Editorial Commentary

Advancing parathyroid surgery: a critical examination of probe-based near-infrared autofluorescence technology

Marco Stefano Demarchi^, Frédéric Triponez

Department of Thoracic and Endocrine Surgery and Faculty of Medicine, University Hospitals of Geneva, Geneva, Switzerland

Correspondence to: Frédéric Triponez, MD, PhD. Department of Thoracic and Endocrine Surgery and Faculty of Medicine, University Hospital of Geneva (HUG), Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Switzerland. Email: frederic.triponez@hug.ch.

Comment on: Kiernan CM, Thomas G, Patel A, *et al.* Does the Use of Probe-based Near-infrared Autofluorescence Parathyroid Detection Benefit Parathyroidectomy?: A Randomized Single-center Clinical Trial. Ann Surg 2023;278:549-58.

Keywords: Near-infrared autofluorescence (NIRAF); parathyroid glands (PGs); thyroid surgery

Submitted Feb 18, 2024. Accepted for publication May 08, 2024. Published online Jun 12, 2024.
doi: 10.21037/gs-24-59
View this article at: https://dx.doi.org/10.21037/gs-24-59

Intraoperative detection of parathyroid glands (PGs) can be challenging, even for experienced surgeons (1). This is even more pronounced among younger and less experienced surgeons who may lack the confidence needed for accurate PG identification. With the inherent difficulty in identifying PGs, coupled with the cost of frozen sections, near-infrared autofluorescence (NIRAF) detection emerges as a promising solution to address this challenge. In light of this, Kiernan and colleagues investigate the efficacy of probe-based NIRAF technology for parathyroid identification during parathyroidectomy (2). The recent study by Kiernan *et al.* is a single-center, randomized clinical trial encompassing 160 patients undergoing parathyroidectomy, who were randomly allocated to either the probe-based NIRAF or control group (visual identification).

The trial was conducted in a high-volume surgical center and involved two endocrine surgeons: a senior surgeon with >20-year experience and a junior surgeon with <5-year experience. The study enrolled adult patients undergoing parathyroid surgery for primary hyperparathyroidism (pHPT) or persistent/recurrent pHPT after a failed prior parathyroidectomy. Exclusion criteria comprised cases of secondary or tertiary hyperparathyroidism, or those undergoing concurrent thyroid procedures. Prior to surgery, patients underwent localization studies, including at least an ultrasound. While patients with radiologically localized disease were considered candidates for focused parathyroidectomy, at the discretion of the surgeon, cases deemed nonlocalized or discordant underwent bilateral neck exploration (BNE). Importantly, the senior surgeon in this study routinely performs BNE. Preoperative imaging studies varied among patients, with ultrasound being standard for all, and additional imaging studies performed based on the surgeons' discretion. Intraoperative parathyroid hormone (ioPTH) monitoring was used in all cases, with cure defined according to the Miami criteria.

In their study, Kiernan *et al.* observe a significant improvement in parathyroid identification rates for both senior and junior surgeons, from 3.2 to 3.6 and 2.2 to 2.5 PGs, respectively. In the probe group, PG identification was even more pronounced for residents. Notably, the probe-based NIRAF approach also led to a significant reduction in the number of frozen sections used. The study concludes that probe-based NIRAF detection serves as a valuable intraoperative adjunct and educational tool, instilling confidence in PG identification and potentially reducing the dependence on frozen sections.

The study exhibits several strengths, including a well-defined methodology and a randomized clinical trial design that involves both experienced and junior surgeons. However, the study also has a number of limitations. These include the variability in surgical approaches, ranging from

^ ORCID: 0000-0002-8419-2980.

routine bilateral cervical explorations to focused approaches, and the potential underestimation of failure rates due to incomplete follow-up. It is worth noting that while Kiernan and colleagues assess the advantages of detecting more PGs, they do not explore the utility of discriminating between normal and diseased PGs, as noted by other authors (3-6).

Although this study aligns with prior research on NIRAF's accuracy in PG identification (7-12), controversies arise when comparing the lower specificity observed in this trial to earlier studies (13). Understanding the reasons behind this specificity difference, such as variations in sample size and tissue types, is essential. The study prompts a critical examination of the technology's limitations and areas for refinement. Yet in most clinical scenarios, experienced surgeons can easily distinguish parathyroid and nonparathyroid tissue, including colloid nodules and brown fat. An additional aspect to consider is that this study is conducted in a high-volume surgical center with experienced surgeons, potentially limiting the generalizability of findings to other settings. These aspects emphasize the need for further validation of the technology across both low- and high-volume centers (14).

