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Parathyroid Preservation During Act of Thyroidectomy

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Abstract:

Background: Parathyroid gland preservation during thyroidectomy remains a critical surgical challenge, as inadvertent injury or devascularization may lead to transient or permanent hypoparathyroidism. Despite advancements in surgical techniques, maintaining parathyroid viability and function is not always guaranteed. Several intraoperative identification and preservation strategies have been developed, including routine identification, use of dyes, and novel imaging modalities. Additionally, parathyroid autotransplantation has emerged as a valuable technique to restore gland function when viability is compromised. This review aims to evaluate the current strategies for parathyroid gland preservation during thyroidectomy, including identification techniques, emerging technologies, and the role of parathyroid autotransplantation.

Keywords: Parathyroid preservation; Thyroidectomy; Hypoparathyroidism; Near-infrared fluorescence; Indocyanine green; Autotransplantation

Introduction:

Thyroidectomy is a commonly performed surgical procedure for a wide range of thyroid disorders; however, it carries a significant risk of postoperative hypoparathyroidism due to inadvertent injury, devascularization, or removal of the parathyroid glands. Even with meticulous surgical techniques, transient hypocalcemia remains relatively frequent, while permanent hypoparathyroidism, although less common, represents a serious and life-altering complication. The preservation of parathyroid gland function is therefore considered a cornerstone of safe thyroid surgery, requiring precise anatomical knowledge and careful intraoperative handling **(Ludwig et al., 2023).**

In recent years, several advances have been introduced to enhance intraoperative identification and assessment of parathyroid gland viability, including near-infrared fluorescence imaging, indocyanine green angiography, and other optical technologies. These modalities aim to improve real-time visualization and reduce the risk of gland ischemia. Additionally, parathyroid autotransplantation has become an established strategy when gland viability is uncertain, helping to minimize the incidence of permanent hypoparathyroidism. Despite these developments, the optimal approach to parathyroid preservation remains a subject of ongoing research and clinical debate **(Rubinstein et al., 2021).**

Parathyroid preservation:

Routine Identification:

The term "**routine identification**" refers to a strategy where the surgeon would try his or her best to identify each and every PG in its orthotopic or non-orthotopic position. This has traditionally been the approach accepted by many surgeons. **(Chang & Lang, 2017)**.

For many years, the fundamental principle of parathyroid preservation during thyroid surgery had been to maintain all the parathyroids in situ on a vascularized pedicle. In addition, there was a belief that any parathyroid apparently preserved, which maintained a tan color, was viable and could thus be left intact **(George et al., 2023)**.

Although the incidence of permanent hypoparathyroidism has always been acceptably low in our unit it still occurred in 1–2% of cases, presumably because of late or unrecognized ischemia of the preserved parathyroid glands. It is now recognized that, not only is dissection of parathyroid glands on a vascularized pedicle a very time-consuming process, especially for those situated high on the thyroid surface, but it does not necessarily guarantee their preservation **(Ludwig et al., 2023).**

Many a parathyroid gland that has been painstakingly dissected on a long pedicle simply infarcts later on as a result of thrombosis of the tenuous vascular supply, or as a result of oedema and swelling of the gland within its dissected capsule. **(Mehta, 2020)**.

Methylene blue:

Methylene blue is a hetero-cyclic aromatic chemical compound which has been widely used in sentinel lymph node biopsies **(Zolfaghari et al., 2009)**.

Methylene blue (MB) was administered at a calculated dose of 5 mg/kg body weight in 500 ml of 5% glucose, intravenous administration of methylene blue resulted in staining of both normal and abnormal parathyroid glands. The administration of high-dose MB can be associated with serious adverse events such as toxic metabolic encephalopathy and can lead to blue staining of the complete surgical field due to leakage of dye into the tissue when the operation takes a long time **(Tummers et al., 2015)**.

High-dose MB (7.5 mg/kg) has many disadvantages. The operative field may be discolored by blue dye, the staining may not be visualized through overlying tissue or fascia, there may be significant discoloration of the patient's skin and urine and patients may suffer severe allergic reaction to the dye. **(Patel et al., 2012)**.

