

## Sentinel Lymph Node Detection Through Radioguided Surgery in Patients With Breast Cancer

**Benedita Andrade Leal de Abreu\*, Adriana de Moraes Santos, Livia de Almeida Soares, Antônio Ricardo dos Santos, Idna de Carvalho Barros, Everardo Leal de Abreu, Alexandre Jorge Gomes da Cruz Filho, João Batista de Abreu and Sabas Carlos Vieira**

*Universidade Estadual do Piauí; Centro Federal de Educação Tecnológica do Piauí; Faculdade São Gabriel; Hospital São Marcos; Universidade Federal do Piauí; Teresina - PI - Brasil*

### ABSTRACT

*Biopsy of the sentinel lymphnode (SLNB), the first lymphnode to receive lymphatic drainage from the primary tumor, accurately predicts the axillary lymph node status and, when negative, obviates the need for axillary lymphadenectomy (AL). The aim of this study was, to verify the SLN localization in breast cancer through preoperative lymphoscintigraphy and intraoperative gamma-probe, as well as to demonstrate the benefits of such techniques in preventing complications of AL. Medical records of 228 patients with breast carcinoma, who were underwent SLN localization and, radioguided surgery, from March 2005 to December 2007 were analyzed retrospectively. Data regarding age, tumor characteristic, breast involved, type of surgery, radiopharmaceutical drainage pattern, axillary assessment (SLNB or AL) and number of lymph nodes dissected were collected. It was ascertained that radioguided surgery is a selective method of axillary assessment in breast cancer, which makes this technique a safe alternative to radical assessment of total dissection of axillary lymph nodes and its subsequent complications.*

**Key words:** Breast cancer, sentinel lymph node, lymphoscintigraphy, intraoperative probe

### INTRODUCTION

The sentinel lymph node (SLN) is defined as the first regional lymph node to receive the lymphatic drainage from the primary tumor. The SLN biopsy (SLNB) accurately predicts the regional lymph node status, and when negative, avoids the performance of radical lymphadenectomy.

Due to the trend to conservative treatment for breast cancer (McCready et al., 2005), mainly because of early detection of the disease through mammographic screening, the SLNB has become a standard technique for axillary staging in many centers, with high sensitivity (84%-98%) and low

rates of false-negative (2.0-8.8%), decreasing the number of unnecessary axillary lymphadenectomy (AL), with low rates of axillary recurrence, less post-operative complications and a significant improvement the patient's quality of life (Veronesi et al., 2003; Blanchard et al., 2003; Mansel et al., 2006).

Magaldi et al. (2005), comparing a group of women with breast cancer who underwent AL with women who underwent SLNB, observed that the second group had less lymphedema, pain, shoulder rigidity and paresthesia.

However, there are some controversies regarding SLN in breast cancer: the presence of axillary

\* Author for correspondence

micrometastasis and SLN in the internal mammary chain. The patients with SLN micrometastasis are treated with AL and adjuvant chemotherapy. However, Giuliano et al. (1994) advocate that AL is not necessary where there are micrometastases from T1 and T2 tumors, because the probability of compromising the other lymph nodes is only about 6%.

Patients with metastasis to a lymph node in the internal mammary chain have a poorer prognosis than patients with only axillary metastasis (Veronesi et al., 2002). The assessment of sentinel lymph node from the internal mammary chain remains investigational, and is not performed as routine practice.

This is probably because it is technically more difficult to biopsy internal mammary than axillary lymph nodes.

The aim of this study was to analyze a series of consecutive cases in which the SLN technique, including preoperative lymphoscintigraphy and intraoperative SLNB, was employed.

## MATERIALS AND METHODS

The medical records of 228 patients with breast cancer, who underwent the SLN localization through lymphoscintigraphy, between March 2005 and December 2007, were reviewed.

In this study, patients with cytohistological diagnosis of breast and axillary carcinoma clinically negative were included. The exclusion criteria were: previous chemo, hormone or radiotherapy, pregnancy and breastfeeding. The following variables were analyzed: age, clinical presentation of the lesions, radiopharmaceutical drainage pattern through lymphoscintigraphy, type of breast surgery performed for treatment of the primary tumor, number of sentinel lymph nodes localized and number involved. A descriptive statistical analysis was performed.

The radiopharmaceutical used was the colloid dextran-500, labeled with  $Tc^{99m}$ . The amount of radioactivity injected was adjusted according to the time intervals between lymphoscintigraphy and the surgery, using dose between 0.3-0.6mCi diluted in saline solution, for a total volume of 0.8ml of solution. The radiopharmaceutical was administered intradermally with a 1ml syringe, at four discrete points around the periareolar region with the patient in the supine position. Immediately after the injection, the area was

massaged to promote migration and lymphatic transportation of the radiopharmaceutical particles to the SLN.

