Review Article

Methods for the identification and preservation of parathyroid glands in thyroid surgery: a narrative review

Bin Pan[1,2,3,4#], Yuquan Yuan[1,2,3,4#], Zeyu Yang[1,2,3,4], Dengwei Lu[1,2,3,4], Tengjiang Long[1,2,3,4], Yiceng Sun[4], Supeng Yin[4], Fan Zhang[1,2,3,4]

[1]Graduate School of Medicine, Chongqing Medical University, Chongqing, China; [2]Chongqing Institute Green and Intelligent Technology, Chinese Academy of Sciences, Chongqing, China; [3]Chongqing School, University of Chinese Academy of Sciences, Chongqing, China; [4]Department of Breast and Thyroid Surgery, Chongqing General Hospital, Chongqing, China

Contributions: (I) Conception and design: B Pan, S Yin; (II) Administrative support: Y Sun, F Zhang; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: Z Yang, D Lu, T Long; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work and should be considered as co-first authors.

Correspondence to: Fan Zhang, MD, PhD. Graduate School of Medicine, Chongqing Medical University, Chongqing, China; Chongqing Institute Green and Intelligent Technology, Chinese Academy of Sciences, Chongqing, China; Chongqing School, University of Chinese Academy of Sciences, Chongqing, China; Department of Breast and Thyroid Surgery, Chongqing General Hospital, No. 118, Xingguang Avenue, Liangjiang New Area, Chongqing 401147, China. Email: zhangfancgh@163.com; Supeng Yin, MD, PhD. Department of Breast and Thyroid Surgery, Chongqing General Hospital, No. 118, Xingguang Avenue, Liangjiang New Area, Chongqing 401147, China. Email: yinsupeng@163.com.

Background and Objective: Accurate intraoperative identification and viability assessment of the parathyroid glands (PGs) has always been a crucial but challenging aspect of thyroid surgery. The traditional method, naked-eye (NE) assessment, is significantly associated with the experience of the surgeon. Therefore, various methods have been developed to help surgeons protect PGs, with some benefits and limitations. Recently, near-infrared autofluorescence (NIRAF) and indocyanine green fluorescence imaging (ICGFI) have been demonstrated to be promising in the identification and viability assessment of PGs. Herein, we provide an overview of the methods of intraoperative identification and viability assessment of PGs, focusing on the application of NIRAF and ICGFI.

Methods: We performed a systematic literature search of PubMed, Medline, Cochrane Library databases, Web of Science, and EMBASE to identify all relevant studies published up to March 2023. The keywords were ((autofluorescence) OR (indocyanine green)) AND (parathyroid gland).

Key Content and Findings: In this narrative review, we summarized the benefits and limitations of intraoperative methods for PG identification and viability assessment, focusing on the application of NIRAF and ICGFI.

Conclusions: Intraoperative parathyroid protection methods have developed from traditional subjective identification of PGs to the latest near-infrared (NIR) fluorescence imaging technology. The discovery, development, and application of NIRAF and ICGFI have provided better ways for surgeons to protect PGs intraoperatively.

Keywords: Parathyroid glands (PGs); near-infrared fluorescence imaging; autofluorescence; indocyanine green (ICG); thyroidectomy

Submitted Jun 08, 2023. Accepted for publication Aug 27, 2023. Published online Sep 14, 2023.
doi: 10.21037/gs-23-242
View this article at: https://dx.doi.org/10.21037/gs-23-242

Introduction

Hypocalcemia is one of the most frequent complications of thyroidectomy, which is transient in 19–38% and permanent in 0–3% of patients receiving thyroidectomy (1,2). Nevertheless, the incidence of permanent hypocalcemia is even higher than 0–3%, as it is often underreported (3). Hypocalcemia may prolong hospital stay, increase costs, or even lead to lifelong medication needs and increase the risk of mortality (2,4). Therefore, accurate intraoperative identification and viability assessment of the parathyroid glands (PGs) has always been a crucial but challenging aspect of thyroid surgery. As the characteristics of PGs (size, shape, color, etc.) resemble those of surrounding tissues such as adipose tissue and lymph nodes, it is difficult to distinguish them by the naked eye (NE), leading to inadvertent removal or devascularization of PGs.

The traditional method of identifying and assessing PGs relies on NE visual inspection, which not only depends on the experience of the surgeon but is also subjective and often unreliable. Even when at least two PGs assessed as normally viable by NE were preserved, transient hypoparathyroidism still occurred in 13.6% of patients (5). To overcome this deficiency, a variety of techniques have been developed to improve PG visualization and preservation during thyroid surgery (6-10). In recent years, methods based on near-infrared (NIR) fluorescence imaging, including near-infrared autofluorescence (NIRAF) imaging and indocyanine green fluorescence imaging (ICGFI), have been demonstrated to be promising in the identification and perfusion assessment of PGs. PGs exhibit significantly stronger autofluorescence than the surrounding tissues under NIR light irradiation, which could be used to detect PGs in real time during surgery (6). ICG, a NIR-fluorescing exogenous agent, can rapidly bind to plasma proteins and generate fluorescence under irradiation with NIR light after intravenous injection, which can help surgeons assess the blood perfusion of PGs and predict the occurrence of postoperative hypocalcemia (7,8).

This review aims to provide an overview of the methods of intraoperative identification and viability assessment of PGs, focusing on the application of NIRAF and ICGFI. We present this article in accordance with the Narrative Review reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-242/rc).

Methods

We performed a systematic literature search of PubMed, Medline, Cochrane Library databases, Web of Science, and EMBASE published up to March 2023 to identify all relevant studies. The keywords were ((autofluorescence) OR (indocyanine green)) AND (parathyroid gland). Three reviewers (Yang Z, Lu D, Long T) independently conducted the literature search, and disagreements were solved by consensus. The abstracts of the retrieved studies were reviewed and excluded if deemed irrelevant. The full text was checked to determine the final eligible articles. The search strategy summary is shown in *Table 1*.

Discussion

Overview of the intraoperative methods for PG identification and viability assessment

For the identification of PGs, visual inspection of PGs by the NE is most commonly used in thyroid surgery. However, it is sometimes challenging for surgeons to distinguish between PGs and the surrounding tissues because of their similar characteristics, especially for inexperienced surgeons. Hauch *et al.* conducted a study on the association between the incidence of complications after thyroidectomy and the surgical volume of surgeons (11). The results showed that the incidence of hypocalcemia was significantly higher after surgeries performed by low-volume (defined as <10 thyroidectomies/year) surgeons than after surgeries performed by high-volume (defined as >99 thyroidectomies/year) surgeons (13.67% *vs.* 9.30%). Likewise, the American Thyroid Association suggested that a low-volume surgeon is a risk factor for permanent hypoparathyroidism (12). To improve the ability to identify PGs intraoperatively, surgeons have tried various techniques. For example, carbon nanoparticles can make the thyroid and surrounding lymph nodes black, while the PG will not be dyed black when injected into the area of thyroid tissue, which can help to identify the PG intraoperatively (9,10). However, once injected improperly, the carbon nanoparticles will spill and blacken the surrounding tissue, obscuring the surgical field. In addition, the immune colloidal gold technique to measure parathyroid hormone (PTH) can yield results rapidly but is invasive and damaging. Other methods for identifying PGs are summarized in *Table 2* (9,10,13-29). Currently, NIRAF imaging and ICGFI are promising techniques that will be elaborated upon in the following text.