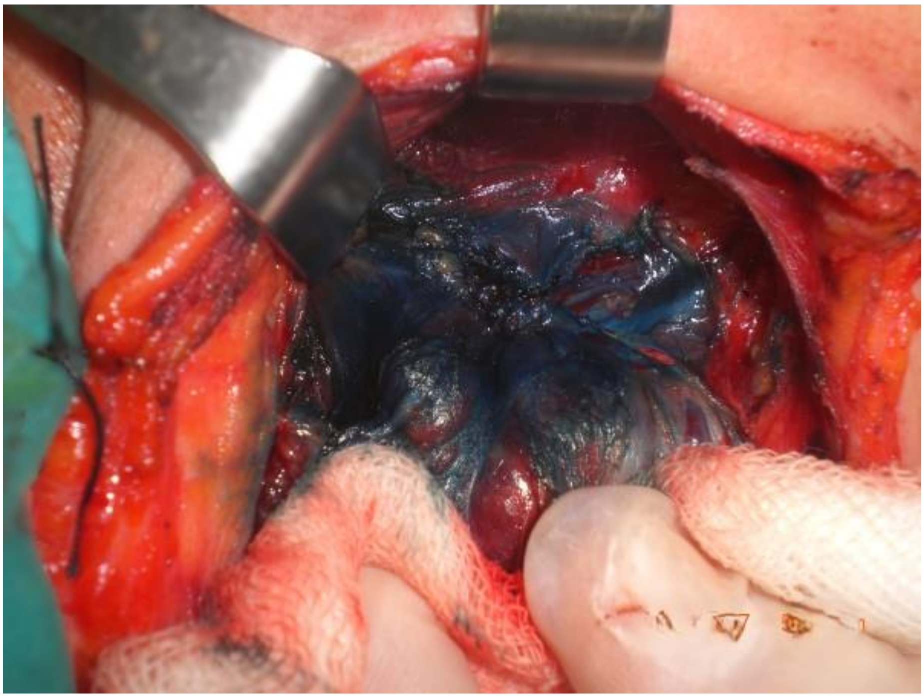

Figure (1): Intra-operative methylene blue spraying. **(Sari et al., 2012)**

Intraoperative optical coherence tomography imaging:

Optical coherence tomography (OCT) is a non-invasive high- resolution imaging technique that permits characterization of microarchitectural features in real time. The technique is capable of distinguishing between parathyroid tissue, thyroid tissue, lymph nodes, and adipose tissue **(Sommerey et al., 2015)**.

Optical coherence tomography (OCT) is a high-resolution microscopic imaging modality that combines a broadband, low- coherent light with interferometry to visualize living tissue microstructure, OCT works in a similar manner to ultrasound but uses near-infrared light instead of sound waves to distinguish intrinsic differences in tissue structures. In general, OCT systems can have an axial resolution of approximately 10 µm with a depth penetration up to 2 mm **(Rubinstein et al., 2021).**

nevertheless, OCT imaging has a limited penetration depth of only 2 mm. It evaluates only the superficial layers of tissues, and in some cases may provide false readings due to tissue samples being surrounded by adipose tissue. This may cause false identification of tissue types is the specific tissue of interest is surrounded by a fat layer. **(Rubinstein et al., 2021)**.

Near-Infrared fluorescence (NIRF):

Is one of several novel technologies that may be useful in early identification and preservation of parathyroid glands during surgery. Fluorophores re-emit light of a higher wavelength when excited by a light source. Some emit light outside of the visible spectrum in the near infra-red region (700–900 nm). NIRF has been used in surgery to aid real-time intraoperative visualization of tissues and differentiate between tissue types including sentinel lymph node mapping **(Tummers et al., 2015)**.

Indocyanine green fluorescent imaging:

ICG is a water-soluble molecule that binds to plasma protein and confined to intravascular compartment. It will emit fluorescent light when being excited by near-infrared light (NIR) thus, the combination of ICG and NIR may provide real-time assessment on tissue perfusion within a focused area reflected by the fluorescent light intensity. ICG fluorescent imaging potentially helps locate PG and thus prevent inadvertent parathyroidectomy or damaging them. **(Lang et al., 2017).**

Moreover, ICG angiography may provide quantitative evaluation of in situ PG perfusion after total thyroidectomy, and could be a good predictor for post-operative hypoparathyroidism. Therefore, ICG fluorescent angiography could potentially be a less invasive option for identifying PGs during thyroidectomy and provide more accurate prediction of parathyroid function **(Chang & Lang, 2017).**

The chance of complications due to intravenous administration of the dye, including neurotoxicity and acute dye-induced phototoxicity, pain at infusion site and nausea is a major drawback of this technique **(Van Den Bos et al., 2019)**.

This method is considered very expensive and requires a special dye is expensive and a special camera is also expensive, so it is difficult to find in most hospitals **(Tummers et al., 2015)**.

