Clinical case



# Utility of using Indocyanine green to locate parathyroid adenoma and predict hypocalcemia

## Summary

**Introduction:** Secondary hypocalcemia due to hypoparathyroidism is a frequent complication of parathyroidectomy, which has certain difficulties in terms of intraoperative localization of the gland, since the surgeon uses his sight, touch and experience, to reach the task of the surgical act.

**Clinical case:** 62-year-old woman, who started her current condition 8 months ago when she was diagnosed with osteoporosis, with hypercalcemia and significant elevation of parathyroid hormone. Cervical ultrasound and 99mTc-MIBI scintigraphy were requested, showing a nodular image compatible with parathyroid adenoma in the left lower thyroid lobe. The patient underwent left inferior parathyroidectomy with the use of indocyanine green.

**Conclusion:** The identification of a parathyroid adenoma intraoperatively with the aid of fluorescence appears to be a reproducible, safe and easy way to use when treating this type of endocrine pathology.

**Keywords:** parathyroid adenoma, indocyanine green, parathormone, parathyroid gland

Volume 12 Issue 2 - 2024

Gallardo Navarro Elias,[1] Adame Paredes Raúl,[1] Vigil Escalera Bejarano Maria,[1] Flores Vite Martha Gabriela,[1] Mansilla Alba Armando,[1] Mancera Steiner Carlos,[2] García Rodríguez Francisco[2]

[1]General Surgery, Oncological surgery, Mexcio
[2]Spanish Hospital of Mexico City, Mexcio

**Correspondence:** Gallardo Navarro Elias, General Surgery, Oncological surgery, Av. Mexican National Army 613, Granada, Miguel Hidalgo, 11520 Mexico City, CDMX, Email gallard18e@gmail.com

**Received:** June 12, 2024 | **Published:** June 24, 2024

## Introduction

Hypocalcemia due to hypoparathyroidism is a frequent complication of thyroid and parathyroid surgery. A common cause of parathyroidectomy is primary hyperparathyroidism, which has certain difficulties in terms of intraoperative localization of the hyperfunctioning gland. The surgeon, in order to successfully perform this surgery, uses his sight, touch and experience, however, this task is not always achieved.[1,2] Primary hyperparathyroidism is an endocrinological disease with clinical features that include kidney stones, pancreatitis, gastric ulcers, bone demineralization and elevated serum calcium levels. Solitary parathyroid adenomas account for approximately 80-89% of cases of primary hyperparathyroidism.[1,3] Indocyanine green angiography (ICG) is a useful tool for predicting post-thyroidectomy hypocalcemia because it quickly and reliably locates the parathyroid glands in real time, thus preventing inadvertent removal of a healthy gland. Intraoperative devascularization and glandular trauma are frequent causes of early hypocalcemia, this complication occurs in a variable percentage of patients, from less than 5% to 49%, this method also helps to locate in a simple way a hyperfunctioning adenoma.[4] In the field of endocrine surgery, surgery of the thyroid, parathyroid and adrenal glands is linked to the use of indocyanine green (ICG), which makes it possible to make anatomical structures visible in real time, both in open and laparoscopic or robotic surgery.[5,6] Some pre-operative factors that increase the risk of injury to a healthy parathyroid gland are simultaneous for parathyroid and thyroid surgery such as modified cervical anatomy either by inflammation or previous cervical surgery. With a planned lymph node resection, we identify a single parathyroid gland with adequate vascularity that is assessed with a high fluorescence intensity objectively to determine the identification and correct function of the parathyroid gland after surgery. In this case we evaluated the usefulness of indocyanine green fluorescence angiography for intraoperative localization of hyperfunctioning adenoma in parathyroidectomy for primary hyperparathyroidism, with its respective benefits.

