

# The Sentinel Lymph Node: a suitable technique in breast cancer treatment?



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## The Sentinel Lymph Node: a suitable technique in breast cancer treatment?

**AIM:** *The sentinel lymph node biopsy (SLNB) was firstly introduced by Giuliano and co. in 1994 for the treatment of breast cancer; in comparison to the axillary lymph node dissection (ALND), the sentinel lymph node biopsy has shown both a lower morbidity and acceptable distance results. We want to show that this technique is reliable and should be used routinely in selected cases.*

**MATERIALS OF STUDY:** *The study on the sentinel lymph node has been carried out, prior informed consent, in 128 patients aged between 27 and 80 years and suffering from non-multicentric infiltrating breast carcinoma, with a diameter not greater than 3 cm, clinically negative axillary, and hospitalized from January 1998 to September 2005 at the Department of Gerontology, Geriatrics and Metabolic Diseases of the Second University of the Study of Naples. For the recruitment of patients subjected to the sentinel lymph node research study, we have respected the inclusion criteria.*

**RESULTS:** *Histological examination of the tumor revealed 95 cases of ductal carcinoma, 16 cases of mucinous carcinoma, 13 of lobular carcinoma and 4 of medullary carcinoma.*

*The sentinel lymph node was detected through lymphoscintigraphy in 96.9% of the cases (124 patients), whereas it was not possible to identify it in 4 patients (3.1% of the cases), 2 of which had previously been subject to excision biopsy.*

**DISCUSSION:** *The SLNB is characterized by an identification rate of SLN > 90% with a false negative rate less than 5%. In our study we have found an SLN identification rate of 96.9% with false-negative rates of 3.9%.*

*Our data show that in only 6.3% of the patients (4 non-identified and 4 false-negative cases) it was necessary to perform ALND because the SLN resulted positive; however no metastasis were observed in level III lymph nodes.*

**CONCLUSIONS:** *Since its inception, the sentinel lymph node technique has gained an increasingly important role in the conservative treatment of the breast carcinoma due to the short duration of the surgery, the decrease of post-operative pain, the risk of lymphedema onset and hospital confinement, the high predictive power and the diagnostic accuracy.*

*We strongly believe that the sentinel lymph node technique is reliable and should be used routinely in selected cases.*

**KEY WORDS:** Axillary lymph node dissection (ALND), Sentinel lymph node (SLN), Sentinel lymph node biopsy (SLNB).

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## Introduction

The sentinel lymph node biopsy (SLNB) was firstly introduced by Cabanas in 1977 for the treatment of penile cancer and reutilized for the treatment of melanoma by Morton in 1992<sup>1,2</sup>. This technique was

used for the breast cancer treatment only in 1994 by Giuliano and co<sup>3</sup>.

In comparison to the axillary lymph node dissection (ALND), the sentinel lymph node biopsy has shown both a lower morbidity and acceptable results at distance<sup>4-8</sup>. Moreover, the guidelines of the American Society of Clinical Oncology and of the American Society of Breast Surgeons affirm that SLNB, as an alternative to ALND, is an appropriate technique<sup>9</sup>. Consequently, SLNB has become the preferred method in the study of the axillary lymph node involvement during breast cancer, in the U.S.A. In fact, only in 2001, this technique was used in 77% of the cases<sup>10-11</sup>.

In the U.S.A., SLNB is largely used as normal therapeutic protocol, whereas in Italy only at specialized centers<sup>12-13</sup>.

The aim of this work is, on one hand, to give more prominence to SLNB, highlighting both its reliability and efficacy, being the latter a parameter already studied in one of our previously published works<sup>14</sup>, and on the other hand, assert that SLNB is a technique used not only in the North of Italy but also in the South. Moreover, we will try to demonstrate that with the proper skills and a minimum organization, this technique can be performed in all breast care centers.