The assessment of PG viability is another necessary part of intraoperative PG protection. A high number of

Table 1 The search strategy summary

Items	Specification
Date of search	2023.03
Databases and other sources searched	PubMed, Medline, Cochrane Library databases, Web of Science, and EMBASE
Search terms used	((autofluorescence) OR (indocyanine green)) AND (parathyroid gland)
Timeframe	2011.06–2023.03
Exclusion criteria	Case report and studies not written in English were excluded
Selection process	Three reviewers (Yang Z, Lu D, Long T) independently conducted the literature search, and disagreements were solved by consensus. The abstracts of the retrieved studies were reviewed and excluded if deemed irrelevant. The full text was checked to determine the final exactly eligible articles

Table 2 Summary of methods for identifying the parathyroid glands intraoperatively

Methods	Description	Advantages	Disadvantages	References
NIRAF imaging	(I) The PGs will emit autofluorescence when stimulated by the near-infrared light at 785 nm wavelength, which is apparently stronger than the fluorescence of the thyroid gland. The surrounding tissues do not emit fluorescence; (II) The PGs can be distinguished from the surrounding tissues according to the fluorescence signal intensity	(I) Label-free and noninvasive technology; (II) Finds more PGs, including isolated PG; (III) Locates the PGs in the operative field; (IV) Reduces the inadvertent removal of the PGs; (V) Reduces the autotransplantation of the PGs; (VI) Reduces the transient hypoparathyroidism	(I) Cannot assess the blood perfusion of the PGs; (II) Interference from electrocoagulated adipose tissue and intragland bleeding; (III) Not available in deep planes; (IV) Turn off the operating room lights; (V) Expensive and cumbersome equipment	Kim *et al.* (13); Kahramangil *et al.* (14); Takahashi *et al.* (15); Kim *et al.* (16); Benmiloud *et al.* (17,18)
ICGFI	(I) Once injected, ICG will rapidly bind to the plasma proteins and fluoresce under the irradiation of near-infrared light, which will be detected by the camera of imaging system; (II) The ICGFI achieves the visualization of the tissues where the dye is present, including the blood vessels of PGs	(I) Rapid metabolism, few adverse effects and repeat injection; (II) Identifies the PGs during the surgery; (III) Assesses the blood perfusion of PGs; (IV) Guides the autotransplantation of PGs; (V) Predicts hypoparathyroidism after surgery	(I) Contraindicated in patients with iodine allergy; (II) Inferior to NIRAF in identifying PGs; (III) Not objective enough; (IV) Affect by the surgeon's learning curve	Hope-Ross *et al.* (19); Zaidi *et al.* (20); Kahramangil *et al.* (21); Lerchenberger *et al.* (22); Di Meo *et al.* (23); Liang *et al.* (24)
Raman spectroscopy	A laser light is used to induce the changes in vibrational and rotational frequency of a molecule, which are measured and analyzed in a spectrometer to biochemically differentiate tissue types	(I) Nondestructive and label-free; (II) Applied in parathyroid surgery to distinguish between parathyroid adenomas, parathyroid hyperplasia and normal parathyroid gland	Current studies are *ex vivo* proof-of-concept studies. *In vivo* studies are needed to validate its usefulness during thyroidectomy and parathyroidectomy	Das *et al.* (25); Palermo *et al.* (26)

Table 2 (*continued*)

Table 2 (*continued*)

Methods	Description	Advantages	Disadvantages	References
Immune colloidal gold technique to measure PTH	Serum samples are collected by the method of fine needle aspiration or tissue block homogenate to measure PTH. The PTH in the sample binds to the colloidal gold–antibody conjugates that are precoated on the conjugate pad to form an immune complex and then captured by the solid-phase chromogenic agent (PTH antibody) located in the test zone on the membrane to form a pink or dark-red ribbon	(I) Rapid, taking only several minutes; (II) Low-cost; (III) Easy operation; no need for expensive equipment or specially trained staff; (IV) A high diagnostic rate of 97.4%	(I) Invasive; may cause some damage to the PGs; (II) The optimal cutoff value of PTH needs further exploration	Xia *et al.* (27); Zhang *et al.* (28)
Carbon nanoparticle injection	(I) Carbon nanoparticles with a diameter of 150 nm are injected into the area of thyroid tissue; (II) Carbon nanoparticles cannot penetrate blood vessels and thus spread to the lymph tubes or lymphatic capillaries. As they gather and deposit in the lymph nodes, the thyroid and its lymph drainage area will be dyed black, while parathyroid glands remain unstained for identification	(I) Minimally prolongs the operation length; (II) No adverse reaction	(I) Once injected improperly, the carbon nanoparticles will obscure the surgical field; (II) Not recommended for larger tumors without apparently normal thyroid tissue; (III) Expensive	Wang *et al.* (9); Shi *et al.* (10)
Dynamic optical contrast imaging	(I) A system consisting of ultraviolet LEDs and an intensified charge-coupled device camera captures images of the fluorescence decay signatures; (II) It extracts relative fluorescence decay information from endogenous fluorophores at various wavelengths and produces contrast imaging based on their different decay rates	(I) Rapid; (II) Does not use invasive dyes or radioactive material	(I) Expensive; (II) *In vivo* imaging needs further improvement	Kim *et al.* (29)

NIRAF, near-infrared autofluorescence; PG, parathyroid gland; ICGFI, indocyanine green fluorescence imaging; ICG, indocyanine green; PTH, parathyroid hormone; LED, light emitting diode.

preserved PGs does not necessarily mean the preservation of parathyroid function because the identification and dissection of PGs may often lead to subtle damage or devascularization (13). Except for assessing the vascular perfusion of PGs by NE, the intraoperative parathyroid hormone (ioPTH) assay can assess whole-PG function, helping predict hypocalcemia (30-32). Lo *et al.* demonstrated that a normal or less than 75% decline in the ioPTH assay can accurately identify normocalcemic patients after thyroidectomy (30). Abdelrahim *et al.* compared the ioPTH assay to ICGFI and found that the diagnostic accuracy of the ICGFI and ioPTH assay was similarly high (82.22% *vs.* 87.78%) (32). Both were higher than the surgeons' diagnostic accuracy of visual inspection (62.22%). However, the mean time needed to identify PGs with ICGFI was 1.2 min ±0.5 SD and for the ioPTH assay was 20 min ±9.49 SD. Neither can assess the function of a single PG, so they cannot guide autotransplantation accurately. Many recent studies have confirmed that ICGFI can assess the blood perfusion of every PG and help surgeons accurately perform PG autotransplantation during surgery (7,8).