Parathyroid auto transplantation:

The concept of parathyroid auto transplantation was first introduced by Halsted in 1909, though systematic clinical application began with the pioneering work of Wells and colleagues in the 1970s. established the fundamental principles of parathyroid tissue fragmentation and heterotopic implantation, demonstrating the feasibility of functional restoration. subsequently expanded upon these techniques, introducing protocols for cryopreservation and delayed transplantation. These early contributions established the foundation for modern parathyroid transplantation approaches and identified key factors influencing graft survival, including tissue preparation methods, recipient site selection, and optimal fragment size. **(Wells et al., 1975).**

Selective parathyroid autotransplantation:

Although there had been sporadic reports of parathyroid auto- transplantation, it has only been in the last 20 years, after Wells confirmed both biochemically and clinically the success of parathyroid autotransplantation in a large series of patients undergoing parathyroidectomy that the technique has become used. In fact, only in recent times has it really become accepted as part of routine clinical practice during total thyroidectomy **(Mehta, 2020).**

The initial approach of the unit was to selectively auto transplant any parathyroid gland that was difficult to dissect or was of dubious viability after dissection. It was during this stage that it was recognized that not all "tan" parathyroids are viable. Venous obstruction in association with pedicle ligation will lead to the classic "black" ischemic parathyroid; however, isolated ligation of the end artery to a parathyroid gland will often lead to the gland becoming ischemic while remaining tan **(Ludwig et al., 2023).**

This led to the use of the “knife” test where the capsule of dubious parathyroid glands is carefully incised – the absence of capillary oozing is an additional indication for autotransplantation. Parathyroid autotransplantation can be readily achieved by the “injection technique”. Each parathyroid gland removed for autotransplantion is made into a suspension of parathyroid cells in 2-mL buffered saline by mincing with scissors. The suspension can then easily be injected into the ipsilateral sternomastoid muscle with a blunt vial access pin **(Mehta, 2020).**

Routine parathyroid autotransplantation:

Although most authors still favor the approach of selective “ready” parathyroid autotransplantation, the unit has now adopted routine autotransplantation, a philosophical approach based on the understanding that while parathyroid autotransplantation is very effective, the viability of in situ vascularized parathyroids remains unpredictable with late ischemia always a possibility. The routine autotransplantation of at least one parathyroid gland during every total thyroidectomy, while unnecessary in most cases, provides insurance in cases where late ischemia of the remaining glands actually occurs **(Ludwig et al., 2023).**

The parathyroid gland chosen for routine autotransplantation is either one determined to be non-viable on the basis of anatomical location or a failed knife-test, or else the least viable appearing of the remaining in situ glands. Routine autotransplantion will be associated with an increase in the rate of temporary hypocalcemia in the short term but has, in theory, the potential to reduce permanent hypoparathyroidism to zero **(Mehta, 2020)**.

Traditional Forearm Implantation technique:

The forearm implantation technique represents the classical approach to parathyroid auto transplantation. This procedure involves several critical steps: 1) Tissue preparation through meticulous removal of surrounding fat and capsule, followed by mincing into 1×1×1 mm fragments; 2) Creation of small muscle pockets within the brachioradialis or flexor muscles of the non-dominant forearm; 3) Implantation of 10–20 tissue fragments into separate muscle pockets; and 4) Marking of the implantation site with non-absorbable sutures or metallic clips for future identification. This approach offers several advantages, including technical simplicity, ease of monitoring through peripheral blood sampling, and accessibility for potential reoperation if necessary. **(Lo, 2002)**

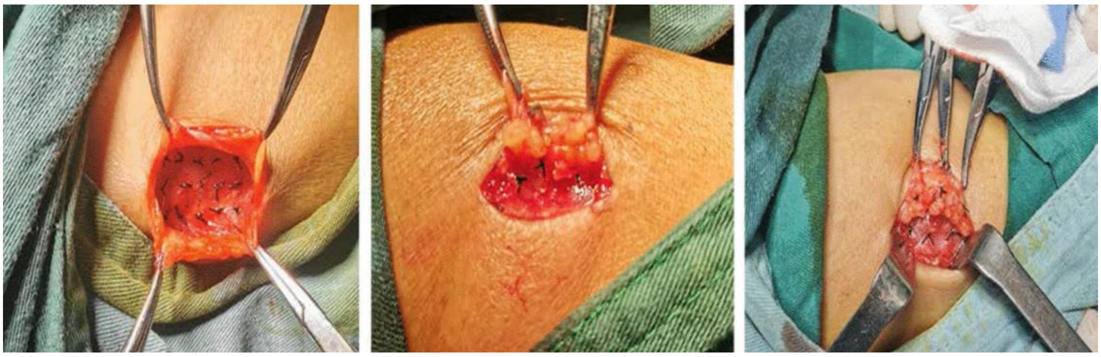

Figure (2): Forearm parathyroid auto transplantation procedure **(Zhou et al., 2021).**

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