

Peer Review File

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Reviewer A

Interesting and covering narrative review on the subject.

My major concern is abstract, that seems to much weaker than the rest of the manuscript regarding the English language. It seems like it has been written separately, perhaps at a later or much earlier timepoint.

Please revise the language of the abstract.

Starting by e.g.: We have witnessed tremendous advances in AI technologies in recent years leading to applications in various....

you cannot have years witnessing advances, it must be a subject.

Replace the word "examination" with serach in the next paragraph

Line 98, add the word current before literature

Authors' response: Thank you for your comment. We have replaced the words "Recent years" with "We" in line 29

Line 36: We have replaced the word "examination" with "search"

Line 97: we have added the word "current" before "literature"

Reviewer B

I would like to appreciate choosing of a hot-discussed topic of AI for their review named Use of Artificial Intelligence in Breast Surgery: A Narrative Review. As the topic of the paper suggests, the review was focused of the use of AI in the breast surgery. Due to my humble opinion, the review focuses mainly on the application of AI in the diagnostic methods of the lesions of the breast gland instead of focus on the breast surgery itself. On the other hand, it provides the extent amount of information about current state of AI in the breast cancer care.

I would suggest these changes:

The topic of the article should be reconsidered as the real surgery-related topics are discussed only in the lines 323-369 and these refers only to the breast cancer surgery, not to benign and plastic or reconstructive surgery.

Authors' response: we have revised the running title of this article to focus on breast surgery and not on plastic or reconstructive surgery.

Line 35: word "neoplasm" . The authors screened for AI and "breast surgery", "breast neoplasm", but not for an usual expression "breast cancer" even though

the main part of the review discuss applications of AI in the breast cancer. I would suggest completing the research with the expression "breast cancer" as well.

Authors' response: we have changed all mention of the word "neoplasm" to "cancer" in line 108.

Line 51: Key word "Plastic Surgery" occurs only once in the text. I do not think that this is a real key word. I would suggest "Breast Imaging" instead as the extent part of the review discuss AI in this area.

Authors' response: we have changed the keyword to "Breast Imaging" Line 60.

Line 61: The definition of AI should be changed as the statement "algorithm" is misleading. The AI is no algorithm on the basis if/then/or.... I would suggest using the definition from cambridge dictionary or oxford dictionary of science or other accepted definition of AI.

Authors' response: we have changed the definition to that of cambridge's. Line 65.

Line 75: The abbreviation deep belief nets (DBN) is not used in the text on the other place as in this line. The DBN is described again in the Fig.1, where it is explained, so I would consider omitting of using the abbreviation DBN in this sentence.

Authors' response: we have omitted it from line 79.

Line 185: The statement: " breast US should therefore be performed by a radiologist for direct interpretation." should be rephrased, as there are gynecologist performing and teaching the breast ultrasound (pre- and intra-operatively) with high expertise in different European countries as standard of care.

Authors' response: we have replaced the word "radiologist" with "expert" in line 191.

Line 201: Autor's suggestion that AI-based-imaging could predict biological subtype of breast cancer and therefore need for the biopsies could be reduce is not supported by any study. This sentence should occur in the discussion instead in the results. In my humble opinion, the histopathological confirmation of a such severe diagnosis as a breast cancer where the various information (histological subtype, Ki67, Grading, Her2 negativity vs. Her2low..) are needed for therapeutical planning will stay in the future as standard of care.

Authors' response: we have removed that sentence from line 222 and shifted it to line 396.

Line 267: There is an unnecessary dot before brackets.

Authors' response: we have removed it in line 274.

Line 308: It is not a current standard of the care that the patient with the complete response to the neoadjuvant therapy (according to the imaging) do not require

surgery. Only the histopathological examination can confirm grade of the regression, what has the implications for postneoadjuvant treatment. The cited study of Heil et al. does not state that the surgery is not required.

Authors' response: we have rephrased the line 319 to say instead that surgery may be held off and not completely recommended against.

Line 340: The studies evaluating postoperative application of AI in breast oncology should be considered to discuss in this part, too. The most discussed AI in the current days is the ChatGPT that was evaluated in the breast oncology as well (e.g. Lukac et al, 2023, DOI: 10.1007/s00404-023-07130-5). I would suggest adding at least a short excursion in this dimension to provide a complex image of adjuvant planning.

Authors' response: we have added that study into the discussion in lines 352-355.

Line 380: There is an unnecessary dot before the brackets.

Authors' response: we have removed that extra dot in line 388.

Line 429: The sentence: "AI models that directly perform breast surgery or assist surgeons could also be introduced in the future." should be explained as the AI is no surgical robot with the capability of physical movements.

Authors' response: we have added the line "akin to the Da Vinci system" into line 443 to better explain how AI can integrate with robotic models. We also added 2 new references.