NIRAF of the PGs

The basis of NIRAF

When irradiated with light at a wavelength of 785 nm, PGs can emit fluorescence that is 2–11 times stronger than the fluorescence of the thyroid gland, a phenomenon called

autofluorescence of the PGs, which is thought to be closely connected to the natural characteristics of PGs (6,25,33,34) Subsequently, the fluorescence will be detected by the NIR camera at a fluorescence peak of 822 nm, whereas the surrounding tissues, such as lymph nodes and adipose tissue, emit significantly less fluorescence. Therefore, according to the fluorescence signal intensity, PGs and surrounding tissues can be distinguished intraoperatively. The fluorescence signal intensity may be influenced by the body mass index, disease state, vitamin D level, and calcium level (34). However, the basis of autofluorescence remains unclear, as no known fluorescent biomolecules have intrinsic fluorescence beyond 700 nm. Calcium-sensing receptors (CaSRs) in parathyroid and thyroid tissues have been regarded as potential candidates, as they are expressed at the highest levels in parathyroid cells and at lower levels in C cells of the thyroid but not in muscle, fat, or lymph of the neck (6,33).

To date, the systems using NIRAF to identify PG can be generally divided into two types: an imaging-based system and a probe-based system (PTeye). The first type is an imaging-based system (Fluobeam-800 and Fluobeam-LX), which has a higher frequency of use. It consists of an NIR light source, a camera, appropriate filters, and a display monitor, which can provide real-time pictures of PGs and achieve the visualization of PGs (35). The second type is a probe-based system (PTeye), which consists of a disposable fiber-optic probe connected to a console housing an NIR light source and interactive display. It provides real-time visual and auditory feedback when the probe touches a PG, which is similar to a nerve-monitoring device. Although it may be convenient to use during surgery, there is currently little research on its application. Many clinical studies are needed to validate its advantages and disadvantages. Therefore, we are mainly concerned about the application of AF imaging systems in thyroid surgery.

The superiority of NIRAF

Das *et al.* first used NIR light to differentiate between parathyroid adenomas and hyperplasia in 2006 (25). Paras *et al.* first detected PGs using NIRAF (785 nm) during endocrine surgery in 2011 (6). Since then, a growing number of studies have been conducted to validate the superiority of NIRAF in protecting PGs intraoperatively (36). In short, as a label-free technique, the autofluorescence of PGs has the following advantages over other methods: (I) identifying and locating PGs in real time during surgery and (II) reducing the incidence of inadvertent removal, autotransplantation of PGs, and temporary hypoparathyroidism or hypocalcemia.

Identifying and locating PGs in real time during surgery

NIRAF can increase the detection rate of PGs. McWade *et al.* performed autofluorescence measurements on 264 PGs in 137 patients, with a 97% correct identification rate (34). Similarly, a multicenter study showed that the detection rate of PGs based on autofluorescence was as high as 97–99% in different centers, and 46% (272/594) of PGs could not be identified during initial visual assessment of the surgical area due to soft tissue coverage, but NIRAF of these glands could be detected without further dissection (14). In contrast, Takahashi *et al.* analyzed 75 specimens that were resected and sent for histological examination (35 PGs, 34 lymph nodes, 5 adipose tissues, and 1 thyroid tissue) by visual inspection *vs.* NIRAF and found no significant differences in the sensitivity (35/35 by visual inspection and 34/35 by NIRAF) or specificity (34/40 by visual inspection and 35/40 by NIRAF) between the two methods (15). For detecting incidentally resected PGs in thyroidectomy specimens, NIRAF showed significantly higher sensitivity than visual inspection by the surgeon (82.9% *vs.* 61.0%). NIRAF can also increase the mean detection number of PGs. Falco *et al.* found that the mean numbers of PGs identified with NIR light (NIRL) and white light (WL) were 3.7 and 2.5 PG, respectively (37). Likewise, Dip *et al.* confirmed that converting WL to NIRL increased the mean number of detected PGs from 2.6 to 3.5 (38). The autofluorescence imaging system can also contribute to finding accidentally removed PGs in isolated tissue and ectopic PGs (39,40). Bellier *et al.* found 24 fluorescent spots in "surgically nude" specimens, of which 13 were confirmed to be PGs. Despite the utilization of the NIRAF system and the surgeons' experience, 15 of 232 PGs remained undetectable, as they were located beneath the thyroid capsule or concealed among a conglomeration of nodules (41).

Visualizing the location of PGs in the early stage can help the surgeon to better dissect surrounding tissues and protect the vascular tissue of PGs. Kim *et al.* investigated the feasibility of real-time autofluorescence imaging of PGs and visualized the entire surgical area, including parathyroid and background tissues (39). Subsequently, in 2018, by using

NIRAF on a total of 69 PGs at various stages, 64 (92.75%) glands could be detected before visual identification (Stage P1), 4 glands were identified after exposure and visual assessment by the surgeon (Stage P2), and 1 gland was identified in a surgical specimen (Stage P3) (16). They confirmed that the location of PGs could be predicted by fluorescence when covered with fat and connective tissues. However, autofluorescence may not be detected when the PGs are deeper than the penetration depth of the NIR light (0.4 to 5 mm in soft tissues) or when the NIR light cannot penetrate the covering tissues, which does not occur frequently (42). After appropriate dissection by the surgeon, autofluorescence was detected again. While they confirmed that NIRAF may be helpful for the early identification of PGs during thyroidectomy, they did not further explore its effect. Therefore, their study in 2021 used NIRAF in three similar stages to detect PGs, which further validated that visualizing the localization of PGs in the early period allowed less inadvertent resection and less postoperative hypoparathyroidism (13).

Reducing the incidence of inadvertent removal, autotransplantation of PGs, and temporary hypoparathyroidism or hypocalcemia

Visualizing the localization of PGs early in operation with an NIRAF imaging system can help surgeons identify PGs better, which means more careful dissection, less inadvertent removal of PGs, and less PG autotransplantation. As a result, the incidence of postoperative temporary hypoparathyroidism or hypocalcemia decreases.

Benmiloud *et al.* conducted a before-and-after controlled study and confirmed that patients in the NIR+ group suffered significantly less autotransplantation (2.1% *vs.* 15.0%), accidental resection (1.1% *vs.* 7.2%) and postoperative transient hypocalcemia (5.3% *vs.* 20.9%) than those in the NIR– group (17). Notably, the mean duration of surgery between the two groups was exactly the same, although the NIR procedure was time-consuming (3–5 min). However, the study period of the NIR+ group was later than that of the NIR– group, which means that the greater surgical experience of the surgeon may have affected the results. Therefore, they conducted a multicenter randomized controlled study, and it had the same result (18). The incidence of parathyroid autotransplantation (3.3% *vs.* 13.3%), inadvertent removal (2.5% *vs.* 11.7%) and transient hypocalcemia (9.1% *vs.* 21.7%) were significantly lower in the NIRAF group than in the standard-care group. However, no statistically significant differences were found between the two groups in permanent hypocalcemia. In addition, in contrast to the previous study, the duration of surgery was significantly longer in the NIRAF group than in the standard-care group.

