Author's response to reviews

Title: An evidential reasoning based model for diagnosis of lymph node metastasis in gastric cancer

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Author's response to reviews: see over
Reply to the reviewers’ comments

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Paper: An evidential reasoning based model for diagnosis of lymph node metastasis in gastric cancer

Authors: Zhi-Guo Zhou, Fang Liu, Li-Cheng Jiao, Zhi-Long Wang, Xiao-Peng Zhang, Xiao-Dong Wang and Xiao-Zhuo Luo

Journal: BMC Medical Informatics and Decision Making

Based on the comments from Editorial team and the reviewers, we have revised the paper carefully. Moreover, the revised contents are highlighted in red font in the revised version.

1. Reply to Editor-in-Chief

<table>
<thead>
<tr>
<th>Number</th>
<th>Comment</th>
<th>Response</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns. We also recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service.</td>
<td>Thanks a lot. Agree and revised. We have revised the manuscript carefully according to the comments of Editorial team and the reviewers. We have asked several colleagues who are native English speakers to check the English. We believe that the language is now acceptable for the review process.</td>
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2. Reply to Review 1

<table>
<thead>
<tr>
<th>Number</th>
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<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Grammar and typos</td>
<td>Thanks a lot.</td>
</tr>
<tr>
<td></td>
<td>Abstract: method: Meanwhile, the output index is that LNM of the patient is positive or negative.</td>
<td>Agree and revised.</td>
</tr>
<tr>
<td></td>
<td>“used for training and test new model”. Missing “the new model”</td>
<td>The first sentences is revised as “The output index determines whether LNM occurs, which is decided by the surgery and histopathology.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The second sentences is revised as “used for training and testing the new Model”.</td>
</tr>
<tr>
<td>2</td>
<td>1 Background:</td>
<td>Agree and revised.</td>
</tr>
<tr>
<td></td>
<td>Second paragraph, page 4, There are a few researches to discuss the diagnostic capabilities of morphological characteristics, besides lymph node size. (See Brown G, Radiology 2003; 227: 371-7. Kim JH, Eur J Radiol 2004; 52: 78-83. Chunyan Cui, Eur J Radiol 2012)</td>
<td>We have added this references as given in red font in the revised manuscript.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>From these articles of the comments, the morphological characteristics including border contour and signal intensity of lymph nodes may partly improve the diagnostic ability of metastasis. But these studies are all about the MRI imaging for rectum cancer. For patients with gastric cancer, abdomen CT is the more common used imaging modality than MRI</td>
</tr>
<tr>
<td>Page</td>
<td>Recommendation</td>
<td>Revised Comments</td>
</tr>
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</tr>
<tr>
<td>3</td>
<td>2 Results: The authors compared the performance of the proposed method with that of the radiologist in terms of sensitivity, specificity, and AUC (89.51%, 80%, 0.829 vs 63.4%, 75.6%, 0.757), and claimed that “it is clear that the proposed model can obtain better performance than the radiologist”. However, we think that the reviewer want to know whether the result is significant difference. By statistical analysis, it is shown that the result is significant difference (P&lt;0.05). It is also revised in the manuscript and given in red font.</td>
<td>Revised.</td>
</tr>
<tr>
<td>4</td>
<td>3 Page 6: “The number of lymph nodes: The number of all visible gastric regional lymph nodes in MDCT images by groups is counted [13].” Since some lymph nodes are tiny, making them indiscernible, the authors are suggested to use more critical criteria to evaluate this. For example, nodes with size less than 3mm is omitted.</td>
<td>Agree and revised.</td>
</tr>
<tr>
<td>5</td>
<td>Page 7, Equation 2-4, the authors are suggested to give a concise explanation of the rational behind Equation 2-3.</td>
<td>Agree and revised.</td>
</tr>
</tbody>
</table>

A concise explanation of Equation 4 is in red font given in ER based model in Section method.
| 6 | 4 There was no explanation which lymph nodes are enrolled in this study. It is important in reliability of this quantitative analysis how to collect the data of lymph nodes for evaluation. Thus, the authors should describe clearly about the inclusion criteria of evaluated lymph nodes enrolled in this study. Besides, matching of nodes after surgery or histopathology with those observed from CT is also a very important issue. This step is vital in that ground truth (positive or negative of lymph nodal status) can be retrieved. | Agree and revised. The indicators from lymph nodes and tumor are manually measured in CT images. The number of lymph nodes is the amount of lymph nodes around the stomach. Maximal lymph node size and lymph node enhancement is extracted from the maximal lymph node that observed from the CT images. Meanwhile, the object of this research is to predict whether LNM occurs other than the maximum lymph node has LNM. Therefore, we need not do the correspondence between lymph node and pathology. |
| 7 | 5 In N staging, diagnostic accuracy of preoperative staging modalities of CT, MRI, and endorectal ultrasound was 60%, 62%, and 65-81%, respectively (Nastro et al. Dig Surg 2005: 22: 6). In lymph node evaluation, CT is not better than other imaging modalities, such as endorectal ultrasound, MRI, and PET/CT. Thus, the author would be better to explain the rationale why they choose the CT as imaging | Agree and revised. According to the international treatment Guideline of gastric cancer, CT is one of The most common application Inspections (reference 17). And other methods such as PET and EUS are selectable check. Therefore, CT is used in this paper. |
In addition, if they could show the data comparing accuracy of quantitative analysis using CT images with those of other imaging modalities, it could provide the strong evidence of this quantitative analysis for lymph node evaluation.

### 3. Reply to Review 2

<table>
<thead>
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<tbody>
<tr>
<td>1</td>
<td>There are many grammar errors. The paper needs to be proofread by a native English speaker.</td>
<td>Thanks a lot. Agree and revised. We have revised the WHOLE manuscript carefully and tried to avoid any grammar or syntax. In addition, we have asked several colleagues who are native English speakers to check the English. We believe that the language is now acceptable for the review process.</td>
</tr>
<tr>
<td>2</td>
<td>The evidence reasoning results should be compared with other learning methods such as SVM (linear, with Gaussian and polynomial kernel), logistic regression, etc. Weka can be used to try many learning methods. The goal</td>
<td>Agree and revised. Five typical methods, which include ANN, SVM (linear, with Gaussian, Polynomial kernel), logistic regression are used for comparisons. This can be seen in Section results and the</td>
</tr>
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</table>
is to predict LNM better, not to promote a particular learning method.

| 3 | Minor issues:  
usually the feature (indicator) vector is denoted by $x$ and the class label by $y$.  
-Eq. (1). If $A$ is used for the training samples, then the notation $T$ is useless and should be replaced by $A$. | experimental results can be seen in Fig. 2 and Table 3.  
Agree and revised.  
The indicator vector is denoted by $x$ and the class label by $y$ in revised manuscript.  
In the revise manuscript, $A$ represents the dictionary and $T$ represents a test sample. |