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**Reviewer A**

1. Mention the limitations and advantages of each imaging modality upfront.

Reply: While our ultrasound section required expansion, we believe the 4DCT section in the introduction adequately outlined the limitation and advantages and only needed minor adjustments (**Lines 109-113**).

Sonography was discussed as the most common first-line imaging modality due to its accessibility, safety, and cost-effectiveness. However, its limitations include difficulty in identifying small, ectopic, and issues with large body habitus.

4DCT's capabilities, including multi-planar imaging and time-based tissue contrast enhancement, are outlined. The literature emphasizes 4DCT's superior sensitivity compared to ultrasound and SPECT/CT.

2. Additional Insights on PET CT Choline

Reply: We added text on PET CT Choline to our manuscript. After some chart review, changes were made to the discussion portion of this manuscript based on literature from the previous 11 years. (**Lines 301-3, 308-20**)

While the article focuses on 4DCT and ultrasound, PET CT choline is noted as a superior modality in evaluating parathyroid gland hyperactivity, which 4DCT does not. This functional information may be important for accurate localization and treatment planning.

3. Ethical Considerations: Emphasize ethical approvals and patient consent to strengthen the study's integrity.

Reply: Patient information was deidentified to protect HPI however it was not clearly stated in our manuscript that this was performed prior to preliminary analysis. This has been corrected.

Changes in text: **Lines 125-8.**

4. Future Directions: Include potential future research or advancements in imaging technology.

Reply: We have included references to newer projects utilizing artificial intelligence to detect parathyroid nodules more accurately and expeditiously. Please also refer to the replies regarding <sup>18</sup>F-choline for advancement in imaging technology.

Changes in the Text: **Lines 312-20.**

5. PET CT Choline Integration: Highlight PET CT choline's role as an emerging modality with superior capabilities in evaluating hyperactivity, suggesting it as a potential replacement or adjunct to 4DCT.

Reply: Enhancements have been made primarily to the discussion portion of this manuscript based on literature from the previous 11 years.

Changes in the Text: **Lines 301-20.**

Reevaluation of Sensitivity and Specificity: Provide a thorough reevaluation of sensitivity and specificity values, addressing any discrepancies or reasons for lower-than-expected performance.

Reply: We agree that the sensitivity and specificity were lower expected. We believe the lower numbers are attributed to the way our statistical analysis was performed i.e. using surgical findings (quadrant) as the gold standard. We believe our stringent standards of “correct” lead to the decreased accuracy, sensitivities and specificities regarding localization but our lateralization values align more closely to those described in the literature. A point worth mentioning is the limited clinical utility of quadrant localization in patients undergoing focused, unilateral surgery. It is our practice to explore the superior and inferior poles of the thyroid when performing unilateral surgery due to the variable anatomic positioning of the parathyroids.

## Reviewer B

1. I recommend slightly expanding the introduction to include a discussion on the utility of the methodologies, particularly ultrasound, in both elective and emergency settings. This paper <https://gs.amegroups.org/article/view/118572/html> may be a useful reference for this purpose.
  - a. Reply: We agree with the reviewer that the introduction did not appropriately outline the utility of ultrasound in the original manuscript. Using the supplied reference and additional review of previously cited texts resulted in an expanded text.
  - b. Changes in the text: **Lines 88-97.**
2. The objective of the study should be made more clear and explicit.
  - a. Reply: This has been revised to more clearly outline our goals of this project. An additional section in the opening paragraph has been added to describe the goals of this paper, which is re-iterated as the introduction concludes.
  - b. Changes in the text:
    - i. **Lines 74-79.**
    - ii. **Lines 118-121.**
3. Change the title to reflect the methodology, explicitly stating that the study evaluates the diagnostic accuracy of the techniques in a single-center, retrospective setting.
  - a. Reply: The title has been adjusted to more clearly reflect the nature of our study
  - b. Changes in the text: “Four-Dimensional Computed Tomography and Ultrasonography for Prediction of Pathological Parathyroid Location, **Retrospective Review of a Single Surgeon’s Patients at a Single Institution**”
4. A thorough revision of the English language is necessary to improve the clarity of the manuscript, especially in the introduction.
  - a. Reply: Several changes were made throughout the paper to improve clarity.
5. The tables need graphical improvements for better clarity. The first table, in particular, requires additional perioperative information on follow-up and healing rates. Additionally, the supplementary table is missing and should be included. There is also an inconsistency in the table references; the tables cited for diagnostic accuracy are 4-6, but they should be 3-6.
  - a. Reply: This project was focused on describing the rates of successful localization of imaging modalities. There was no mention in our paper regarding follow up of these patient but could be a secondary project to evaluate patient outcomes, possibly comparing those who underwent focused single gland parathyroidectomy vs. those who underwent bilateral exploration.