Similarly, Kim *et al.* followed up on the levels of PTH and ionized calcium during the hospital stay and 1, 3, and 6 months after surgery to compare the NIRAF group and the control group (13). The results showed that patients in the NIRAF group had a significantly lower incidence of hypoparathyroidism during hospitalization and 1 month after surgery (33.7% *vs.* 46.6% during hospital stay, 8.8% *vs.* 18.9% at postoperative 1 month), while there was no difference in the permanent hypoparathyroidism rate (6 months after surgery) between the NIRAF group and control group (4.2% *vs.* 4.6%). Furthermore, the number of inadvertently resected PGs was significantly lower in the NIRAF group (6.9% *vs.* 12.8%). Unlike Benmiloud *et al.* (17), they found no difference in the incidence of hypocalcemia (iCa. <1.09 mmol/L) at any follow-up time between the two groups, and there was no difference in the number of autotransplanted PGs between the two groups. They concluded that the calcium level can be affected by postoperative fluid infusion or vitamin D or calcium intake, while the PTH level is a direct measure of PG function.

In conclusion, the NIRAF imaging system can help surgeons identify more PGs and detect them more accurately by visualizing their location in real time, which contributes to better dissection and preservation of the vascular tissues of PGs. As a result, fewer autotransplantations and accidental removals of PGs occur intraoperatively, and ultimately, there is a lower incidence of transient hypoparathyroidism or hypocalcemia after surgery. Unfortunately, NIRAF was not superior in reducing postoperative permanent hypoparathyroidism.

The shortcomings of NIRAF

Although NIRAF imaging has many unique advantages in identifying PGs, there are still some shortcomings. Previous studies have highlighted several shortcomings that can impact its application during operation. First, NIRAF imaging cannot provide information regarding the blood perfusion of PGs or their viability (43). PGs can emit autofluorescence even when their vessels are damaged, which is a characteristic of PGs that can be used to find isolated PGs. Additionally, NIRAF imaging can be affected by

electrocoagulated adipose tissue and intragland bleeding, which can cause false positives and false negatives (14). In false-negative cases, autofluorescence cannot be detected when there is massive bleeding in the PG, which is potentially absorbed by hemoglobin in erythrocytes. In false-positive cases, electrocoagulated tissue has similar fluorescence intensity (FI) compared to PG. Furthermore, the autofluorescence cannot be detected when the PG is in a deep plane or covered by many fat tissues, which requires more dissections to detect the autofluorescence again (16). The need to turn off the operating room lights to capture the images is one of the drawbacks of the NIRAF imaging system, as it may prolong the surgery (43). For Fluobeam LX, room ceiling lights can remain on, while the remaining light sources should be switched off (35). For a probe-based system (PTeye), ambient operating room lights do not interfere with its function (35). Last, the high cost of NIRAF imaging equipment and cumbersome operations may limit its widespread adoption. Oh *et al.* demonstrated the early feasibility of a portable hand-held imager (44). The imager was held approximately 20–30 cm from the surgical field. The system has two modes: mode 1 permits label-free, noninvasive localization of PGs using NIRAF, and mode 2 enables continuous visualization of the vasculature and viability assessment of PGs using real-time dye-free angiography using an 830 nm laser source, which means that it can allow both PG detection and viability assessment. However, its clinical value needs further exploration.

NIR ICGFI

The basis of NIR ICGFI

Indocyanine green (ICG), a sterile, water-soluble fluorescent dye with rapid metabolism and few adverse effects, was first approved for clinical use by the FDA in 1956 (7,19). Once injected, ICG rapidly binds to plasma proteins and generates fluorescence under irradiation with NIR light, which is detected by the camera of the imaging system (16). As a result, ICGFI achieves visualization of the tissues where the dye is present, including the blood vessels of PGs. It is then taken up by hepatocytes and excreted into the bile (45). ICG has a half-life of 3.4±0.7 min, which allows repeated injections (46).

The superiority of NIR ICGFI

Since its approval for clinical use, ICG angiography has been widely used in neurosurgery, bypass coronary surgery, flap operations in reconstructive surgery, laparoscopic surgery, oncology, sentinel lymph node harvesting, and other applications (7). In 2015, Suh *et al.* first applied the ICGFI to the detection of PGs in dogs (47). In 2016, Vidal Fortuny *et al.* used ICGFI during thyroid surgery and built an ICG scoring system (48) (a similar system in our center is shown in *Figure 1*). Since then, multiple clinical studies have used ICGFI for human thyroid or parathyroid surgery (49,50). In summary, ICGFI makes the following contributions to surgery: (I) identifying PGs during surgery; and (II) visualizing the PG blood vessels, assessing PG viability, determining the autotransplantation of PGs and predicting the occurrence of postoperative hypoparathyroidism.

Identifying PGs during surgery

In 2016, Zaidi *et al.* found that the majority (84%) of PGs exhibit ICG fluorescence during total thyroidectomy (TT) and suggested that PGs could be identified by ICGFI prior to thyroid dissection (20). However, the identification may be prevented by the fact that the thyroid gland demonstrated intense fluorescence with ICG administration. In the same year, Yu *et al.* first applied ICGFI to robotic thyroidectomy and confirmed that patients in the ICG group had significantly lower rates of incidental parathyroidectomy than those in the control group (0 *vs.* 15.9%) (51). However, patients in the two groups had similar rates of transient hypoparathyroidism and permanent hypoparathyroidism.