## Materials and methods

The study on the sentinel lymph node has been carried out, with prior informed consent, in 128 patients aged between 27 and 80 years and suffering from non-multicentric infiltrating breast carcinoma, with a diameter not greater than 3 cm, clinically negative axillary, and hospitalized from January 1998 to September 2005 at the Department of Gerontology, Geriatrics and Metabolic Diseases of the Second University of the Study of Naples. For the recruitment of patients subjected to the sentinel lymph node research study, we have respected the inclusion criteria<sup>15-16</sup>:

- presence of breast cancer detected by either ago biopsy or needle aspiration cytological test;
- clinically negative axillary;
- absence of clinical/radiological multi-focal and multicentric lesions;
- absence of ongoing pregnancy and breast-feeding;
- tumor mass < 3 cm (T1-T2).

For the study, we administered the 99m-Tc nanocolloids of human albumin (particle size: < 80 nm) to the patients. The pre-operative inoculation of marked albumin nanocolloids was performed subdermally with a 25 G needle in proximity of the tumoral lesion.

The lymphoscintigraphic control was initially performed within the first 3-5 minutes after injection and then after 4-5 hours, searching for the area with the highest emission of radioactivity, probably corresponding to the seat of the sentinel lymph node, which was marked with a

dermographic marker. It is always advisable to apply dynamic scintigraphy, recording images for 15 minutes from the inoculation and, probably, static images also after 12 hours. To identify the seat of the sentinel lymph node, front-oblique projections were performed, keeping the surface of the gamma camera head parallel to the axillary cavity, so a point source highlighted the projection.

During surgery, we utilized a probe to detect the emission of gamma radiation. Such probe converts the revealed radiations into an analog acoustic signal with intensity and frequency varying according to the emission of radiation. The probe should be highly sensitive and calibrated in order to discriminate between two nearby regions. Firstly, we searched for the confirmation of the external radioactive signal, in correspondence to the spots detected by the gamma probe. After the skin incision, the lymph node or “hot” lymph nodes were identified using a sterile probe linked to a portable gamma camera.

After the sentinel lymph node removal, we have always checked for the possible presence of any residual radioactivity within the axilla.

In the cases of presence of residual radioactivity within the axilla, we have continued surgical intervention with the removal of other axillary lymph nodes which have been sent for histological examination.

Where, finally, the extemporaneous examination of the SLN showed a positive result, we continued surgical intervention with the ALND.

## Results

The histological examination of the tumor revealed 95 cases of ductal carcinoma, 16 cases of mucinous carcinoma, 13 of lobular carcinoma and 4 of medullary carcinoma (Fig. 1).

The sentinel lymph node was detected by lymphoscintigraphy in 96.9% cases (124 patients), whereas

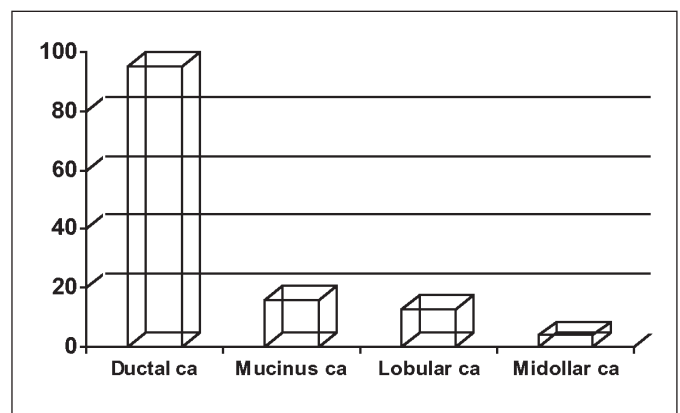


Fig. 1: Tumoral histology.

TABLE I - *Our experience*

N. Patients	% SLN identified	% False negatives
128	96,9	3,9

it has not been possible to detect it in 4 patients (3.1% cases), 2 of which had previously been subjected to excisional biopsy.