## Clinical case

A 62-year-old female patient, with no relevant history, allergies denied, began her current condition 8 months ago when she was diagnosed with osteoporosis, which was treated with alendronate, in addition to referring adynamia and osteopenia, complementary studies were requested where hypercalcemia and significant elevation of parathyroid hormone (PTH) were evidenced. On physical examination, no alterations were observed in the neck, without the presence of adenomegaly and visible or palpable alterations. Laboratories: Serum calcium of 13 mg/dl and parathyroid hormone level of 234 pg/ml (normal values range from 10 to 55). Pathological history: Osteoporosis (T-score > 2.5 SD below maximum bone mass). Cervical ultrasound was requested, showing a nodular image compatible with parathyroid adenoma in the left lower thyroid lobe. The 99mTc-MIBI scan showed a hyperintense MIBI uptake compatible with hyperfunctioning parathyroid tissue in the left lower thyroid pole. He underwent left inferior parathyroidectomy with the use of indocyanine green.

## Surgical technique

The parathyroid glands were accessed through a 3 cm incision in anterior neck region 2 cm from the sternal fork. The prethyroid muscles were visualized and laterally rejected, the thyroid gland was luxated to the right to identify the enlarged left inferior parathyroid gland. After objectifying the suspicious lesion, the anesthesiologist administered 5 mg of ICG (5 mg / ml ICG dissolved in 10 cc sterile water) as an intravenous bolus, subsequently using laparoscopy optics designed to capture the fluorescence of the administered ICG (Figure 1). The left inferior parathyroid gland obtained a higher fluorescent enhancement one minute after the injection (Figure 2 & 3). After confirming the fluorescence with ICG, the vascular pedicle of the parathyroid gland was ligated, and the gland was sent for transoperative study with the pathology service which reported parathyroid adenoma.

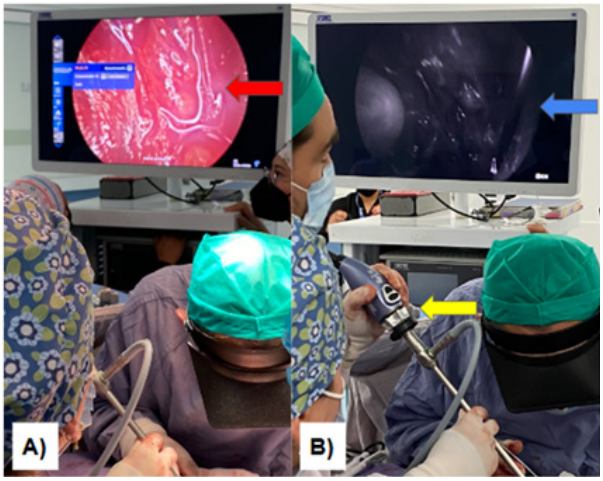


**Figure 1** (A) Red arrows show the laparoscope with LED light (B) Blue arrow with laparoscope image in monochromatic mode, yellow arrow shows the surgeon directing directly to the parathyroid gland.

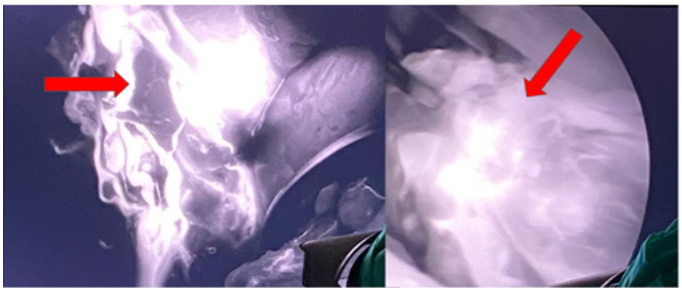

**Figure 2** (A) Red arrow shows in monochromatic mode the hyperfunctioning parathyroid gland at 5 min (B) Red arrow shows in monochromatic mode the hyperfunctioning parathyroid gland at 10 min with a marked vascularization of the same.

