



Near-infrared fluorescence imaging plus indocyanine green fluorescence in patients undergoing a total thyroidectomy and central neck lymph node dissection: is it worth it?

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Thyroid surgery has seen a dramatic evolution since its precarious beginnings when mortality approached 40% (1) and the procedure was banned by the French Academy of Medicine (2). The modern thyroid surgeon enjoys a practice where serious adverse events are uncommon, and most patients safely recuperate in the outpatient setting. Despite these advances, postoperative hypoparathyroidism remains a frequent and challenging complication leading to decreased patient quality of life and increased health care costs (3,4). Patients requiring a central neck dissection for thyroid cancer are at increased risk of postoperative hypoparathyroidism compared to patients undergoing thyroidectomy alone because of removal and devascularization of the parathyroids during removal of the lymph nodes (5). It is in this setting that surgeons have been searching for technology to help them identify and protect parathyroid glands during thyroid surgery.

In 2013, McWade *et al.* published their sentinel study on the use of near-infrared autofluorescence (NIRAF) for identification of parathyroid glands during thyroid surgery (6). NIRAF technology relies on the intrinsic property of tissue to emit autofluorescence when exposed to the near-infrared spectrum of light (7,8). Parathyroid autofluorescence is notably distinct from surrounding tissues including fat, muscle, and thyroid, which allows for parathyroid tissue to be identified and protected using NIRAF technology (8). NIRAF can be coupled with

indocyanine green angiography (ICGA), which is used for vascular mapping and assessing tissue perfusion. When used together, NIRAF and ICGA have shown promise as surgical adjuncts to help surgeons identify, protect, and assess the perfusion of parathyroid glands during thyroid surgery, leading to decreased rates of postoperative hypoparathyroidism (9).

In the study entitled “Impact of near-infrared fluorescence imaging plus indocyanine green fluorescence on postoperative hypoparathyroidism rates after total thyroidectomy and central neck lymph node dissection”, Di Lorenzo *et al.* compared the efficacy of NIRAF-alone, NIRAF + ICGA, and a control group using only visual identification of the parathyroids. These three groups were evaluated in their ability to protect against postoperative hypoparathyroidism in patients undergoing a total thyroidectomy with central neck dissection. In this retrospective evaluation of prospectively collected data, the authors found a significantly lower rate of transient hypoparathyroidism (less than six months) in the NIRAF + ICGA group compared with the visual identification and NIRAF-alone groups. There was no significant difference in the rates of permanent hypoparathyroidism (lasting over six months) between the three groups, but there was a trend toward improvement in both NIRAF groups, with no patients in the NIRAF + ICGA group experiencing permanent hypoparathyroidism. The authors also found

a higher number of identified parathyroid glands and parathyroid gland auto-transplantation in the NIRAF-alone and NIRAF + ICGA groups compared to the control group. There were no significant differences between operative time, length of stay, and final pathology (10).

NIRAF + ICGA technology represents an exciting new frontier in thyroid surgery, but like the implementation of recurrent laryngeal nerve monitoring in the 2000's, the adoption of NIRAF technology has been somewhat measured. The Di Lorenzo *et al.* study is part of a growing wealth of data that supports the use of NIRAF in thyroid surgery. Benmiloud *et al.* reported a multicenter randomized control trial using NIRAF during total thyroidectomy and found a decreased incidence of temporary hypoparathyroidism and an increased rate of parathyroid preservation during total thyroidectomy (11). Similarly, Dip *et al.* published a single institution randomized control trial and found that NIRAF during thyroidectomy increased intraoperative identification of parathyroid glands and decreased the incidence of postoperative hypocalcemia (12). Rossi *et al.* conducted a prospective randomized single institution study which showed that a significantly higher number of parathyroid glands were identified in patients who had their surgery using NIRAF + ICGA along with a decreased risk of postoperative symptomatic hypocalcemia (13). Bergenfelz *et al.* also performed a randomized controlled trial and discovered a lower rate of hypoparathyroidism on the day after surgery among patients undergoing central lymph node dissection with NIRAF compared to the control group (14). Taken with the study by Di Lorenzo the volume of data supporting the use of NIRAF (with or without ICGA) has heightened the excitement about the potential of this technology.

As with most new surgical technology, questions as to the cost effectiveness and whether the technology truly improves outcomes remain. Theoretically, NIRAF would be most beneficial for surgeons who are less experienced or who perform a lower volume of thyroid surgeries. But this population may be less willing to spend the money to acquire the technology as their practice does not have the volume to justify the cost. Sturgeon *et al.* found that low volume surgeons were less likely to adopt nerve monitoring technology during its initiation (15). The reason for this hesitancy by low volume surgeons is unclear, but in addition to the cost, new technology may also have a steep learning curve which lessens efficiency or is time consuming. Furthermore, the cost benefit of NIRAF is difficult to justify when most patients with temporary hypoparathyroidism are

managed as an outpatient with low-cost calcium and vitamin D supplementation. More cost-benefit analyses are needed to investigate the financial effectiveness of NIRAF. Finally, data on the benefit of NIRAF in reducing the incidence of permanent hypoparathyroidism remains sparse, despite this being the group that would benefit the most from preventing this complication.

In summary, NIRAF + ICGA is an evolving and promising technology for surgeons to minimize the most common complication of thyroid surgery. As demonstrated again by Di Lorenzo *et al.* NIRAF + ICGA may have a role in mitigating the risk of hypoparathyroidism, especially for patients at high risk for parathyroid disruption, such as those undergoing a central neck dissection. Other high-risk cases that could benefit from NIRAF include patients with extensive malignancy or re-operations in patients who may have previously experienced injury to the parathyroid glands. Although questions still exist on its best use, cost effectiveness, and long-term benefits, it represents an exciting new tool that may hold the potential to improve patient outcomes and improve health care costs.

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