In the broader context of parathyroid surgery, Kiernan and colleagues address a critical need for improved intraoperative tools. The findings of this study underscore the potential of probe-based NIRAF in this context, not only in enhancing surgeon confidence, but also in reducing the need for frozen section analyses, and potentially lowering costs associated with parathyroidectomy. Kiernan and colleagues address the practical implications of integrating advanced technologies into routine surgical practices. Notably, their study contributes significantly to the existing literature by being the first randomized controlled trial evaluating probe-based NIRAF during parathyroid surgery for pHPT. As highlighted in a recent population-based cohort study by Annebäck *et al.* (15), the risk of hypoparathyroidism after total thyroidectomy remains a significant concern, emphasizing the need for follow-up and improved tools to minimize such complications.

Although NIRAF technologies are frequently used to detect PGs and minimize postoperative hypoparathyroidism, there is a notable research gap regarding their impact in parathyroid surgery. Previous studies have shown NIRAF's superiority over naked eye visualization during surgery (16). This study, consistent with recent research in other low-volume institutions (17,18), offers valuable insights into the impacts that autofluorescence guidance may have on surgical outcomes, particularly for less experienced surgeons.

Within the field of NIRAF imaging, there are currently two types of systems: probe-based and image-based modalities. The former includes the PTeye system (Medtronic, Minnesota, MN, USA) and provides quantitative and auditory feedback upon contact with parathyroid tissue. The latter utilizes a near-infrared light source with a filtered camera, enabling identification of autofluorescence signals on display monitors, and includes the Fluobeam-800/Fluobeam-LX (Fluoptics, France), EleVision™ IR Platform (Medtronic, Minnesota, MN, USA), PDE Neo II (Hamamatsu, Shizuoka Pref. Japan), among others. Concerning parathyroid surgery, both systems offer distinct benefits and limitations. Image-based devices may be particularly advantageous in the hands of young, less experienced surgeons. This can be attributed to a broader simultaneous field of examination compared to probe-based devices, where the probe should be positioned on already visually suspicious parathyroid tissue as a confirmation. Image-based devices, which enable identification of fluorescent signals and thus help detect the heterogeneous fluorescent pattern of adenomas, may contribute to a more accurate prediction of the disease characteristics of a parathyroid adenoma (4-6). Yet both modalities can effectively detect and differentiate between normal and diseased PGs, as diseased PGs can be 30% less fluorescent than normal PGs. This may explain the presence of two false negatives in two parathyroid adenomas in this study. It is worth acknowledging that probe-based systems also hold a practical advantage over image-based modalities in this context, as the small size of the probe proves for surgical procedures conducted through (very) small neck incisions.

The ultimate goal of NIRAF technology is to reduce the incidence of postoperative complications, particularly persistent hyperparathyroidism, but also hypoparathyroidism in cases of multiglandular disease. Yet because experienced centers already have low complication rates (<5% and <1%, respectively), it is likely that no study will be sufficiently powered to address this question. In this context, the number of detected PGs serves as a surrogate marker, wherein detecting more PGs will lead to a reduction in complication rates. The authors should be congratulated for their effort in enhancing patient care.

Despite certain limitations, the integration of probe-based NIRAF in parathyroid surgery represents a promising avenue for improved PG identification. This study marks

a pioneering effort in evaluating the utility of probe-based NIRAF in parathyroid surgery. And while it sheds light on the potential benefits of real-time identification, further research is essential to address limitations and establish the broader applicability of this technology in diverse clinical settings.

Acknowledgments

We would like to thank Dr. Ilaria Di Meglio for her invaluable assistance in editing this editorial commentary.
Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Gland Surgery*. The article has undergone external peer review.

