

Peer Review File

Article information: <https://dx.doi.org/10.21037/gS-22-11>.

Reviewer A

The reviewed article decently summarizes some topics regarding the use of DL in digital pathology of breast cancer. It is acceptable after minor revisions listed below:

1. Sections 1 and 2 need more recent references. Citations (8-11) are from 2010-2015, (27,28) are from 2016, (32-33) are from 2006(!), and so on. Please provide more recent references.

Reply: Thank you so much for your careful check. We have added relevant and up-to-date references. (p3 line 66, p5 line 106-1117, p6 line 118-128)

2. The references should be more relevant to the text where are they cited. Ref(13) is about dermatology not breast cancer or microscopy evaluation. Ref(14,15) it is difficult to establish connection with surgery. Ref(23,24) are both about frozen samples not about paraffin embedded. Ref(31-35) are not relevant to digital pathology.

Reply: Thank you so much for your careful check. We have changed the references. (p4 line 68-69, p4 line 73, p5 line99, p6 line120)

3. I strongly suggest citing the references right after the name of the author instead of the end of the sentence. For example: Spanhol et al. (37) and Bayramoglu et al. (38) used CNN [...]. If this contradicts with Journal policy then disregard this comment.

Reply: We have made changes to the reference locations based on your suggestions.

4. It is not clear if the provided search keywords were used all at once or in some combination or separately. Please clarify.

Reply: We have provided the keywords search method. (p4 line82-84)

5. I would suggest not using too vague expressions like "great deal of expertise" or "longer training" (both: p.6, line 116) as you never specify what kind of expertise nor longer than what. I suggest rephrasing this sentence and other in similar manner.

Reply: We have changed the way this statement is described. (p7 line140-143)

6. Please explain all abbreviations when first used. For example DeCAF (page 6) is never expanded nor explained.

Reply: DeCAF is a technical term, not an abbreviated form, and we add a subordinate clause to introduce the method. (p7 line146-149)

7. I suggest to keep one notation of accuracy throughout the entire review (this one 95% OR this one 0.95).

Reply: We have expressed all descriptions such as accuracy in one form. (95%)

8. (page 8, line 171) "experimental setup as in 47" if you mean reference 47 then it seems illogical. Please check.

Also, the "40x" is almost self-explanatory but I suggest to put a word "magnification" there just to make sure the reader is not confused.

Reply: We have changed the description form. (p10 line206)

We have put the word "magnification" there. (p10 line207)

9. (page 8, lines 174-176) The last sentence on page 8 seems unnecessary as it cites 2 works

without explaining them and claiming they have inferior results to previous works. I suggest deletion of this sentence.

We have deleted this sentence.

10. (page 10, line 207) The expression "large image clusters" is confusing, I suggest rephrasing.

Reply: We have changed the description form. (p12 line245)

11. (page 14, lines 299-304) No numerical results (accuracy/precision/F1-score) are presented of these methods as opposed to previously described works. I suggest expanding this section or explaining why no numerical data is provided.

Reply: For the method in Ref. 101, we added numerical results. (p17 line357)

For the method in Ref. 102, the method focuses on predicting gene expression, which can be used for biomarkers but does not give specific numerical results in the article.

12. (page20, line 426) At least one reference should be provided for that sentence.

Reply: We have added references in this location.(p23 line505)

13. There is no mention in the review about explainable deep learning models that are becoming more popular in medical application as well as in digital pathology. (refs: DOI: 10.1007/978-3-030-50402-1_6; arXiv:2007.00311; arXiv:1712.06657; DOI: 10.1038/s41598-020-62724-2)

Reply: We have carefully read the relevant references you provided and integrated them into this review. (p24 line516-520)

14. The target of this review is enigmatic. The level of detail is without depth, technical details are poorly introduced and not explained in the article. On the other hand, a lot of abbreviations and technical names are used frivolously that might confuse medical-oriented reader.

Reply: The contents of the deep learning model have been modified, and the revised version was attached to the email and submitted to our website. To make it understandable for the reader, we have added technical correlations in the preliminary part of the paper and introduced the terminology of the specialized models presented in the later papers, please see the second part of the paper. (p5 line91-109)

All in all, the review seems superficial and only touches some topics giving hints about it and where to look further. The narrative review suffers from authors biased choice of works. But I hope it will find targeted audience.

In my personal opinion after a few first pages the quality of the paper picks up, and I liked Section 4 (Challenges) very much - its a good summary of challenges in digital pathology, although it could be more discussed.

Reply: Thanks a lot for your comments, we think it significantly improved the quality of the review and we have revised it.

Reviewer B

This review article on progress on deep learning in breast cancer is very interesting. The side topics in the artificial intelligence in the breast cancer are very useful for the readers new to breast cancer research. Here are my suggestions for the improvement in the challenges in the clinical application and in discussion.

1. There is a need to add few validation studies on the DL in the clinical settings if needed.
Reply: Thanks for your advice. However, it is very unfortunate that deep learning methods are not yet applied to practice clinical diagnosis, we will follow the development of this field and update in future reviews.
2. Highlighting the cons of DL based approach in detail in the discussion will be useful.
Reply: Thanks for your suggestion and we have summarized their cons and shortcomings, please see the fourth part of the text. (p22 line474)