

Peer Review File

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Reviewer A

This is an interesting study with good data regarding pre-operative localisation studies, some of which reaches statistical significance.

The title and main conclusion of the paper is that choline PET is superior in terms of diagnostic yield for small multiple adenomas - however this conclusion is not supported by the data in this study, as the diagnostic yield of choline PET in correctly identifying the location of adenomas did not reach statistical significance due to small sample size (56 patients).

It has also been previously demonstrated in numerous studies (and subsequent review articles) that choline PET is superior to US and SPECT/CT in pre-operative localisation of parathyroid adenomas - therefore an additional study in which conclusions cannot be reached due to a lack of statistical significance to the data is of limited value.

There is however a great deal of interesting data in this paper which reaches statistical significance and would be of value to publish. I would recommend the authors consider re-configuring this article, as although unable to draw clear conclusions from the data regarding the diagnostic yield of choline PET, there are many other interesting conclusions regarding other imaging modalities that would support existing studies.

Comments to reviewer A

Thank you for your detailed review and the numerous comments to our work.

Reply

I agree with you that the statements and conclusions lack confirmation from the presented statistics and tables, or they are difficult to comprehend. Despite this, the data collected show a significant superiority of PET/CT over the other imaging modalities for accurate localization especially of small parathyroid adenomas.

To highlight this clearly, we evaluated the ability of each imaging modality to detect the sought adenomas separately for the small and large adenoma subgroups as well as adenomas in MGD. We have added the findings in supplemental tables 2c and 3b and in the “results” and “discussion” sections of the manuscript.

We have refined the definition of the correct side by including all patients in whom imaging has identified the correct quadrant. The inferiority of SPECT/CT in detecting the correct side of small adenomas has now reached a significant level. The rest of the calculations have not changed.

Changes in the manuscript

The subgroups of large and small adenomas were analyzed separately based on the imaging methods' detection ability. We added Table 2c containing the results, which were also added to the “Results” section (page 9) and discussed in the “Discussion” section (page 13).

The analysis of patients with MGD was similarly complemented by an analysis of the imaging modalities in their ability to detect the sought PA. Addition of Table 3c with the results and their discussion in the text (pages 10 and 13). Adaptation of the abstract and the conclusion (page 1 and 14).

Editing all tables, adding percentage values and IQR. Adding the explanation of abbreviations.

Reviewer B

This is a nice study showing that choline SPECT CT is the most accurate preoperative localizing study in patients with primary hyperparathyroidism.

Questions:

- 1) Was IV contrast used for the CT portion of the choline SPECT CT? We have found the a CT neck with parathyroid protocol using IV contrast to be very accurate in localizing parathyroid adenomas.
- 2) It would be nice to have Figures that show examples of the choline SPECT CT since most readers do not have this at their institution.

Comments to reviewer B

Thank you for reviewing the work and sharing your comments and questions with us. Following our point-by-point answers:

Question 1

Was IV contrast used for the CT portion of the choline SPECT CT? We have found a CT neck with parathyroid protocol using IV contrast to be very accurate in localizing parathyroid adenomas.

Answer 1

SPECT/CT imaging was conducted after IV injection of 550 MBq Tc-99m Sestamibi 20 minutes and 120-150 minutes after injection. PET/CT images were acquired 20 minutes after the intravenous injection of 120-150 MBq 18F-Fluorocholine. According to our radiologists, this indeed shows a higher accuracy in the correct localization of PAs.

No changes in the manuscript

Question 2

It would be nice to have Figures that show examples of the choline SPECT CT since most readers do not have this at their institution.

Answer 2

This is a good point. An image comprising a negative SPECT/CT and a positive PET/CT of the identical patient was added to illustrate the capabilities of the methods.

Changes in the manuscript:

Addition of figure 2 and a corresponding note in the text (page 9).