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-59/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-59/coif). F.T. reports consulting fees from Medtronic and Fluoptics part of Getinge. The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Benmiloud F, Godiris-Petit G, Gras R, et al. Association of Autofluorescence-Based Detection of the Parathyroid Glands During Total Thyroidectomy With Postoperative Hypocalcemia Risk: Results of the PARAFLUO Multicenter Randomized Clinical Trial. JAMA Surg 2020;155:106-12.
2. Kiernan CM, Thomas G, Patel A, et al. Does the Use of Probe-based Near-infrared Autofluorescence Parathyroid Detection Benefit Parathyroidectomy?: A Randomized Single-center Clinical Trial. Ann Surg 2023;278:549-58.
3. Lee SM, Dedhia PH, Phay JE. Heterogeneous parathyroid near-infrared autofluorescence patterns are associated with single adenomas in primary hyperparathyroidism. Head Neck 2024;46:592-8.
4. Demarchi MS, Karenovics W, Bédat B, et al. Autofluorescence pattern of parathyroid adenomas. BJS Open 2021;5:zraa047.
5. McWade MA, Sanders ME, Broome JT, et al. Establishing the clinical utility of autofluorescence spectroscopy for parathyroid detection. Surgery 2016;159:193-202.
6. Kose E, Kahramangil B, Aydin H, et al. Heterogeneous and low-intensity parathyroid autofluorescence: Patterns suggesting hyperfunction at parathyroid exploration. Surgery 2019;165:431-7.
7. Wolf HW, Runkel N, Limberger K, et al. Near-infrared autofluorescence of the parathyroid glands during thyroidectomy for the prevention of hypoparathyroidism: a prospective randomized clinical trial. Langenbecks Arch Surg 2022;407:3031-8.
8. Yin S, Pan B, Yang Z, et al. Combined Use of Autofluorescence and Indocyanine Green Fluorescence Imaging in the Identification and Evaluation of Parathyroid Glands During Total Thyroidectomy: A Randomized Controlled Trial. Front Endocrinol (Lausanne) 2022;13:897797.
9. Kim DH, Lee S, Jung J, et al. Near-infrared autofluorescence-based parathyroid glands identification in the thyroidectomy or parathyroidectomy: a systematic review and meta-analysis. Langenbecks Arch Surg 2022;407:491-9.
10. Kose E, Rudin AV, Kahramangil B, et al. Autofluorescence imaging of parathyroid glands: An assessment of potential indications. Surgery 2020;167:173-9.
11. Falco J, Dip F, Quadri P, et al. Cutting Edge in Thyroid Surgery: Autofluorescence of Parathyroid Glands. J Am Coll Surg 2016;223:374-80.
12. Demarchi MS, Karenovics W, Bédat B, et al. Intraoperative Autofluorescence and Indocyanine Green Angiography for the Detection and Preservation of Parathyroid Glands. J Clin Med 2020;9:830.

13. Thomas G, Solórzano CC, Baregamian N, et al. Comparing intraoperative parathyroid identification based on surgeon experience versus near infrared autofluorescence detection - A surgeon-blinded multicentric study. Am J Surg 2021;222:944-51.
14. Iacobone M, Scerrino G, Palazzo FF. Parathyroid surgery: an evidence-based volume-outcomes analysis : European Society of Endocrine Surgeons (ESES) positional statement. Langenbecks Arch Surg 2019;404:919-27.
15. Annebäck M, Osterman C, Arlebrink J, et al. Validating the risk of hypoparathyroidism after total thyroidectomy in a population-based cohort: plea for improved follow-up. Br J Surg 2024;111:znad366.
16. Rao KN, Rajguru R, Dange P, et al. Lower Rates of Hypocalcemia Following Near-Infrared Autofluorescence Use in Thyroidectomy: A Meta-Analysis of RCTs. Diagnostics (Basel) 2024;14:505.
17. Abood A, Rolighed L, Ovesen T, et al. Autofluorescence-guided hemithyroidectomy in a low-volume thyroid institution with no experience in parathyroid surgery: randomized clinical trial. Br J Surg 2024;111:znae075.
18. Abood A, Ovesen T, Rolighed L, et al. Hypoparathyroidism following total thyroidectomy: high rates at a low-volume, non-parathyroid institution. Front Endocrinol (Lausanne) 2024;15:1330524.

Cite this article as: Demarchi MS, Triponez F. Advancing parathyroid surgery: a critical examination of probe-based near-infrared autofluorescence technology. Gland Surg 2024;13(6):1137-1140. doi: 10.21037/gs-24-59