The number of the removed sentinel lymph nodes was 1 in 62,7% cases, multiple for the remaining percentage, with an average of 3 lymph nodes (between 2 and 6), because it resulted residual radioactivity within the axilla.

The sentinel lymph node metastization was detected in 39 cases (30.5%), in 13 of which the sentinel lymph node resulted to be the only one affected by metastasis. In 3 cases the SLN resulted negative at the freezer and positive at the final histological examination.

Regarding the correlation between the sentinel lymph node status and the axillary lymph nodes, the percentage of false negatives was 3.9% (4 cases); the accuracy was 96.9%, and the sensitivity was 96,8% (see Table I).

## Discussion

The SLNB is characterized by an identification rate of SLN > 90% with 5% or less false negative rate <sup>9,17-20</sup>. However, Giuliano and co. had already announced these rates in the U.S.A. in 1999 <sup>21,22</sup>. Our study, as well, confirms the percentages found in literature; in fact, we had a SLN identification rate of 96,9% with a false negative rate of 3,9%.

SLNB, thanks to the increasing number of breast cancers diagnosed at an early stage, has given to surgeons the possibility to reduce the number of axillary dissections. Moreover, many studies have demonstrated:

- scarce involvement of axillary lymph nodes at an early stage of breast cancer <sup>23</sup>;
- excessive occurrence of complications following axillary dissection and its low therapeutic validity <sup>6,8,24</sup>.

Our data show that in only 6,3% of the patients (4 not identified and 4 false negative cases) it has been necessary to perform ALND because the SLN resulted positive; however, no metastasis were found in level III lymph nodes.

It should be kept in mind that SLNB is an approach that requires harmony of action by the whole medical team (surgeons, nuclear physicians, anatomopathologists) and also a long learning period <sup>13-15</sup>.

Another widely controversial parameter in literature is the kind of technique to be used for the lymph node mapping <sup>25,26</sup>.

The use of vital dye alone doesn't seem to be the best technique. Indeed, it needs a long time to be learned

and a high surgical commitment; whereas the use of lymphoscintigraphy allows for a faster and more efficient proceeding.

Moreover, it is important to read the images with the precise timing. Data in literature about this topic are quite variable; in general, the timing should not be too short in order to permit a sufficient concentration of the tracer in the lymph node, and at the same time not too long in order to avoid the scintigraphical detection of other lymph nodes <sup>27,28</sup>.

Generally, the gamma probe should not be used 4-5 hours prior to the inoculation of the radioactive tracer, although it is preferable to perform the inoculation the afternoon before surgical operation, between 16 and 20 hours earlier <sup>29,30</sup>. The most preferable inoculation site of the tracer is the subdermic one, as shown by Veronesi and co. in several studies, according to which the breast parenchyma and the skin have the same lymphatic drainage due to the common ectodermic origin <sup>31</sup>. However, the peritumoral way is to be considered for tumors located in deeper regions of the mammary gland <sup>32</sup>.

It is fundamental to select the cases in which this technique can be performed: the tumoral dimensions should be less than 3 cm, the axillary should be clinically negative, the tumor should have been detected by ago biopsy or needle aspiration cytology, absence of radiological and/or clinically multifocal or multicentric lesions, absence of on-going pregnancy or breast-feeding.

Finally, the hystopathological study of lymph nodes should not be overlooked; in this regard, there are conflicting data in literature about the use of different procedures on the number of sections which could be obtained for the extemporaneous examination and, for the use, at a later time, of immunohistochemistry to examine lymph nodes in cases of doubt <sup>33,34</sup>.

The method we used involved a number of sections less than 10 and the use of immunohistochemistry only in cases of doubt. It has proved to be particularly reliable in limiting the number of false negatives, which in literature are less than 5%; in our experience the values were 3,9%; moreover, immunohistochemistry allowed for the detection of micrometastasis not otherwise identifiable.

