

## Continuing Education

Review of the role of the sentinel node biopsy in neoadjuvant chemotherapy in women with breast cancer and negative or positive axillary node at diagnosis<sup>☆</sup>

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## ARTICLE INFO

## Article history:

Received 1 May 2017

Accepted 29 June 2017

## Keywords:

Breast cancer

Neoadjuvant chemotherapy

Sentinel node

## ABSTRACT

The role of the selective sentinel node biopsy (SNB) is increasing in relevance in breast cancer women with indication of neoadjuvant chemotherapy (NAC). The Radiosurgery Working Group of the SEMNIM is aware of the necessity of establishing the need for SNB before or after NAC, and also how to manage patients with axillary node-negative or node-positive. There is sufficient data to assess that the SNB with radioisotope techniques is feasible and safe in all these scenarios. An adequate axilla evaluation prior to surgery and the possibility of marking prior to NAC the nodes infiltrated must be the two main pillars to guarantee the success of the SNB. It has been shown that to incorporate the SNB in breast cancer women with indication of NAC increases the rate of a conservative treatment of the axilla that will be a clear benefit for these patients.

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### Actualización de la biopsia del ganglio centinela tras quimioterapia neoadyuvante en el cáncer de mama sin y con afectación ganglionar al diagnóstico

## RESUMEN

Esta actualización pretende contextualizar la relevancia de la biopsia selectiva del ganglio centinela (BSGC) en mujeres con cáncer de mama e indicación de quimioterapia neoadyuvante (QTN). El Grupo de Trabajo de Cirugía Radioguiada de la SEMNIM es consciente de la variabilidad existente en nuestro país sobre todo en cuanto al momento de realizar la técnica (previa o tras la QTN) y en cuanto al manejo de pacientes con axila negativa o positiva al diagnóstico. Existe suficiente experiencia contrastada para aseverar que mediante técnicas radioisotópicas la BSGC es factible, eficaz y segura en estos escenarios. Una adecuada valoración mediante técnicas de imagen de la situación tumoral a nivel de la axila previa a la cirugía y la posibilidad del marcaje previo a la QTN de cualquier ganglio infiltrado deben ser los pilares fundamentales para garantizar el éxito de la BSGC. Es un hecho que incorporar la BSGC en el cáncer de mama con indicación de QTN favorece un tratamiento conservador de la axila, lo cual redonda en claro beneficio de las pacientes.

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## Palabras clave:

Cáncer de mama

Quimioterapia neoadyuvante

Ganglio centinela

<sup>☆</sup> Please cite this article as: Ruano Pérez R, Rebollo Aguirre AC, García-Talavera San Miguel P, Díaz Expósito R, Vidal-Sicart S, Cordero García JM, et al. Actualización de la biopsia del ganglio centinela tras quimioterapia neoadyuvante en el cáncer de mama sin y con afectación ganglionar al diagnóstico. Rev Esp Med Nucl Imagen Mol. 2018;37:63–70.

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## Introduction

In aim of this review is to describe the importance of sentinel lymph node biopsy (SLNB) in patients with breast cancer (BC) treated with neoadjuvant chemotherapy (NAC) prior to surgery.

The objective of the Radioguided Surgery Working Group of the Spanish Society of Nuclear Medicine and Molecular Imaging is to describe the situation of this indication in this subgroup of patients with advanced BC and establish a series of recommendations for safely and effectively performing SLNB using radioisotopic techniques based on studies published in the literature.

Historically, Nuclear Medicine in our country has played a fundamental role in the development of SLNB in BC at both an international and national level. Since 2001 several multidisciplinary consensus on the management of BC have been published in Spain, considering SLNB as the best axillary staging technique, after having replaced systematic axillary lymph node dissection more than 10 years ago.<sup>1</sup>

Indeed, based on the NSABP B-32 and the recently updated ACOSOG Z0011 studies published in 2010 on the treatment of early stage BC, SLNB allows adequate lymph node staging and may even avoid the need for posterior axillary lymph node dissection in cases with lymph node involvement limited to one or two lymph nodes candidates for breast-conserving surgery.<sup>2–4</sup>

In view of the relevance of ruling out avoidable axillary lymph node dissection in patients with BC, Breast Cancer Units have progressively widened the indications of SLNB to larger sized, multicentric and/or multifocal tumors.<sup>5</sup> These tumors involve greater resection of breast tissue which, on occasions, requires complete mastectomy leading to subsequent functional and emotional damage to the woman. The use of chemotherapeutic agents in neoadjuvant treatment approaches prior to surgery is increasingly more frequent in order to preserve the breast.

