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EDITORIAL – ENDOCRINE TUMORS

Autofluorescence and Artificial Intelligence: The Future of Parathyroid Surgery?

Quan-Yang Duh, MD, and Stephanie N. Davis, MD

Department of Surgery, University of California, UCSF Mount Zion, San Francisco, CA

Postsurgical hypoparathyroidism is a clinically significant complication occurring in about 5–10% of patients undergoing total thyroidectomy. Hypoparathyroidism decreases quality of life and increases the risks of cardiovascular disease, renal failure, and death.[1] The risk of unintentional devascularization or removal of parathyroid glands during thyroidectomy is lower at high-volume centers, especially if parathyroid glands are routinely identified, but unintentional parathyroid removal still occurs in 15–20% of thyroidectomies.[2]

Parathyroid tissue has much higher near-infrared autofluorescence (NIRAF) than thyroid and other background tissues. NIRAF detection devices have been developed to help surgeons identify parathyroid glands intraoperatively. Both image-based and probe-based NIRAF detection devices have been approved by the Food and Drug Administration (FDA) as adjuncts to help identify and protect parathyroid glands during thyroidectomy. Several studies, including a multicenter prospective randomized study, have shown an association between using an image-based NIRAF detection device (Fluobeam, Fluoptics) and a lower risk of transient postoperative hypoparathyroidism.[3]

The experienced thyroid surgeon finds parathyroid glands in varying anatomical locations, informed by their anticipated embryological development. The surgeon visually assesses the color, appearance, and vascularization of the candidate parathyroid glands. When in doubt, their identity can be confirmed by histology or aspiration for PTH assay. With an image-based NIRAF device, the brightness of the NIRAF signal is assessed visually to further confirm (or exclude) the candidate as a parathyroid gland. This process is relatively accurate but is also subjective, like reading an X-ray film. Artificial intelligence (AI) can help with image interpretation. Deep learning describes a class of machine-learning algorithms that uses multiple layers of learning to progressively extract higher-level features from raw input. Computer vision is a field of AI that processes digital images to derive higher-level visual information. Deep learning has been used to process digitized images from ultrasonography for the diagnosis and management of thyroid nodules.[4]

In this issue, Dr. Avici and colleagues used deep machine learning to develop a model for detecting normal parathyroid glands using NIRAF images obtained during thyroid or parathyroid operations.[5] They used 466 parathyroid-specific NIRAF images from 197 patients who underwent thyroid or parathyroid operations. These images were uploaded into Google's AutoML Vision API, a commercially available platform; 80% of the images were used for training, 10% for testing, and 10% for validation. They showed that their model performed very well with recall (sensitivity) of 90.5% and precision (positive predictive value) of 95.7%. It correctly predicted the location of parathyroid glands in 91.9%.

There are several obstacles to overcome for more widespread use of deep-learning models for NIRAF identification of parathyroid glands. False positives and false negatives can only be estimated without histology. For example, a parathyroid gland situated deeper than a millimeter will likely not be identified either by the surgeon visually or by NIRAF imaging (thus false negative for both). False positives from brown fat, colloid nodules, and lymph nodes can only be confirmed with certainty by histology. Since normal-appearing glands are not usually

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Q.-Y. Duh, MD
e-mail: quan-yang.duh@ucsf.edu

biopsied, there is no histological confirmation of their identity. In such a study, the surgeons' visual assessment of tissues (that were not removed or biopsied) was assumed to be correct and used as the gold standard for parathyroid identification. Studies in which all tissues can be removed and tested (by histology or by PTH assay) would be most accurate, but such studies can only ethically be done in deceased donors. These limitations, in addition to the uncertainty of the potential presence of supernumerary parathyroid glands, makes it almost impossible to calculate the true sensitivity, specificity, and positive and negative predictive value of the model.

Recent preliminary studies showed that NIRAF devices may improve the confidence and speed of parathyroid identification, especially for less experienced surgeons;[6] these devices may be good teaching tools to shorten the learning curve. We can speculate that imaging processing by AI may add to this improvement in learning.

For now, the problems of false negatives and false positives, the bulkiness of the imaging system, and the time required for image processing are all obstacles, albeit surmountable. We may soon have artificial intelligence-augmented intraoperative imaging devices to help identify parathyroid glands faster and better than surgeons. Endocrine surgeons are taught to treat every parathyroid gland like it is the patient's last one; AI-augmented intraoperative devices may become one more tool to help us prevent injury to them.

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