Moreno-Llorente *et al.* reported different results (52). Compared to the control group, patients in the ICGFI group, in whom ICGFI was used to guide thyroidectomy and assess perfusion after thyroidectomy, suffered transient hypocalcemia less frequently (5.6% *vs.* 26.2%) and similarly for permanent hypocalcemia (0 *vs.* 11.9%). In addition, the number of glands left *in situ* with an ICG score of 2 in the ICGFI group was higher than that in the control group. However, the two cohorts were not operated on in the same period. Although the surgery was performed by one endocrine surgeon, as time passed, the experience of the surgeon in the two periods may have

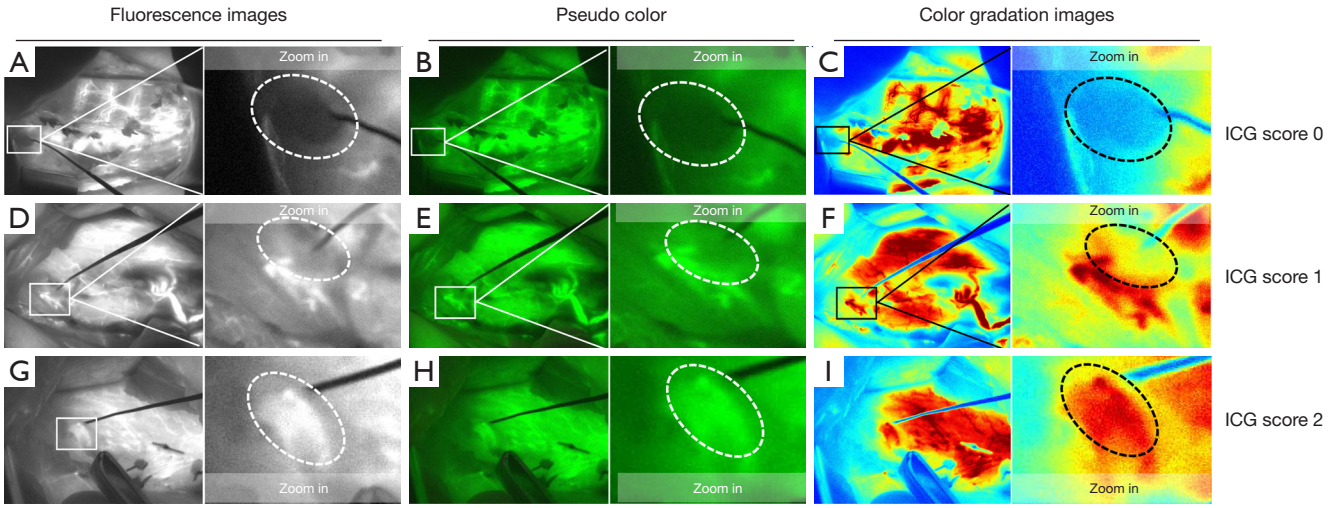

Figure 1 Representative parathyroid indocyanine green fluorescence images from our research. (A-C) Black parathyroid gland indicates no blood perfusion (ICG score 0). (D-F) Gray parathyroid gland indicates partial blood perfusion (ICG score 1). (G-I) White parathyroid gland indicates adequate blood perfusion (ICG score 2). ICG, indocyanine green.

been different, which may be the reason that worse results were obtained in the historical control group. Similarly, Demarchi *et al.* conducted a study to determine whether the introduction of ICGFI resulted in a reduced incidence of hypoparathyroidism on postoperative day POD 1 (53). On the one hand, the reduction in hypoparathyroidism after the introduction of ICGFI may be the result of modifications in the surgical technique over time. On the other hand, it may be the result of the Hawthorne effect, which can be explained by the fact that surgeons may have noted the possibility of evaluating PGs with ICGFI and thus would subconsciously engage in a more meticulous dissection of the vascular pedicle when using ICGFI.

In terms of the difference between ICGFI and other methods in the identification of PGs, Kahramangil *et al.* first compared ICGFI and AF during thyroidectomy (21). The results showed that AF and ICGFI had similar detection rates for PGs (98% *vs.* 95%) but differed in the timing of identification. AF could detect PGs more frequently than ICGFI before NE (52% *vs.* 6%), whereas the transient postoperative hypocalcemia rates in both groups were not significantly different (9% *vs.* 5%). Consistent with Zaidi *et al.* (20), they also found that ICG uptake in the thyroid gland significantly limited their ability to identify PGs. Likewise, Lerchenberger *et al.* compared ICGFI and AF and found that both were helpful in identifying PGs intraoperatively, finding a sensitivity of 82% for AF and 81% for ICGFI (22). However, they thought the two techniques were not sufficiently sensitive to serve as screening tools that would help to localize parathyroid tissue at an early stage of the operation, as the AF will not appear when the PGs are covered by a sheath of adipose tissue and even minor bleeding at the operating site can obscure the ICG fluorescence. In 2021, Di Meo *et al.* applied ICGFI to the intraoperative localization of pathological PGs in 37 patients with hyperparathyroidism (23). The ICGFI successfully identified 59 of the 62 PGs. They performed a subanalysis of 30 patients (55 PGs) whose PGs were identified by all three tests: ultrasonography (US), technetium-99m sestamibi scintigraphy (MIBI) and ICGFI. The sensitivity of PG detection by ICGFI was 96% (53/55), which was significantly higher than that of US (55%; 35/55) and MIBI (63%; 37/55).

Visualizing the PG blood vessels, assessing PG viability, determining the autotransplantation of PGs and predicting the occurrence of postoperative hypoparathyroidism

Angiography is undoubtedly useful for assessing blood vessels. Prior to thyroid resection, angiography was performed to precisely identify and preserve the parathyroid pedicle (50,52). In 2016, Vidal Fortuny *et al.* found that all patients who had at least one well-vascularized PG by ICGFI had PTH levels in the normal range on POD 1 and 10, and only one patient exhibited asymptomatic hypocalcemia on POD 1 (48). They suggested that

treatment for hypoparathyroidism is unnecessary for patients who have at least one well-vascularized PG by ICGFI. Subsequently, they applied ICGFI to parathyroidectomy and validated the usefulness of ICGFI in parathyroid surgery (49). In 2018, their randomized controlled study also suggested that TT can be performed safely in patients with at least one well-perfused PG by ICGFI, without the need for systematic calcium/PTH measurements, without the need for systematic calcium supplementation, and without the risk of hypocalcemia (8). In the study, 146 of the 196 patients who had at least one well-vascularized PG by ICGFI were randomized to receive standard follow-up (measurement of calcium and PTH on POD 1 and systematic supplementation with calcium and vitamin D; control group) or no supplementation and no blood test on POD 1 (intervention group). The results showed that no hypoparathyroidism was observed in either group. The 50 patients who were not included in the randomized part of the study failed to demonstrate at least one well-perfused PG by ICGFI. Eleven of the 50 patients presented with postoperative hypoparathyroidism, which was significantly more than was found in randomized patients. Furthermore, ICGFI was thought to change the management of PG autotransplantation, as 23 of the 37 PGs were auto-transplanted based on ICGFI, indicating the absence of perfusion. Similarly, in 2021, Liang *et al.* applied ICGFI to transoral endoscopic thyroidectomy and found that patients who retained at least one well-perfused PG on ICGFI during TT had higher PTH levels and were less likely to develop hypoparathyroidism on POD 1 than those without any well-perfused PG on ICGFI (24).