## Conclusions

Since its inception, the sentinel lymph node technique, has gained an increasingly important role in the conservative treatment of the breast carcinoma for the short duration of the surgery, the decrease of the post-operative pain, the risk of lymphedema onset and hospital confinement, the high predictive power and the diagnostic accuracy <sup>35</sup>.

Data in the international literature <sup>36-38</sup> show an identification rate of SLN > 90% with < 5% false negatives; in agreement with these results, in our study we have a

SLN identification rate of 96,9% with a false negatives percentage of 3.9%.

Furthermore, the predictive role of LS has proven to be reliable with a very small number of false negatives; therefore, the method can be used as standard procedure in the surgical treatment of patients with breast cancer; one fundamental point is to have a minimum organization and interdisciplinary collaboration.

In conclusion, we strongly believe that the sentinel lymph node technique is reliable and should be routinely used in the selected cases.

Currently, it is desirable that this technique be exercised only in specialized centres where there can be a multidisciplinary approach by surgeons, nuclear physicians and anatomopathologists in order to obtain optimal responses. It is also possible to perform this technique in minor centres which have a minimum organization and the appropriate multidisciplinary expertise, working in synergy and collaboration.

## Riassunto

**OBIETTIVO:** La biopsia del linfonodo sentinella è stata introdotta per la prima volta da Giuliano e coll nel trattamento nel cancro della mammella nel 1994; è caratterizzata sia da una ridotta morbidità, sia da buoni risultati a distanza rispetto alla dissezione linfonodale completa del cavo ascellare. Noi vogliamo dimostrare che tale tecnica è affidabile e deve essere utilizzata di routine in casi selezionati.

**MATERIALI E METODI:** La ricerca del linfonodo sentinella è stata effettuata, previo consenso informato, in 128 pazienti di età compresa tra i 27 e gli 80 anni affette da carcinoma infiltrante della mammella non multicentrico, di diametro non superiore ai 3 cm, con ascella clinicamente negativa, ricoverate dal gennaio 1998 al settembre 2005 presso il Dipartimento di Gerontologia, Geriatria e Malattie del Metabolismo della Seconda Università degli Studi di Napoli.

Nel reclutamento delle pazienti da sottoporre alla ricerca del linfonodo sentinella abbiamo rispettato i criteri di inclusione.

**RISULTATI:** Dall'esame istologico del tumore sono risultati 95 casi di carcinoma duttale infiltrante, 16 casi di carcinoma mucinoso, 13 di carcinoma lobulare e 4 di carcinoma midollare.

Il linfonodo sentinella alla linfoscintigrafia è stato identificato nel 96,9% dei casi (124 pz), solo per 4 pazienti non è stato possibile la sua identificazione (3.1% dei casi), due delle quali avevano subito in precedenza una biopsia escissionale.

**DISCUSSIONE:** La SLNB è caratterizzata da un tasso di identificazione del SLN > 90% con un tasso di falsi-negativi < al 5%. Nel nostro studio abbiamo riscontrato un tasso di identificazione del SLN del 96.9% con un tasso di falsi-negativi del 3.9%.

I dati della nostra esperienza mostrano che solo nel 6,3% delle pazienti (4 casi non identificati + 4 falsi-negativi) è stato doveroso effettuare l'ALND, in quanto il SLN risultò positivo; ciononostante i linfonodi di III livello risultarono senza metastasi.

**CONCLUSIONI:** La tecnica del linfonodo sentinella, dalla sua nascita, ha acquisito un ruolo sempre più importante nel panorama del trattamento conservativo del carcinoma mammario per la ridotta durata dell'intervento, per la riduzione del dolore post-operatorio, del rischio di comparsa di linfedema e della degenza ospedaliera, per l'elevato potere predittivo e per l'accuratezza diagnostica. A nostro giudizio, la tecnica del linfonodo sentinella è affidabile e deve essere utilizzata di routine nei casi selezionati.

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