Based on greater knowledge of the molecular subtypes of the tumors which allows not only preservation of the breast gland but also achieves a higher percentage of pathological complete response (pCR), neoadjuvant methods are now increasingly more frequently used as a step prior to surgery in most centers in our country. In this context, the Departments of Nuclear Medicine play a predominant role, and axillary lymph node evaluation by SLNB has also been included in the staging process of BC.

## Indications for selective sentinel lymph node biopsy

Selective SLNB is indicated in all cases of BC except in inflammatory type carcinomas in which the absence of axillary involvement is specifically observed at diagnosis or after neoadjuvant treatment. This assumption is fundamental to perform the procedure with maximum guarantees within the context of health care.

### *Indication pre- or post-neoadjuvant chemotherapy*

In most centers in our country SLNB is carried out during surgery after neoadjuvant treatment. However, some centers prefer to do this procedure during initial staging. Both strategies are valid since they fulfill the main objective of SLNB which is to avoid unnecessary lymph node dissection in women without lymph node disease, although it is clear that important differences must be taken into account. The most relevant is the presence or not of clinical axillary involvement prior to neoadjuvant therapy. It is evident that on histological confirmation by metastatic lymph node puncture, SLNB prior to NAC is contraindicated and should only be performed afterwards. However, in the absence of clinical suspicion or ultrasound evidence of lymph node involvement, SLNB may be considered both before and after chemotherapy.

The performance of SLNB before neoadjuvant therapy can establish the presence of lymph node involvement prior to NAC and determine the possible need for axillary lymph node dissection at the time of the second surgery and whether adjuvant axillary radiotherapy is indicated. This allows better planning regarding the type of surgical intervention to perform, especially if immediate reconstruction is foreseen since the results of the reconstruction may be altered if mammary and/or axillary radiotherapy is carried out.<sup>6</sup>

To the contrary, in this surmise there is the disadvantage of submitting patients to 2 surgical interventions; one for sentinel lymph node (SLN) resection and another after neoadjuvant therapy at the mammary and axillary level in cases in which the SLN is affected.

Another disadvantage is that patients never benefit from the effect of chemotherapy to the lymph nodes since axillary lymph node dissection is performed in all the cases with SLN involvement at diagnosis, increasing the morbidity associated with the procedure. The option of performing a second SLNB in this case is a strategy which is neither viable nor safe.<sup>7</sup> In addition, this ruling out of the possibility of complete axillary response implies the paradox of having to perform axillary lymph node dissection in patients with pCR after NAC of the breast, which occurs in 33.6% of triple negative tumors and up to 50% of human epidermal growth factor receptor 2 (HER2) positive tumors treated with trastuzumab.<sup>8</sup>

The second option is to perform the SLNB at the end of neoadjuvant treatment. In this case the first advantage is that the procedure is carried out in a single surgical intervention, with intraoperative use of one-step nucleic acid amplification (OSNA) being feasible for the study of the SLN.<sup>9</sup> In addition to this advantage, there is the possibility of salvage treatment in women with lymph node involvement at diagnosis who have shown complete response to chemotherapy, which occurs in 33–50% of the patients.<sup>8,10</sup>

It should be noted that from a methodological point of view there are no large pre- or post-NAC differences with the radioactive isotope technique, although as described later, the injection of the radiotracer and the detection rate may differ according to the technique performed.

In the current context of surgical management of BC which prioritizes conservation of the breast and greater preservation of the axilla, it seems more coherent to perform the SLNB after neoadjuvant treatment.

Nonetheless, as mentioned above, both possibilities are feasible and the decision is made by multidisciplinary committees in each hospital which consider the best option for each individual case as stated in the informed consent forms signed by the patients.

## Evaluation of the axillary lymph nodes

In order to specify and ensure that the process is as effective as possible, thorough evaluation of the axillary lymph nodes is necessary at diagnosis as well as after neoadjuvant treatment.

It is well known that the possibility of axillary lymph node involvement is directly related to the size of the primary tumor, and thus, the proportion of axillary metastasis in T1 tumors of less than 1 cm is of around 15%, being 20% in T1c, 30–35% in T2 tumors less than 3 cm and 45–50% in tumors larger than 3 cm.<sup>11,12</sup> Therefore, in the context of a large sized tumor requiring neoadjuvant treatment, in depth evaluation of the axillary lymph nodes should be performed, including physical examination and imaging techniques.

### *Axillary lymph node evaluation prior to neoadjuvant chemotherapy*

Ultrasound is the imaging technique of choice at diagnosis for detecting axillary lymph node disease, presenting a sensitivity of

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