

# Use of Indocyanine Green Fluorescence (ICG) as an alternative for sentinel node identification in breast cancer: Experience in a third level center.

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**BACKGROUND:** Sentinel lymph node biopsy is based on two main precepts: The anatomical support of the existence of an orderly and predictable pattern of lymphatic drainage towards a regional lymph node and the functioning of a first node as an effective relay site that filters neoplastic cells.

Since that demonstration to achieving the concept of sentinel lymph node biopsy in breast tumors that is currently performed, it has gone through great changes, from the use of colloid gold, patent blue and finally the use of gamma probe (lymphoscintigraphy and radioimaging-guided biopsy), which represents the diagnostic method that, combined with a dye, offers the best performance in our time. Recently, the use of indocyanine green fluorescence as a means of identifying the sentinel node has shown good results and is considered an alternative in centers that do not have the necessary infrastructure to use nuclear medicine.

**KEY WORDS:** Sentinel lymph node, Indocyanine Green Fluorescence.

## Introduction

**S**entinel lymph node biopsy is based on two main precepts: The anatomical support of the existence of an orderly and predictable pattern of lymphatic drainage towards a regional lymph node and the functioning of a first node as an effective relay site that filters neoplastic cells<sup>[1]</sup>.

Since that demonstration to achieving the concept of sentinel lymph node biopsy in breast tumors that is currently performed, it has gone through great changes, from the use of colloid gold, patent blue and finally the use of gamma probe (lymphoscintigraphy and radioimaging-guided biopsy), which represents the diagnostic method that, combined with a dye, offers the best performance in our time. Recently, the use of indocyanine green fluorescence as a means of identifying the sentinel node has shown good results and is considered an alternative in centers that do not have the necessary infrastructure to use nuclear medicine.

## History

The concept of sentinel node has its first clinical approach more than 70 years ago. In 1951, Gould<sup>[2]</sup> sent after a total parotidectomy, a lymph node found at the confluence of the anterior and posterior facial veins, which in the histopathological study revealed metastatic invasion of the lymph node, this finding favored that in the following parotidectomies by cancer a transoperative study of this lymph node will be performed in its usual location, making the

decision according to the result on whether or not to perform a radical neck dissection.

However, was in 1977 when Morton et al<sup>[3]</sup> started cutaneous lymphography with gold colloid and introduced the concept of "Lymphatic mapping with sentinel node biopsy" to identify early metastases in melanomas, considering the sentinel node as the first site of metastatic disease. The same Morton's group, at the John Wayne Cancer Institute, adopted the use of patent blue dye in lymphatic mapping for their reported work in 1992<sup>[4]</sup>, using this dye for the first time, whose use prevails to this day.

Giuliano<sup>[5]</sup> was the first surgeon to use lymphatic mapping and sentinel node biopsy in breast tumors. He identified the possibility and usefulness of performing sentinel node in axillary nodes for patients with malignant breast neoplasms, in order to avoid the deleterious effects of an axillary dissection<sup>[6-9]</sup>.

## Objective

As we are in a tertiary level and national reference center for oncological surgery in our institution, we receive a large number of patients to perform breast cancer surgery. As reported by the world literature, sentinel lymph node biopsy is useful in making decisions regarding whether or not to perform axillary dissection and is indicated in early stages of breast cancer, with clinically negative axillary (T1-T2/N0)<sup>[10-13]</sup>.

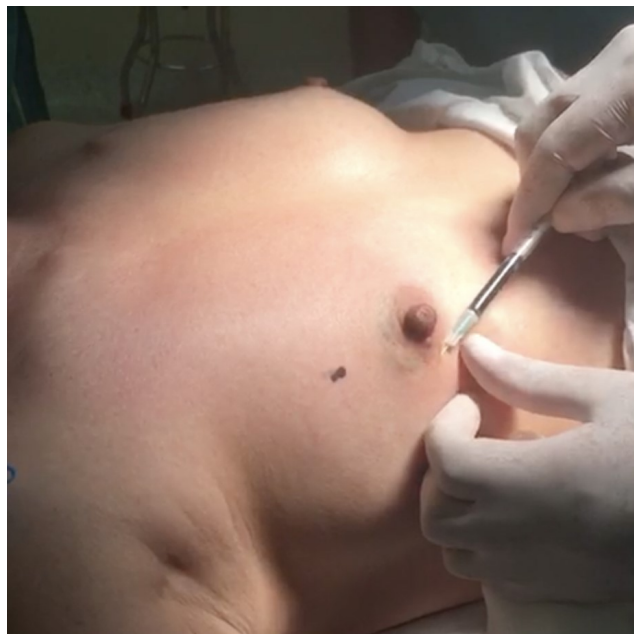
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<b>1. Table of results.</b>		
Age, (years)		
	Range= 37-78	Mean = 52,5 / Median = 48 ( SD $\pm$ 14,6)
	> 50 years	3
	< 50 years	4
BMI (kg/m <sup>2</sup> )		
	Range= 22.47-41.44	Median= 27.34 ( SD $\pm$ 4.6)
	< 18.5, n (%)	0
	18.5 – 25, n (%)	2
	25-30, n (%)	2
	30-35, n (%)	2
	>40, n (%)	1
Size of tumor (pT)		
	Tis	
	T1	2
	T2	3
	T3	1
	T4	
Location of tumor		
	Unknown	
	RSEQ	3
	RIEQ	0
	LSEQ	3
	LIEQ	0
Pathology, malignancy (%)		
	Invasive carcinoma, n(%)	4
	No invasive carcinoma, n(%)	1
Markers and receptors		
	Estrogen receptors, n (%)	4
	Progesterone receptors, n (%)	4
	HER2, n (%)	1
Surgical time (minutes)		
	Range= 40 - 130	Median= 80 (SD $\pm$ 30)
	<60	1
	>60	6
Number of lymphatic nodes		
	Range = 0 - 8	Mean= 2,8 / Median= 3, (SD $\pm$ 3,2)
	No nodes	1
	< 0 = 2	1
	3 – 4	2
	> 4	3

**Table 1.** RSEQ: right superoexternal quadrant, RIEQ: right inferoexternal quadrant, LSEQ: left superoexternal quadrant, LIEQ: left inferoexternal quadrant.

