

Peer Review File

Article information: <https://dx.doi.org/10.21037/aot-22-31>

Reviewer A Comments:

The authors summarized the history of parathyroid glands autofluorescence detection during thyroid procedures. Overall, the paper is well written and authors described the technical advances and current limitations. Please correct the comments in the below.

Thank you for your review. Please see below our responses to each one of your valuable comments.

Comment 1: The abstract doesn't outline the purpose of the paper nor the methodology.

Reply 1: Thank you for your comment. We have stated the purpose of the invited review.

Changes in the text: Line 37-40.

Comment 2: The paper could benefit from adding some figures to expand on the difference in technology.

Reply 2: Thank you for your comment. We have added some figures.

Changes in the text: End of the document.

Comment 3: Line 124 - 132, only described dyes and not actual imaging technology.

Reply 3: Thank you for your comment. We agree with you, we have removed the word imaging.

Changes in the text: Line 134.

Comment 4: Adding a table summarizing the studies results could be helpful.

Reply 4: Thank you for your comment. We considered doing a summarizing table, however this will add to many figures and will not be compliant with the journal style.

Changes in the text: No change done.

Comment 5: In lines 197 - 200, recent AI-based parathyroid detection relevant publications should be added, for examples,

1) Kim, Y., Lee, H. C., Kim, J., Oh, E., Yoo, J., Ning, B., Lee, S. Y., Ali, K. M., Tufano, R. P., Russell, J. O., Cha, J., J. *Biophotonics* 2022, 15(8), e202200008. <https://doi.org/10.1002/jbio.202200008>

2) Apostolopoulos, I.D.; Papandrianos, N.I.; Papageorgiou, E.I.; Apostolopoulos, D.J. Artificial Intelligence Methods for Identifying and Localizing Abnormal Parathyroid Glands: A Review Study. *Mach. Learn. Knowl. Extr.* 2022, 4, 814-826. <https://doi.org/10.3390/make4040040>

Reply 5: Thank you for your comment. We have added this valuable references.

Changes in the text: Line 208 – 209.

Comment 6: The reviewer suggests that authors add perfusion assessment in the discussion part since the title implies preservation of parathyroid glands. In particular, label-free imaging approach would be a good addition for the future directions. e.g.,

1) Emmanuel A. Mannoh, Giju Thomas, Naira Baregamian, Sarah L. Rohde, Carmen C. Solórzano, and Anita Mahadevan-Jansen. Assessing Intraoperative Laser Speckle Contrast Imaging of Parathyroid Glands in Relation to Total Thyroidectomy Patient Outcomes. *Thyroid* 2021 31:10, 1558-1565

2) Oh, E, Lee, HC, Kim, Y, Ning, B, Lee, SY, Cha, J, et al. A pilot feasibility study to assess vascularity and perfusion of parathyroid glands using a portable hand-held imager. *Lasers Surg Med.* 2022; 54: 399–406. <https://doi.org/10.1002/lsm.23478>

Reply 6: Thank you for your comment. We have added this valuable references.

Changes in the text: Lines 220-226

Comment 7: To sum up, the paper reviewed journal articles published relevant to the Parathyroid autofluorescence imaging in detection and preservation. The reviewer believes that the paper can be strengthened by improving those comments with revisions and will be of great interest from broader readership.

Reply 7: Thank you for your comment. We have made your suggested changes.

Changes in the text: Throughout the text.

Reviewer B Comments:

Comment 1: The article lacks of novelty and is just similar to many already published articles. Moreover I find the abstract completely inadequate and doesn't explain the aim of this article and doesn't resume at all the article presented.

Reply1: Thank you for your comment. This is an invited review. We agree the topic of autoflorescence has been covered in prior publications. However, we wanted to offer a timeline description of the development of autoflorescence to the readers. We have modified the abstract accordingly.

Changes in the text: Lines 25-40

Comment 2: Line 42: As a result of these increased postoperative rates of hypo and hypercalcemia - what does the author mean?

Reply 2: Thank you for your comment. We agree this line was confusing and we have deleted from the manuscript.

Changes in the text: Line 50.

Comment 3: Why in the introduction talk about hyperparathyroidism if the title state thyroid surgery?

Reply 3: Thank you for your comment. We agree this is confusing and we have deleted it from the manuscript.

Changes in the text: Line 44-58.

Reviewer C Comments:

The concept and idea is interesting and will definitely be useful for the literature. However, there

are some major issues:

Thank you for your review. Please see below our responses to each one of your valuable comments.

Comment 1: Initially, the title and paper just reads like a narrative and history paper of how NIRAF has come into use, rather than a paper on the effectiveness of NIRAF in reducing hypocalcaemia during total thyroidectomy.

Reply 1: Thank you for your comment. Yes, the purpose of the paper is to do a history of how NIRAF has come into use until its point of use during thyroidectomy to reduce hypocalcemia. We have made edits in the introduction to describe this.

Changes in the text: Lines 44-63

Comment 2: No aim of the study – just has introduction and then sections on various different modalities.

Reply 2: Thank you for your comment. We have include this as requested.

Changes in the text: Lines 61-65.

Comment 3: No method as to how these studies were selected and what the inclusion and exclusion criteria were set for paper inclusion/exclusion. Reads as if suitable papers were cherry picked rather than a systematic review of the literature being performed.

Reply 3: Thank you for your comment. The purpose of the review was not to perform and exhaustive systematic review. But rather to provide the reader with landmark papers which led to the development of this technology and its application in thyroidectomy.

Changes in the text: Lines 61-65.

Comment 4: If including a section on other technologies, be good to read about their results in comparison to NIRAF. Otherwise, just focus on NIRAF.

Reply 4: Thank you for your comment. The aim of the review was not to compare NIRAF versus other technologies. We consider that mentioning these alternatives and their disadvantages to NIRAF will offer the reader other alternatives.

Changes in the text: No changes made.

Comment 5: No clear results section reporting on the overall efficacy and safety of NIRAF. Individual papers are and the authors' institution's numbers are quoted, but no meta-analysis attempted – obviously may not have been possible. If so, would have been good to mention this. Also, line 156 – “to the best of our knowledge” – this does not sound like a proper literature review has been performed looking for the relevant papers.

Reply 5: Thank you for your comment. This is a review. This is by no mean a systematic review or meta-analysis. We acknowledge the limitations of the review.

Changes in the text: We have removed “to the best of our knowledge”, line 166.

Comment 6: Also, seems a lot of this paper is just paraphrasing other authors' results/work. There has been no attempt to collate the data.

Reply 6: Thank you for your comment. This is a review. This is by no mean a systematic review or meta-analysis.

Changes in the text: No changes.

Comment 7: The idea of the paper is interesting and would be a good addition to the literature, but needs significant amendments.

Reply 7: Thank you for your comment. We have made the edits as suggested.

Changes in the text: Throughout the text.