However, Rudin *et al.* argued that there was significant correlation between at least two well-vascularized PGs by ICGFI (using the ICG scoring system) and normal postoperative PTH levels, which may predict postoperative PG function (54). They found that detecting at least one normal gland by ICGFI had 57% accuracy in predicting normal postoperative PTH, with a sensitivity of 58% and specificity of 50%, while there was no correlation between finding at least one vascularized PG by ICGFI and normal postoperative PTH levels. When patients had at least two normal glands by ICGFI, the accuracy and sensitivity increased by 63% and 72%, respectively. The reasons why ICGFI was not accurate enough to predict normal postoperative PTH could be that ICGFI is subjective and the researchers did not have enough experience. Moreover, for the PG with impaired venous drainage, ICGFI may not accurately assess its function. The result that patients in the ICGFI group suffered from autotransplantation of PGs more frequently than those in the control group (36% *vs.* 12%) confirmed the usefulness of ICGFI in PG autotransplantation.

Therefore, PG assessment of ICGFI using the ICG scoring system is a qualitative method that may not be objective enough to assess PG perfusion, as it can be affected by the learning curve of the operator. Importantly, Lang *et al.* developed a quantitative method to calculate the FI of each identifiable *in situ* parathyroid gland (ISPG), which was expressed as the intensity ratio between it and the anterior trachea (55). They analyzed 70 patients who had 4 identifiable PGs that were confirmed on histology and calculated the FI of each ISPG and found that the greatest FI was significantly correlated with PTH on POD 0, PTH on POD 1 and % drop in PTH from preoperative to POD 0. When the greatest FI was >150% (i.e., a FI >150% in at least one ISPG), the risk of developing subsequent hypocalcemia was 0/59. Iritani *et al.* used the maximum intensity ratio (MIR) to quantitatively assess blood perfusion, which was calculated as the maximum FI after ICG injection divided by the intensity before ICG injection (56). They found that MIR was useful in predicting postoperative PG function, and the optimal MIR cutoff value for predicting postoperative hypoparathyroidism was 2.14, which had an area under the curve =0.904 (sensitivity: 0.769 and specificity: 1.00).

In our opinion, ICGFI has a relatively limited role in the identification of PGs during surgery because there is background interference from the thyroid gland. The benefits of ICGFI in decreasing the postoperative hypoparathyroidism or hypocalcemia rates require further exploration. ICGFI can assess the vessels of PGs at the site after thyroidectomy to guide the autotransplantation of PGs. The presence of at least one well-perfused PG by ICGFI can predict normal postoperative PTH levels, which means that there is no need for systematic calcium supplementation.

The shortcomings of NIR ICGFI

ICGFI has emerged as a promising technique for assessing the blood perfusion of PGs. However, it is essential to acknowledge some of the shortcomings of this method. First, known or suspected allergy to iodine or shellfish is an absolute contraindication to ICGFI (44,57). Additionally, ICGFI is inferior to NIRAF in locating PGs, as it may be prevented by ICG uptake in the thyroid gland. Moreover,

ICGFI is considered "passive", as it allows the assessment of PG vascularization only after the completion of thyroid resection, failing to provide the blood perfusion of preserved PGs in real time. Finally, the assessment of PG perfusion by ICGFI with the ICG scoring system is not sufficiently objective, as it is rated by the surgeon and affected by the learning curve. For PGs with an ICG score of 1, there is still no clear explanation of whether they should be auto-transplanted, which needs further exploration. Aside from quantitative methods to assess the FI, a recent study validated the feasibility of applying computer-assisted deep learning models to recognize and localize parathyroid-specific NIRAF on intraoperative NIR images (58). Therefore, the development of deep learning models to judge the images of PGs to guide their autotransplantation may be the next step.

Combined use of NIRAF imaging and ICGFI

NIRAF imaging is uniquely superior in identifying PGs, which can help surgeons find and locate PGs in real time before any dissection. The operator can dissect the tissues surrounding the PGs carefully, according to their location. Regardless of how careful surgeons are at dissecting the tissues, subtle damage or devascularization is inevitable. Therefore, assessing blood perfusion is essential for protecting PGs. NIRAF cannot evaluate the blood perfusion of PGs, but ICGFI can accurately assess the blood perfusion of PGs and help operators perform the autotransplantation of PGs. Explaining that some advantages and disadvantages of the two novel NIR optical technologies are complementary, some researchers believe that combining the two methods in one fluorescence system may protect the PGs more comprehensively.

In 2018, Vidal Fortuny *et al.* proposed the idea of using NIRAF to identify PGs, followed by ICGFI to confirm their vascularization, which was not achieved as a result of the limitation of equipment (8). Afterward, Alesina *et al.* first demonstrated the feasibility of combining autofluorescence and ICG angiography in video-assisted neck surgery (59). However, its ability to reduce the incidence of postoperative hypoparathyroidism was unproven, which may be related to the small sample size of that study. Subsequently, in 2021, a video study confirmed that in TT, the systematic application of NIRAF and ICGFI can guide surgeons in the early identification and autotransplantation of PGs to prevent and predict postoperative hypoparathyroidism (60).

A prospective randomized controlled study conducted by our research team showed that patients who underwent TT in the NIR fluorescence imaging (including NIRAF and ICGFI) group (NIFI group) suffered from less transient hypoparathyroidism than those in the control group (27.8% *vs.* 43.3%) (61). In addition, more PGs were identified (3.6±0.5 *vs.* 3.2±0.4), and more PGs were preserved *in situ* (1.3±0.6 *vs.* 1.0±0.5) in the NIFI group than in the control group. Among the patients with at least one well-perfused PG in both groups, the rate of postoperative hypoparathyroidism in the NIFI group was significantly lower than that in the control group (4.5% *vs.* 34.6%), which meant that the accuracy of assessment of PG perfusion by NIFI was significantly higher than that by NE. There was no significant difference in the number of auto-transplanted PGs between the two groups, which may be the result of the offset effect: NIRAF can identify more PGs to reduce PG autotransplantation, while ICGFI may increase PG autotransplantation. Similarly, Rossi *et al.* reported that their NIFI group had a significantly higher number of identified PGs than their NE group and that having at least 2 well-vascularized PGs correlated with lower rates of transient hypocalcemia (62).

Overall, the combined use of NIRAF and ICGFI can not only identify PGs in real time before any dissection but also assess the blood perfusion of PGs *in situ* to guide autotransplantation after thyroidectomy and decrease the rate of postoperative hypoparathyroidism, achieving full protection of PGs in thyroid or parathyroid surgery.

Conclusions

Intraoperative parathyroid protection methods have developed from traditional subjective identification of PGs to the latest NIR fluorescence imaging technology. Although NIRAF and ICGFI have some limitations, their discovery, development and application have provided better ways for surgeons to protect PGs intraoperatively. The concerns that remain to be resolved include the following. First, the limitation of fluorescence equipment affects its clinical application. Miniaturization, portability, integration of functions and ease of operation are the trends in the development of fluorescent equipment. In our opinion, the development of equipment similar to intraoperative neuromonitoring devices may be the next hot topic in PG protection. Second, the scoring system of ICGFI is not objective enough to assess the viability of PGs. Although explorations in that direction have been undertaken before, finding a quantitative method to clarify PG viability by

ICGFI is an outstanding need. Additionally, applying deep learning to ICGFI is a promising research direction that needs further exploration.