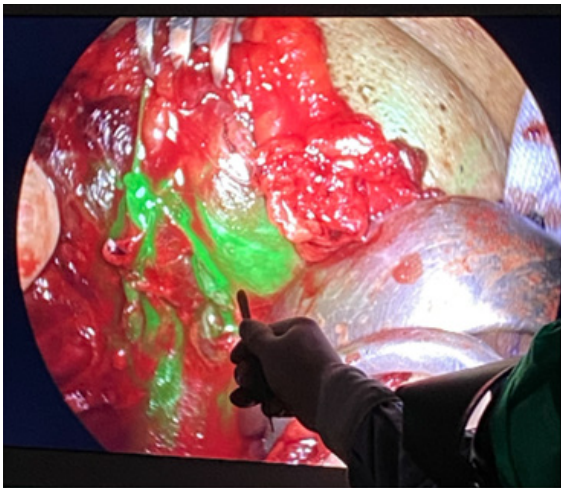

**Figure 3** Marked vascularization and fluorescein green color IN LED mode at 5 min.

The surgical technique was successfully completed, corroborating that the parathyroid adenoma removed corresponded to the one located preoperatively. Parathyroid hormone levels were taken 10 minutes after resection with a decrease of more than 50 percent. The sample was taken in the jugular vein, fulfilling the surgical objective. He had an adequate postoperative period and was discharged the following day with normal serum calcium and PTH, in adequate clinical conditions and without calcium supplements.

## Discussion

The parathyroid glands have anatomical variability and little macroscopic differentiation from the surrounding tissues, for this reason it makes the visualization of these structures difficult in the surgical act, especially of the thyroid tissue by which they are surrounded.[6,7] The extreme locations of the parathyroid glands have been little described in the literature, but they have been found in the mediastinum and in the bifurcation of the carotid artery.[7,8] Embryologically the inferior parathyroids originate in the third pharyngeal pouch, while the superior parathyroids descend from the fourth, the epithelium of the pharyngeal pouches forming the outlines of the parathyroids, proliferate forming small nodules between which the vascularized mesenchyme penetrates to form the stroma of the glands. Subsequently, these are disconnected from the pharynx and are fixed to the thyroid gland, the inferior parathyroids are the ones that travel a greater distance, therefore, they have higher rates of ectopia.[8,9] There are several mechanisms involved in post-surgical hypocalcemia, from direct damage to the glands, lesion of the vascularization system, mechanical damage or by inadvertent or voluntary partial or complete excision of the glands. Parathyroid vascularization is complex and its variants make the surgical act difficult. Most frequently, the inferior thyroid artery is the dominant vessel providing irrigation to both inferior and superior parathyroids, which also usually receives a blood supply from the superior thyroid artery. Nevertheless, there are individuals with dominance of some of the arteries.[10,11] Another predictor of early hypocalcemia is intraoperative PTH levels lower than 7-17.9 pg/ml, as well as postoperative PTH decreases greater than 62.5-80%. Also low levels of intact PTH, generally <10-15 pg/ml, in the first 24 hours postoperatively have shown high sensitivity and specificity to predict the development of hypocalcemia.[10,12] Primary hyperparathyroidism is a disease produced by alterations in the parathyroid glands, which produce an elevated secretion of PTH. Physiologically, the elevated secretion of PTH produces hypercalcemia due to an increase in the tubular reabsorption of calcium, phosphaturia and stimulation of bone reabsorption.[9,13] Parathyroidectomy with neck exploration is the surgical treatment of choice, currently various strategies have been The parathyroid glands have anatomical variability and little macroscopic differentiation from the surrounding tissues, for this reason it makes the visualization of these structures difficult in the surgical act, especially of the thyroid tissue by which they are surrounded.[6,7] The extreme locations of the parathyroid glands have been little described in the literature, but they have been found in the mediastinum and in the bifurcation of the carotid artery.[7,8] Embryologically the inferior parathyroids originate in the third pharyngeal pouch, while the superior parathyroids descend from the fourth, the epithelium of the pharyngeal pouches forming the outlines of the parathyroids, proliferate forming small nodules between which the vascularized mesenchyme penetrates to form the stroma of the glands. Subsequently, these are disconnected from the pharynx and are fixed to the thyroid gland, the inferior parathyroids are the ones that travel a greater distance, therefore, they have higher rates of ectopia.[8,9] There are several mechanisms involved in post-surgical hypocalcemia, from direct damage to the glands, lesion of the vascularization system, mechanical damage or by inadvertent or voluntary partial or complete excision of the glands. Parathyroid vascularization is complex and its variants make the surgical act difficult. Most frequently, the inferior thyroid artery is the dominant vessel providing irrigation to both inferior and superior parathyroids, which also usually receives a blood supply from the superior thyroid artery. Nevertheless, there are individuals with dominance of some of the arteries.[10,11] Another predictor of early hypocalcemia is intraoperative PTH levels lower than 7-17.9 pg/ml,