Reviewer C

Excellent narrative review that thoroughly explores the role of AI in all aspects of breast surgery. Congratulations to the authors.

There are a few minor, slightly trivial comments which I reckon requires addressing. A few statements are made which provides some new thinking points worth exploring too.

All areas in the paper worth addressing are highlighted in the [PDF attached](#).

Highlight 1: A very good introduction, however, a little more insight into what the other deep learning models are generally used for/ capable of might allow the layperson to be more informed on the differences between them early on. You have done a good job in outlining what convolutional neural networks are specifically used for but not the others. One sentence explaining the utility of the other models would be useful.

Authors' response: we have included 2 additional sentences to discuss LLMs and their usage in medicine thus far, including 10 new references. Lines 81-84.

Highlight 2: I understand that the authors wanted to capture an extensive narrative review, however, I can't seem to understand the rationale behind starting the search strategy from 1901! The first AI research did not even begin until the late 50s!

Authors' response: apologies! We have revised the search strategy to start from 1955 onwards.

Highlight 3: Very good point. I have written a systematic review and performed a meta-analysis on the use of AI radiomics in differentiating malignant and benign breast lesions on mammography, US and MRI. Worth a read!
<https://pubmed.ncbi.nlm.nih.gov/38024014/>

Authors' response: very interesting read! We have added that reference in!

Highlight 4: Not sure if I agree with this point. Although I do agree that AI is a valuable tool in the interpretation of breast radiology, I do not think they have the potential to replace obtaining a biopsy. The gold standard work-up of any breast lesion is a thorough triple assessment which includes a history/physical exam, radiology and biopsy. AI can assist in radiology and can assist in the interpretation of histopathological images, however, a biopsy is still required for this to be obtained. A biopsy not only gives us information regarding receptor status but tells us the cancer grade (which is a histopathological definition) and also tells us what is the margin involvement, evidence of lymphatic and neurovascular invasion. I believe biopsies are here to stay!

Authors' response: we have removed that line from line 381.

Highlight 5: A bit more insight into what characteristics the DL model uses from breast lesions to predict this outcome would be useful.

Authors' response: we have added 2 more sentences to lines 391-393 to elaborate further on how DL is used in breast lesions.

Highlight 6: Tru-cut core needle biopsies are actually done as part of triple assessment clinics in most institutions at first patient presentation. They don't give you results instantly but are not time consuming. couple of days for histopath analysis.

Authors' response: we have removed the part about it being time consuming from line 566.

Highlight 7: Not all the time. early cancers which are large in size (> 5cm), tumors affecting women with small breasts, patients with multiple previous re-excisions, cancers close to the nipple-areolar complex, multiple small tumors affecting a single breast or fungating/ ulcerated tumors are all candidates for mastectomy relative to breast-sparing surgery.

Authors' response: we have revised the phrasing. Instead, we said "the preferred" method instead of the "current standard".

Highlight 8: What about the other post-operative complications?

Authors' response: We have read the paragraph below. Very interesting thoughts! We have added the complication of nerve damage during axillary clearance and how AI could be integrated. However, at the time of writing, we were unable to find any studies on this. Definitely a topic to investigate further. Lines 780-787.

A rare but devastating complication of axillary clearances are injury to the long thoracic nerve and intercostobrachial nerve (this sometimes has to be intentionally sacrificed). One useful role of AI in the pre-operative/ surgical planning phase could be to determine certain characteristics of breast tumors and axillary lymphadenopathy that make it more likely to encroach nearby neurovascular structures. AI can also be used to investigate patient anatomy from pre-operative breast radiology. This could help predict or calculate the risk of nerve injury intra-op. This could help anticipate neurovascular injuries early on. This prediction or risk calculation reminds the surgeon to be more judicious and also results to a more tailored informed consent process, highlighting the higher than average risk of neurovascular complications for certain patients. Something to think about. I wonder if there are any papers investigating this? It would be a great addition to your review.

Highlight 9: usually associated with axillary procedures like clearances rather than breast surgery itself.

Authors' response: thank you for the clarification, we have replaced "breast surgery" with " axillary procedures, such as mastectomy with axillary clearance," in lines 755-756.

Highlight 10: examples? NPI? BCSS?

Authors' response: we have added mention of the NPI and BCSS in lines 848-849.

Highlight 11: Plausible in countries with public health systems like the NHS in the UK or the HSE in Ireland. Very hard in privatised health systems like in America. Ethical laws regarding transfer of sensitive patient information should also be considered. (i.e GDPR in Europe)

Authors' response: we have added that point into lines 884-885.

Overall, this is an excellent review. It truly is eye-opening. Very excited to see the direction surgery is taking.