Acknowledgments

Funding: This work was supported by the Chongqing Medical Scientific Research Project (Joint Project of Chongqing Health Commission and Science and Technology Bureau) (No. 2023QNXM017) and the Chongqing Health Appropriate Technology Promotion Project (No. 2022jstg036).

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-242/rc

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-242/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-242/coif). The authors have 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. Christou N, Mathonnet M. Complications after total thyroidectomy. J Visc Surg 2013;150:249-56.
2. Edafe O, Antakia R, Laskar N, et al. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. Br J Surg 2014;101:307-20.
3. Annebäck M, Hedberg J, Almquist M, et al. Risk of Permanent Hypoparathyroidism After Total Thyroidectomy for Benign Disease: A Nationwide Population-based Cohort Study From Sweden. Ann Surg 2021;274:e1202-8.
4. Almquist M, Ivarsson K, Nordenström E, et al. Mortality in patients with permanent hypoparathyroidism after total thyroidectomy. Br J Surg 2018;105:1313-8.
5. Ji YB, Song CM, Sung ES, et al. Postoperative Hypoparathyroidism and the Viability of the Parathyroid Glands During Thyroidectomy. Clin Exp Otorhinolaryngol 2017;10:265-71.
6. Paras C, Keller M, White L, et al. Near-infrared autofluorescence for the detection of parathyroid glands. J Biomed Opt 2011;16:067012.
7. Alander JT, Kaartinen I, Laakso A, et al. A review of indocyanine green fluorescent imaging in surgery. Int J Biomed Imaging 2012;2012:940585.
8. Vidal Fortuny J, Sadowski SM, Belfontali V, et al. Randomized clinical trial of intraoperative parathyroid gland angiography with indocyanine green fluorescence predicting parathyroid function after thyroid surgery. Br J Surg 2018;105:350-7.
9. Wang B, Qiu NC, Zhang W, et al. The role of carbon nanoparticles in identifying lymph nodes and preserving parathyroid in total endoscopic surgery of thyroid carcinoma. Surg Endosc 2015;29:2914-20.
10. Shi C, Tian B, Li S, et al. Enhanced identification and functional protective role of carbon nanoparticles on parathyroid in thyroid cancer surgery: A retrospective Chinese population study. Medicine (Baltimore) 2016;95:e5148.
11. Hauch A, Al-Qurayshi Z, Randolph G, et al. Total thyroidectomy is associated with increased risk of complications for low- and high-volume surgeons. Ann Surg Oncol 2014;21:3844-52.
12. Orloff LA, Wiseman SM, Bernet VJ, et al. American Thyroid Association Statement on Postoperative Hypoparathyroidism: Diagnosis, Prevention, and Management in Adults. Thyroid 2018;28:830-41.
13. Kim DH, Kim SW, Kang P, et al. Near-Infrared Autofluorescence Imaging May Reduce Temporary Hypoparathyroidism in Patients Undergoing Total Thyroidectomy and Central Neck Dissection. Thyroid 2021;31:1400-8.
14. Kahramangil B, Dip F, Benmiloud F, et al. Detection of Parathyroid Autofluorescence Using Near-Infrared

Imaging: A Multicenter Analysis of Concordance Between Different Surgeons. Ann Surg Oncol 2018;25:957-62.
15. Takahashi T, Yamazaki K, Ota H, et al. Near-Infrared Fluorescence Imaging in the Identification of Parathyroid Glands in Thyroidectomy. Laryngoscope 2021;131:1188-93.
16. Kim SW, Lee HS, Ahn YC, et al. Near-Infrared Autofluorescence Image-Guided Parathyroid Gland Mapping in Thyroidectomy. J Am Coll Surg 2018;226:165-72.
17. Benmiloud F, Rebaudet S, Varoquaux A, et al. Impact of autofluorescence-based identification of parathyroids during total thyroidectomy on postoperative hypocalcemia: a before and after controlled study. Surgery 2018;163:23-30.
18. 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.
19. Hope-Ross M, Yannuzzi LA, Gragoudas ES, et al. Adverse reactions due to indocyanine green. Ophthalmology 1994;101:529-33.
20. Zaidi N, Bucak E, Yazici P, et al. The feasibility of indocyanine green fluorescence imaging for identifying and assessing the perfusion of parathyroid glands during total thyroidectomy. J Surg Oncol 2016;113:775-8.
21. Kahramangil B, Berber E. Comparison of indocyanine green fluorescence and parathyroid autofluorescence imaging in the identification of parathyroid glands during thyroidectomy. Gland Surg 2017;6:644-8.
22. Lerchenberger M, Al Arabi N, Gallwas JKS, et al. Intraoperative Near-Infrared Autofluorescence and Indocyanine Green Imaging to Identify Parathyroid Glands: A Comparison. Int J Endocrinol 2019;2019:4687951.
23. Di Meo G, Karampinis I, Gerken A, et al. Indocyanine Green Fluorescence Angiography Can Guide Intraoperative Localization During Parathyroid Surgery. Scand J Surg 2021;110:59-65.
24. Liang TJ, Wang KC, Wang NY, et al. Indocyanine Green Angiography for Parathyroid Gland Evaluation during Transoral Endoscopic Thyroidectomy. J Pers Med 2021;11:843.
25. Das K, Stone N, Kendall C, et al. Raman spectroscopy of parathyroid tissue pathology. Lasers Med Sci 2006;21:192-7.
26. Palermo A, Fosca M, Tabacco G, et al. Raman Spectroscopy Applied to Parathyroid Tissues: A New Diagnostic Tool to Discriminate Normal Tissue from Adenoma. Anal Chem 2018;90:847-54.
27. Xia W, Zhang J, Shen W, et al. A Rapid Intraoperative Parathyroid Hormone Assay Based on the Immune Colloidal Gold Technique for Parathyroid Identification in Thyroid Surgery. Front Endocrinol (Lausanne) 2020;11:594745.
28. Zhang A, Gao T, Wu S, et al. Feasibility of using colloidal gold immunochromatography for point-of-care identification of parathyroid glands during thyroidectomy. Biochem Biophys Res Commun 2018;507:110-3.
29. Kim IA, Taylor ZD, Cheng H, et al. Dynamic Optical Contrast Imaging. Otolaryngol Head Neck Surg 2017;156:480-3.
30. Lo CY, Luk JM, Tam SC. Applicability of intraoperative parathyroid hormone assay during thyroidectomy. Ann Surg 2002;236:564-9.
31. Gupta S, Chaudhary P, Durga CK, et al. Validation of intra-operative parathyroid hormone and its decline as early predictors of hypoparathyroidism after total thyroidectomy: A prospective cohort study. Int J Surg 2015;18:150-3.
32. Abdelrahim HS, Amer AF, Mikhael Nageeb R. Indocyanine Green Angiography of Parathyroid Glands versus Intraoperative Parathyroid Hormone Assay as a Reliable Predictor for Post Thyroidectomy Transient Hypocalcemia. J Invest Surg 2022;35:1484-91.
33. McWade MA, Paras C, White LM, et al. A novel optical approach to intraoperative detection of parathyroid glands. Surgery 2013;154:1371-7; discussion 1377.
34. McWade MA, Sanders ME, Broome JT, et al. Establishing the clinical utility of autofluorescence spectroscopy for parathyroid detection. Surgery 2016;159:193-202.
35. Solórzano CC, Thomas G, Berber E, et al. Current state of intraoperative use of near infrared fluorescence for parathyroid identification and preservation. Surgery 2021;169:868-78.
36. Sehnem L Jr, Noureldine SI, Avci S, et al. A multicenter evaluation of near-infrared autofluorescence imaging of parathyroid glands in thyroid and parathyroid surgery. Surgery 2023;173:132-7.
37. Falco J, Dip F, Quadri P, et al. Increased identification of parathyroid glands using near infrared light during thyroid and parathyroid surgery. Surg Endosc 2017;31:3737-42.
38. Dip F, Falco J, Verna S, et al. Randomized Controlled Trial Comparing White Light with Near-Infrared