**Citation:** Elias GN, Raúl AP, Maria VEB, et al. Utility of using Indocyanine green to locate parathyroid adenoma and predict hypocalcemia. *MOJ Surg.* 2024;12(2):73–75. DOI: 10.15406/mojs.2024.12.00265

as well as postoperative PTH decreases greater than 62.5-80%. Also low levels of intact PTH, generally <10-15 pg/ml, in the first 24 hours postoperatively have shown high sensitivity and specificity to predict the development of hypocalcemia.[10,12] Primary hyperparathyroidism is a disease produced by alterations in the parathyroid glands, which produce an elevated secretion of PTH. Physiologically, the elevated secretion of PTH produces hypercalcemia due to an increase in the tubular reabsorption of calcium, phosphaturia and stimulation of bone reabsorption.[9,13] Parathyroidectomy with neck exploration is the surgical treatment of choice, currently various strategies have been studied to improve the identification of the parathyroid glands. In 1971 Dudley described the use of methylene blue for this surgery, but the appearance of toxic encephalopathy in certain patients decreased its use. Similarly, aminolevulinic acid is another tool that has been used, but the need to previously photosensitize the patient and protect him/her from light for 48h after surgery has also hindered its use.[7,8,14] In head and neck surgeries, ICG was initially used to help preserve the parathyroid glands during thyroidectomy with a dose of 25 mg of ICG powder in 10 ml of sterile water administered intravenously in a dose of 3 ml, which can be repeated up to a maximum of 5 mg/kg.[15–17] In a study comparing 2 scoring systems (ICG-2 vs. ICG-4), in which they used the classification used to measure the vascularity of the glands, which divides the color of the glands as: black for not vascularized (Score 0), gray as partially vascularized (Score 1) and white, as a well vascularized (Score 2). The ICG-4 system based on the sum of the score value of the 4 glands translates to a score of 2 in at least one gland of the ICG-2 has a higher diagnostic accuracy than that obtained from the sum of the score of each gland and for the cut point ≤3 of ICG-4. In the study of Galvez-Pastor, in patients with all 4 glands identified, it is mentioned that the ICG-2 scoring system has higher diagnostic accuracy in terms of the quality of a single parathyroid with score 2 than that of ICG-4, thus avoiding the need to systematically identify all parathyroid glands during thyroidectomy. These results are consistent with the usefulness of ICG angiography for in situ assessment of parathyroid gland perfusion and function to prevent early hypocalcemia.[17] Zaidi et al. demonstrated the usefulness of fluorescence imaging, specifically for patients undergoing initial surgery for primary hyperparathyroidism, showing that 92.9% of the glands visible to the naked eye demonstrated ICG uptake and that all 33 patients in the study were biochemically cured of their hyperparathyroidism after surgery.[15,16] In another study involving 60 patients, 54 patients underwent preoperative sestamibi scintigraphy, of which 36 patients were identified as having a parathyroid adenoma, while 18 patients had no abnormalities. However, of these 18 patients, a fluorescent adenoma on indocyanine green imaging was found. This tool has the potential to help surgeons identify parathyroid gland abnormalities quickly with minimal intraoperative risk.[18] ICG appears to intraoperatively facilitate identification of the vascular pedicle of the parathyroid gland offering a decrease of inadvertent resection of a healthy gland or identification of an adenoma, as in our case.