- b. Changes in the text: The Supplementary table is attached to this reply.
6. A statistical comparison regarding diagnostic accuracy could be a useful addition. Is there a significant difference between the two methodologies? Have they always been used in combination, thus precluding a direct comparison? Can we discuss combined accuracy?
- a. Reply: There could be benefit of comparing the two imaging modalities, however this project's goal was not to compare the two methods but to describe each one individually. It is of our opinion they should not be compared to one another as they have synergistic effect when used together. The combined accuracy for lateralization is stated in lines 228 and 266-267 in the manuscript. No changes were made to the text.

### Reviewer C

1. It is not clear from title, aim and methodology that study population includes primary, secondary and tertiary hpt. On the other hand, only less than 3% of patients other than phpt maybe is not appropriate for statistical analysis. It is more appropriate to analyze only phpt patients.
- a. Reply: Our project was designed to include all patients undergoing dual-modality imaging with initial plan for focused parathyroidectomy to treat primary hyperparathyroidism. We elected to include all comers to give a more heterogenous mixture of patients that would be characteristic of a practicing surgeon's patient population. No changes were made to the text.
2. In Methods, it's stated that all patients without 4dct are excluded, still there are 6 patients without it.
- a. Reply: This sentence was an accidental inclusion from a previous version of the paper where statistical analysis was attempted on only on patients who underwent BOTH modalities. In the paper's current form this is no longer applicable and has therefore been removed.
  - b. Changes in the text: Deletion of the sentence in line 136-137.
3. How many ectopic parathyroid glands were found and where? Intrathyroid localization?
- a. Reply: Based on review of the patients, there were 13 patients with intrathyroidal parathyroid glands identified surgically. A total of 53 ectopic parathyroid glands were identified in total. This has been added to the results section of the manuscript.
  - b. Changes in the text: A small portion of our patients were found to have ectopically located parathyroid glands after surgical excision. A total of 53 ectopic glands were identified surgically and 4DCT and ultrasound identified 44 and 10 glands respectively. Thirteen of the ectopic parathyroid glands were identified within the thyroid gland. When detected by imaging the accuracy of surgically identifying the ectopic gland was 86.5% (Table 6).
4. It's not clear how quadrants were defined. Even more important, by dividing neck on quadrants, one cannot get info about precise location of parathyroid gland, because upper gland can be found in lower quadrant, and vice versa. Also, precise anatomical presentation usually can be predicted if enlarged parathyroid is identified, which is crucial for successful surgery.
- a. Reply: In the discussion section (Lines 282-283), we describe that superiorly vs. inferiorly situated glands were based upon the surgical findings of ZukerKandl's tubercle and the passage of the recurrent laryngeal nerve. An additional mention of this

differentiation has been added to the methods section to more clearly define how our localization was performed.

- b. Changes in the text: A retrospective chart review was performed of all eligible patients with the following data extracted: demographics; preoperative images (4DCT scan and ultrasound) and identified parathyroid location(s); parathyroid size on image; final pathology (single adenoma, double adenoma, hyperplasia, or parathyroid carcinoma); pathology measured gland dimensions and mass; and reported parathyroid surgical location(s). **Lines 135-138.**