Autofluorescence for Parathyroid Gland Identification During Total Thyroidectomy. J Am Coll Surg 2019;228:744-51.
39. Kim SW, Song SH, Lee HS, et al. Intraoperative Real-Time Localization of Normal Parathyroid Glands With Autofluorescence Imaging. J Clin Endocrinol Metab 2016;101:4646-52.
40. De Leeuw F, Breuskin I, Abbaci M, et al. Intraoperative Near-infrared Imaging for Parathyroid Gland Identification by Auto-fluorescence: A Feasibility Study. World J Surg 2016;40:2131-8.
41. Bellier A, Wazne Y, Chollier T, et al. Spare Parathyroid Glands During Thyroid Surgery with Perioperative Autofluorescence Imaging: A Diagnostic Study. World J Surg 2021;45:2785-90.
42. Stolik S, Delgado JA, Pérez A, et al. Measurement of the penetration depths of red and near infrared light in human "ex vivo" tissues. J Photochem Photobiol B 2000;57:90-3.
43. 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.
44. Oh E, Lee HC, Kim Y, et al. A pilot feasibility study to assess vascularity and perfusion of parathyroid glands using a portable hand-held imager. Lasers Surg Med 2022;54:399-406.
45. Desmettre T, Devoisselle JM, Mordon S. Fluorescence properties and metabolic features of indocyanine green (ICG) as related to angiography. Surv Ophthalmol 2000;45:15-27.
46. Sadowski SM, Vidal Fortuny J, Triponez F. A reappraisal of vascular anatomy of the parathyroid gland based on fluorescence techniques. Gland Surg 2017;6:S30-7.
47. Suh YJ, Choi JY, Chai YJ, et al. Indocyanine green as a near-infrared fluorescent agent for identifying parathyroid glands during thyroid surgery in dogs. Surg Endosc 2015;29:2811-7.
48. Vidal Fortuny J, Belfontali V, Sadowski SM, et al. Parathyroid gland angiography with indocyanine green fluorescence to predict parathyroid function after thyroid surgery. Br J Surg 2016;103:537-43.
49. Vidal Fortuny J, Sadowski SM, Belfontali V, et al. Indocyanine Green Angiography in Subtotal Parathyroidectomy: Technique for the Function of the Parathyroid Remnant. J Am Coll Surg 2016;223:e43-9.
50. Benmiloud F, Penaranda G, Chiche L, et al. Intraoperative Mapping Angiograms of the Parathyroid Glands Using Indocyanine Green During Thyroid Surgery: Results of the Fluogreen Study. World J Surg 2022;46:416-24.
51. Yu HW, Chung JW, Yi JW, et al. Intraoperative localization of the parathyroid glands with indocyanine green and Firefly(R) technology during BABA robotic thyroidectomy. Surg Endosc 2017;31:3020-7.
52. Moreno-Llorente P, García-Barrasa A, Pascua-Solé M, et al. Usefulness of ICG Angiography-Guided Thyroidectomy for Preserving Parathyroid Function. World J Surg 2023;47:421-8.
53. Demarchi MS, Flaris AN, Fortuny JV, et al. Effect of introduction of indocyanine green angiography of parathyroid glands on postoperative hypoparathyroidism after total thyroidectomy. BJS Open 2022;6:zrac059.
54. Rudin AV, McKenzie TJ, Thompson GB, et al. Evaluation of Parathyroid Glands with Indocyanine Green Fluorescence Angiography After Thyroidectomy. World J Surg 2019;43:1538-43.
55. Lang BH, Wong CK, Hung HT, et al. Indocyanine green fluorescence angiography for quantitative evaluation of in situ parathyroid gland perfusion and function after total thyroidectomy. Surgery 2017;161:87-95.
56. Iritani K, Teshima M, Shimoda H, et al. Intraoperative quantitative assessment of parathyroid blood flow during total thyroidectomy using indocyanine green fluorescence imaging - surgical strategies for preserving the function of parathyroid glands. Laryngoscope Investig Oto 2022;7:1251-8.
57. Dip F, Alesina PF, Anuwong A, et al. Use of fluorescence imaging and indocyanine green during thyroid and parathyroid surgery: Results of an intercontinental, multidisciplinary Delphi survey. Surgery 2022;172:S6-S13.
58. Avci SN, Isiktas G, Berber E. A Visual Deep Learning Model to Localize Parathyroid-Specific Autofluorescence on Near-Infrared Imaging : Localization of Parathyroid Autofluorescence with Deep Learning. Ann Surg Oncol 2022. [Epub ahead of print]. doi: 10.1245/s10434-022-11632-y.
59. Alesina PF, Meier B, Hinrichs J, et al. Enhanced visualization of parathyroid glands during video-assisted neck surgery. Langenbecks Arch Surg 2018;403:395-401.
60. Noltes ME, Metman MJH, Jansen L, et al. Parathyroid Function Saving Total Thyroidectomy Using Autofluorescence and Quantified Indocyanine Green Angiography. VideoEndocrinology 2021;8:ve.2021.0008.
61. 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.
62. Rossi L, Vasquez MC, Pieroni E, et al. Indocyanine green fluorescence and near-infrared autofluorescence may improve post-thyroidectomy parathyroid function. Surgery 2023;173:124-31.

Cite this article as: Pan B, Yuan Y, Yang Z, Lu D, Long T, Sun Y, Yin S, Zhang F. Methods for the identification and preservation of parathyroid glands in thyroid surgery: a narrative review. Gland Surg 2023;12(9):1276-1289. doi: 10.21037/gs-23-242