Our institution does not have a nuclear medicine department (gamma-probe), which combined with a dye, represents the method with the best results for the identification of the sentinel node<sup>[14-16]</sup>, so methods with dyes such as methylene blue or patent

blue were used to identification of sentinel node. However, since 2021 the use of fluorescence with indocyanine green became more accessible for our hospital, so in view of the good results obtained by other groups<sup>[19-24]</sup>, we decided to use this technological



**Figure 1.** A standard periareolar infiltration technique was used immediately after orotracheal intubation.

tool and report our experience with the first 7 procedures performed by our oncology surgery service.

## Methods

A total of 7 consecutive patients were registered, who underwent sentinel lymph node biopsy with ICG for the location of the first nodule, the first two patients had no histopathological diagnosis of malignancy and the rest ( $n = 5/7$ ) had an established diagnosis of breast carcinoma. Immediately after placement of the laryngeal mask airway or endotracheal tube, 1-2 milliliters of a dilution with indocyanine green (5mg/mL) were infiltrated periareolar and into the subcutaneous space using an "standard technique" (figure 1) and gently massaged the region for at least 5 minutes, finally starting the procedure an average of 20 to 30 minutes after having infiltrated indocyanine green in all cases.

The first lymph node found following the lymphovascular pathway oriented by fluorescence was considered the sentinel node. The criteria for sentinel node was a Fluorescent ganglia observed in gray scale using the IC-Flow Imaging System (Figure 2A) or those observed in green using the IMAGE1 STM RUBINA™ device (KARL STORZ) (Figure 3), or lymph nodes that at first sight were stained with the green dye (figure 4), these nodes were biopsied and sent for histopathological study, in some cases intraoperatively and in others for definitive study, in order to determine the number of lymph nodes obtained during the biopsy.



**Figure 2.** Fluorescence of the areola after infiltration with indocyanine green using the IC-Flow system. A tail of fluorescence is observed extending into the axilla.

## Results

Seven procedures were performed, all in women, with a mean age of 52.5 years (median 48,  $SD \pm 14.6$ ), of whom 5 had a preoperative histopathological diagnosis of breast carcinoma. A total of 27 lymph nodes were removed in 7 procedures, which were identified by ICG.

The ICG fluorescence method identified an average of 3.8 nodes ( $SD \pm 3.2$ ) and with a detection rate of 85%; In all procedures, subcutaneous lymphatic vessel patterns are detected by fluorescence. Regarding the surgery time (range 40-130 minutes), there was a mean of 82.1, with a median of 80 minutes ( $SD \pm 30$ ). Positive lymph nodes for tumor invasion were identified in four of the patients who underwent the procedure, 2 were reported free and one of the tissue samples sent did not report lymph nodes due to pathology.

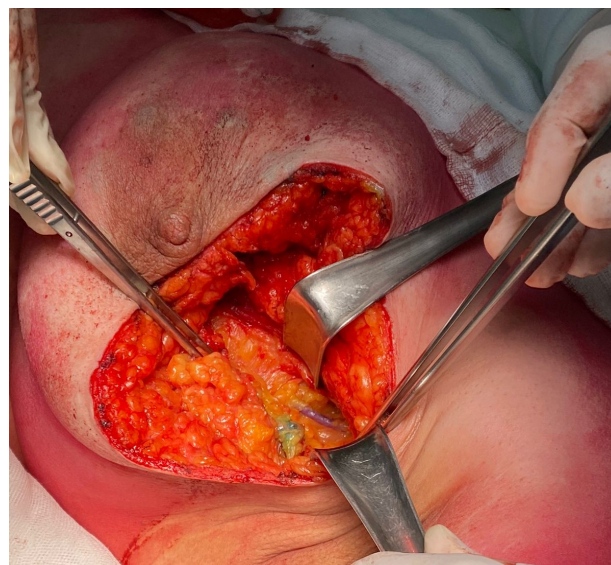
## Conclusion

Fluorescence using ICG offers an alternative as there gamma probe is not available as a tool for the identification and biopsy of the sentinel node in the context of patients with breast carcinoma and clinically negative axilla (cN0), however it requires a learning curve, so who needed in the first procedures, perform lymph node scanning in patients who did not





**Figure 3.** Visualization of the areola using the IMAGE1 STM RUBINATM device (KARL STORZ) after periareolar infiltration of indocyanine green.



**Figure 4.** ICG-stained node observed by direct visualization in the surgical field.

have oncological pathology, in order to avoid the risk of unidentified metastases, however it is useful in seeking to achieve less morbidity (lymphedema, pain and sensory alterations of the extremity), with respect to the effects of radical axillary dissection. We will continue this sentinel lymph node protocol in our hospital to report the results obtained by analyzing a larger population.

### Conflicts of interests

There was no conflict of interest during the study, and it was not funded by any organization.

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