

June 16, 2020

Prof. Xue-Li Chen
Editor-in-Chief,
Artificial Intelligence in Medical Imaging

RE: Resubmission of manuscript number 57292 “Breast DCE-MRI and radiomics: state of art”

Dear Prof. Xue-Li Chen,

We want to thank you and the reviewers for the thoughtful comments concerning our manuscript 57292 “Breast DCE-MRI and radiomics: state of art”.

We are resubmitting the revised manuscript and we would like to have the opportunity to respond to each of the suggestions and criticisms of the reviewers.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

Reviewer #1, comment #1

The topic of this article is relatively new. It uses radiology model and texture analysis to distinguish the heterogeneous histopathological subtypes of breast cancer and the entropy-based features in the symbiotic matrix, and describes the current application of radiomics in breast dynamic contrast-enhanced MRI, which has certain scientific significance.

Reply:

We thank the reviewer for the positive comments concerning our manuscript.

Reviewer #1, comment #2

The author should include more references to the correlation between DCE-MRI and breast cancer receptor status, and it is best to specify the results of the correlation.

Reply:

According to the reviewer comment we have added:

“According to the molecular subtypes different strategies, including surgery, adjuvant or neoadjuvant therapies, can be undertaken[28-31]. Current assessment of molecular subtypes is mostly based on immunohistochemistry (IHC)[32]. When IHC is tested in tissue specimens obtained by needle biopsy, could be not totally representative of the entire tumor or provide inconclusive results due to insufficient material. In this setting, according to prior studies, DCE-MRI may provide information suggesting the molecular subtype of breast cancer. In 2018, the AJCC updated the breast cancer staging guidelines to add other cancer characteristics to the TNM system to determine a cancer’s stage, including receptor status[33]. When developing a treatment plan, a correct assessment of receptor status is crucial. Several published studies revealed that rim enhancement, heterogeneous internal enhancement, and peritumoral edema are more frequently associated with TN than Luminal subtypes[34,35]. In the study of Blaschke et al.[36] HER2-enriched tumors showed the percent volume with >50% and >100% early phase uptake higher than Luminal A/B lesions at kinetic assessment. TN tends to be more frequently round in shape[32,37], Her2 cancers with smooth margins than other subtypes[37]. Controversial results

were reported for diffusion-weighted imaging, suggesting that high ADC values are associated with HER2 subtypes[38] or with Luminal A[39], and for spectroscopy, suggesting that high values of tCho are statistically correlated to the TN subtype for some authors[39,40], and with non-TN and Luminal B[41].”

References from #28 to #41 have been added according to the reviewer comment.

Reviewer #1, comment #3

The application of DCE-MRI to predict the pathological reaction of neoadjuvant chemotherapy in breast cancer patients is correlated with the stage of breast cancer and the type of chemotherapy drugs used. Although there is currently controversy, it cannot be generalized when it is elaborated.

Reply:

Thank you for the comment. In order to better discuss this point we have added that:

“Neo-adjuvant systemic therapy (NST) is often the first line treatment for those patients diagnosed with locally advanced breast cancer, with several potential advantages, including the reduction of tumor size to allow breast-conservative surgery instead of mastectomy, as well as a prognostic indicator[68]. The pathologic complete response (pCR) rate range from 0.3–38.7%, depending on cancer subtype and breast cancer stage[69].”

“According to another recent meta-analysis, accuracy in detection of residual malignancy with breast MRI varies also in consideration of the treatment type, with AUC values ranging from 0.83 to 0.89, and on the basis of response definition, for instance volume reduction, absence of enhancement or enhancement equal or less than breast parenchyma[71,72]. The wide heterogeneity of studies, with controversial results, suggests to standardize definitions and primary endpoints to produce clinically significant results[73].”

Reviewer #1, comment #4

The authors can increase the content of whether DCE-MRI radiology can predict axillary lymph node residual metastasis in patients with neoadjuvant chemotherapy or negative imaging for breast cancer, and further explain whether it can replace the pathological evaluation of axillary lymph nodes for breast cancer, so as to increase the validity of this technique in the evaluation of axillary lymph node metastasis.

Reply:

We thank the reviewer for the suggestions. We have increased the content as follow:

“Sentinel lymph node biopsy has replaced axillary lymph node dissection in patients who convert to node-negative status after NST. Several studies assessed whether breast MRI can be used to assess lymph node residual metastasis after NST allowing breast cancer patients to avoid unnecessary axillary surgery. In the study of Hyun[91], DCE-MRI was able to rule out the presence of advanced nodal disease with a NPV of 94% in NAC patients. Nevertheless, in the work of Mattingly et al[92], post-treatment MRI and surgical pathologic findings revealed a slight strength of agreement and DCE-MRI revealed specificity and sensitivity of 63% and 55%, respectively. Ha et al[93] found different results, with sensitivity and specificity of 57% and 72%, with positive estrogen receptor status significantly associated with misdiagnosis by MRI. These latter evidences, revealing that post-treatment MRI findings were not exactly predictive of residual axillary disease, suggest to use DCE-MRI results with caution when planning treatment and to avoid to omit sentinel lymph node biopsy or axillary lymph node dissection for staging in women determined to be node-positive pre-treatment. In this setting, convolutional neural networks (CNN), were employed to predict the likelihood of axillary LN metastasis and NAC treatment response, using MRI datasets prior to initiation of NAC in few studies with controversial results[94-97]. Ha et al[96] reported an accuracy of 83% with AUC of 0.93 for CNN in predicting axillary response. Nevertheless, in the study of Golden et al[97] the GLCM texture features extracted from pre- chemotherapy MRI was able to predict pCR and residual lymph node metastasis with an AUC of 0.68.”

Reviewer #1, comment #5

It is recommended to accept after modification.

Reply:

Once again we thank you and the reviewers for the thoughtful comments that have improved the manuscript. We hope that we may anticipate a favorable response to this revision and that we may anticipate publication in Artificial Intelligence in Medical Imaging.