td>Morphology+Kinetic</td>
<td>0</td>
<td>1</td>
<td>62.19</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Morphology+ADC</td>
<td>0.16</td>
<td>0.837</td>
<td>68</td>
<td>0.579</td>
</tr>
<tr>
<td></td>
<td>Morphology+Texture+Kinetic</td>
<td>0</td>
<td>1</td>
<td>62.19</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Entire*%</td>
<td>0.154</td>
<td>0.846</td>
<td>65.46</td>
<td>0.556</td>
</tr>
</tbody>
</table>

Remark 1: Entire*% refers to using entire feature set, i.e., Morphology+Texture+Kinetic+ADC, and the subscript*% denotes the increased ratio from Morphology+Texture+Kinetic to Morphology+Texture+Kinetic+ADC.

6. The meaning of Scenario 2 is that ADC is highly diagnostic and it can improve the performance of classification. Does it need to consider other feathers’ influence? If every feather’s combination with feather i has a good or bad effect on the classification, it can be calculated by a contribution function designed by ourselves. We then can get every feather i’s function value and a sorting table. The paper will be more enriched with the analysis of the items in the sorting table.

We appreciate the valuable comments from the Reviewer 2. In Scenario 2, we analyzed the contribution of ADC when adding it with other feature types, including kinetic feature of SER, morphology, and combination of morphology, texture with kinetic feature. By the simple add-and-remove scheme, ADC is shown to be highly diagnostic. For example, the specificity was increased from 0.445 to 0.630 when adding ADC to morphology, 0.611 to 0.685 when adding ADC to combination of morphology, texture with kinetic feature. An enriched analysis of contribution function for each feature is a valuable suggestion. However in our experiment, the sample size is in limited and therefore the bias in estimating the contribution value will be large. We will consider this nice comment in analyzing our expanding database of breast cancer patients.

Again, we thank the Reviewers and the Editor for their constructive comments and positive remarks.