## Conclusion

The identification of a parathyroid adenoma intraoperatively with the aid of fluorescence appears to be a reproducible, safe and easy to use way to treat this type of endocrine pathology with adequate visual and histopathological correlation.

## Acknowledgments

None.

## Conflicts of interest

The authors declare that there are no conflict of interest.

## References

1. Roy M, Mazeh H, Chen H, et al. Incidence and localization of ectopic parathyroid adenomas in previously unexplored patients. *World J Surg.* 2013;37:102–106.
2. Ruda JM, Hollenbeak CS, Stack BC Jr. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. *Otolaryngol Head Neck Surg*. 2005;132(3):359–372.
3. Gila Bohórquez A, Suárez Grau J, Gómez Menchero J, et al. Indocyanine green fluorescence-guided primary hyperparathyroidism parathyroidectomy. *Cirugía Andaluza.* 2020;31(3):326–329.
4. Puzziello A, Rosato L, Innaro N, et al. Hypocalcemia following thyroid surgery: Incidence and risk factors. A longitudinal multicenter study comprising 2,631 patients. *Endocrine.* 2014;47:537–542.
5. Behrns KE. *Surgical anatomy and technique: a pocket manual*. Mayo Clin Proc. Elsevier; 2016;70(10):1022.
6. Meruane M, Smok C, Rojas M. Face and neck development in vertebrates. I*nt J Morphol [Internet]. Sociedad Chilena de Anatomía*; 2012;30(4):1373–1388.
7. Dudley NE. Methylene blue for rapid identification of the parathyroids. *Br Med J.* 1971;3(5776):680–681.
8. Prosst RL, Weiss J, Hupp L, et al. Fluorescence-guided minimally invasive parathyroidectomy: Clinical experience with a novel intraoperative detection technique for parathyroid glands. *World J Surg.* 2010;34(9):2217–2222.
9. Zaidi N, Bucak E, Okoh A, et al. The utility of indocyanine green near infrared fluorescent imaging in the identification of parathyroid glands during surgery for primary hyperparathyroidism. J Surg Oncol. 2016;113(7):771–774.
10. Castro A, Del Rio L, Gavilan J. Stratifying the risk of developing clinical hypocalcemia after thyroidectomy with parathyroid hormone. *Otolaryngol Head Neck Surg.* 2018;158(1):76–82.
11. Huguet I, Muñoz M, Cortés M, et al. Postoperative thyroid hypocalcemia diagnosis and management protocol. *Revista de Osteoporosis y Metabolismo Mineral [Internet*]. 2020;12(2):71–76.
12. Lombardi CP, Raffaelli M, Princi P, et al. Early prediction of postthyroidectomy hypocalcemia by one single iPTH measurement. *Surgery.* 2004;136(6):1236–1241.
13. 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;29:2811–2817.
14. Sound S, Okoh A, Yigitbas H, et al. Utility of indocyanine green fluorescence imaging for intraoperative localization in reoperative parathyroid surgery. *Surg Innov*. 2019;26(6):774–779.
15. 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(7):775–778.
16. Rupp GE, Barba P, Goldhaber NH, et al. Indocyanine green fluorescence guided resection of parathyroid adenoma of the carotid sheath: a case report and review of the literature. *Gland Surg.* 2023;12(4):548–554.
17. Moreno Llorente P, García Barrasa A, Francos Martínez JM, et al. Intraoperative indocyanine green (ICG) angiography of the parathyroids glands in prediction of post-thyroidectomy hypocalcemia: Diagnostic accuracy of the ICG score 2 versus the 4-ICG score. *Cirugía Española.* 2022;100(5):274–280.
18. DeLong JC, Ward EP, Lwin TM, et al. Indocyanine green fluorescence-guided parathyroidectomy for primary hyperparathyroidism. *Surgery.* 2018;163(2):388–392.

**Citation:** Elias GN, Raúl AP, Maria VEB, et al. Utility of using Indocyanine green to locate parathyroid adenoma and predict hypocalcemia. *MOJ Surg.* 2024;12(2):73–75. DOI: 10.15406/mojs.2024.12.00265