

## Peer Review File

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### Reviewer A

This is a single center retrospective data analysis of 704 patients who underwent thyroid surgery. Specimen were analyzed for inadvertently resected parathyroid glands. When found, their location was classified by histopathology as intracapsular or extracapsular, with the latter further subdivided according to their location between the thyroid capsule and thyroid tissue. They found most of the removed glands inside the thyroid capsule, with more than 50% partially covered by thyroid tissue. The authors promote this as a new histopathological location.

The data is well analyzed and presented. Results are adequately illustrated with graphics.

My comments in detail

1) The proportion of carcinoma patients in your study population seems high. Did you exclude all patients with capsular invasion, as this could influence the detection of intracapsular PGs?

**Reply 1:** According to our own policy, thyroidectomy of benign lesion is not common in our hospital, therefore the proportion of carcinoma population is high. We did not exclude patients with capsular invasion, and we showed the proportion of extrathyroidal extension in groups of partially buried + subcapsular location and extracapsular location in Table 3.

**Change in the text:** no change has been made

2) What is the key message of your work for the reading surgeons? What should they look out for, what should they change? This key message also needs to be discussed in more detail with the results of other papers dealing with similar issues.

**Reply 2:** Since partially buried parathyroid gland can act as an inevitable risk factor of unintended parathyroidectomy under the naked eye, surgeons do not necessarily need to be embarrassed or be frustrated about the pathologic report of unintended parathyroidectomy, and thereby do not have to routinely perform an excessive manipulation for identification of parathyroid gland next time because it can increase direct trauma or disrupt blood supply on parathyroid glands. However, meticulous capsular dissection of thyroid glands is still crucial principle of thyroid surgery

**Changes in the text:** see Page 9, line 15~21

3) NIR AF is a well-known tool to assist the detection of PGs, but a known limitation is the poor tissue penetrance (Wolf HW et al, LAOS 2022). This should be discussed regarding the glands covered by tissue.

**Reply 3:** We have modified our text as advised

**Changes in the text:** see Page 11, line 1~13

**Reviewer B**

I have read with great interest the manuscript entitled “A new histopathological location of parathyroid gland with high possibility of unintended parathyroidectomy”. In this study the authors investigated 743 patients with 13% inadvertent parathyroidectomy. The authors divide the cases into intra and extra capsular. The intracapsular cases are further divided into subcapsular, partially and completely buried.

Comments:

1. While it seems that this is a new classification I fail to see the clinical relevance.

**Reply 1:** Partially buried parathyroid gland can act as a risk factor for unintended parathyroidectomy comparable to intrathyroidal parathyroid gland, but partially buried parathyroid glands have more chance to be saved if newly invented visualizing technique such as near-infrared autofluorescence technique is adopted than intrathyroidal parathyroid glands. It is worth using near-infrared autofluorescence technique if allowed while performing meticulous capsular dissection.

**Changes in the text:** See page 9, line 15~21, and page 10, line 18~25, page 11, line 1~13

2. Although suggested, you have not shown that using ICG or autofluorescence instruments help in identifying these parathyroids.

**Reply 2:** We could not find the relevant references specifically using autofluorescence to identify the partially buried parathyroid glands, but added more references using autofluorescence to identify parathyroid glands before visual inspection. We deleted one previous reference introducing carbon nanoparticle

**Changes in the text:** We deleted the following paragraph:

“Another recent study reported the use of carbon nanoparticles to identify parathyroid glands during thyroid surgery and this technique was based on the concentration of carbon pellets in thyroid and lymph nodes, and not in parathyroid glands”

See page 10, line 18~25

3. It seems that certain percentage of inadvertent parathyroidectomy is inevitable. How does this classification assist in preventing such cases?

**Reply 3:** Newly introduced classification does not significantly prevent inadvertent parathyroidectomy of partially buried parathyroid glands when it is performed with the naked eye. However, partially buried parathyroid glands have more chance to be saved than intrathyroidal parathyroid glands in the future if appropriate visualizing technique is adopted.

**Changes in the text:** No change was done. We have already mentioned that in

conclusion.

4. Consider adding a reference on intrathyroidal parathyroids (Surgery 2012).

**Reply 4:** we added the above reference and modified our text as advised.

**Changes in the text:** Page 5, line 11, page 9, line 15, page 10, line 5~8

### **Reviewer C**

I think it's obviously already well established that parathyroids can easily be inadvertently removed due to their variable anatomy, small size and location often being subcapsular and intrathyroidal (whether fully or partially) and therefore susceptible despite capsular dissection. But I found this review looking at the specifics of how often they were found in each location was interesting. It doesn't necessarily have a direct clinical application, but the point is made that it could be relevant to consider these anatomical variations when applying additional visualisation techniques for parathyroids.

So overall, well written and interesting topic. Well done.

Just a few minor spelling/grammar issues to fix:

Page 10, Line 9 - spelling "newley"

**Reply:** we have made changes as advised

**Changes in the text:** see page 10, line 9

Page 10, Line 17 - sentence needs editing "Autofluorescence imaging makes surgeons to utilize...", perhaps "Autofluorescence imaging allows surgeons to utilize..."

**Reply:** we have made changes as advised

**Changes in the text:** see page 10, line 17

Page 10, Line 23 - spelling "parathyrid" and "advance" ?should be advances

**Reply:** we have made changes as advised

**Changes in the text:** see page 11, line 15, 16