Six hours after administering the radiopharmaceutical, static images in anterior and lateral projection were obtained on gamma camera (Genesys Epic®) using a low energy high resolution collimator, a 256x256 matrix, and 20% energy window centered on 140 keV. Afterwards, a  $^{99m}Tc$  point source was used to identify the cutaneous projection of the sentinel lymph node, with dermography of the area.

The exams were done preferably on the day before surgery. However, in cases which were not possible to mark the SLN on the 6-hour images, images were obtained on the following day (surgery day).

In the operation room, the SLN localization was done with a *gamma-probe* (EUROPROBE® - REM). Not only the high score radioactive lymph node was considered SLN, but also those which eventually scored at least 10% of the first. Once detected and dissected, the SLN was submitted to intraoperative frozen-section, and, later, to examination with hematoxylin-eosin (HE).

## RESULTS AND DISCUSSION

The patients' ages ranged between 26 and 81 years, with a mean age of 54.6 years. The lesion (tumor) was localized in the right breast in 51.8% (118/228). The tumor diameter varied from 0.7cm to 6cm in its largest axis, with a mean of 2.42cm. The tumor was clinically palpable in 77.6% (177/228) of the cases.

The predominant histological type was infiltrating ductal carcinoma (IDC) representing 83.8% (191/228), followed by ductal carcinoma in situ 6.1% (14/228).

The predominant degrees of nuclear differentiation were degrees II and III, present in 42.1% (96/228) and 34.7% (79/228) of the cases, respectively.

The surgical treatment was conservative in 61% of the cases, with 42.1% (96/228) of the patients treated with sectorectomy and 18.9% (43/228) with quadrantectomy.

Lymphoscintigraphy with periareolar subdermal injection of the radiopharmaceutical identified SLN in 98.6% (225/228) of the cases. However, 6-hour imaging localized the SLN in 96% (219/228) of the cases. Of these, in 93.4% (213/219), the radiopharmaceutical migrated to the axillary chain

and in 2.6% (6/219) to the axillary and internal mammary chains simultaneously. No migration occurred exclusively to the internal mammary chain. There was no SLN detected in 6-hour imaging in 4% (9/228) of the cases.

Coelho-Oliveira et al., (2004) observed that in both injection techniques (peritumoral and intradermal) 100% of the SLN were localized in the axilla, independently from the lesion topography, without identifying paraaxillary lymph nodes, even in the peritumoral injection group.

The periareolar or subareolar injection stands out for representing a converging point of all the mammary lymphatic drainage pathways, before the axillary and internal mammary chains (Quadros and Gebrim, 2007).

Barros et al. (2005) verified through lymphoscintigraphy of 112 patients that in 86.6% of the cases SLN localization was in the axillary lymphonodal chain, in 8.9% in the axilla and also in the internal mammary chain, and in only 4.5% the radiopharmaceutical migrated exclusively to the internal mammary chain.

Of the nine cases in which there was no migration of the radiopharmaceutical in the 6-hour imaging,

the SLN identification was possible in the images taken on the following day in 66.7% (6/9) of the cases. However, in 33.3% (3/9), no SLN was ever seen and these patients, then, underwent AL. In these three cases, the exam with HE ascertained that 71.9% (46/64) of the dissected lymph nodes were involved with tumor (Table 1)

Urban et al. (2001) and Xavier et al. (2005) found that advanced age can contribute to radiopharmaceutical failure in identifying the SLN, possibly due to liposubstitution of the lymphoid tissue. Birdwell et al., (2001) suggested that lower rates of SLN identification related to age were due to decreased breast tissue turgor in older women, resulting in lower hydrostatic pressure in the lymphatic channels and lower impulsion power of the radiocolloid, besides the decreased phagocytic function of the lymph node itself, which in older women shows reduction of the sinusoidal spaces due to liposubstitution.

Another factor that can lead to failure in lymphoscintigraphic and surgical identification is metastatic involvement of the SLN itself, where a mechanic obstruction of the lymphatic way or of the SLN is caused by neoplastic cells (Van Lancker et al., 1995; Brenot-Rossi et al., 2003).

**Table 1** - Profile of patients whose 6-hour lymphoscintigraphy failed to identify the SLN.

Age	Size of the Tumor (cm)	Degree of Differentiation	SLN in the day-after image	Axillary approach
38	3.2	3	No	AL
49	2.4	2	Yes	AL
54	2.3	2	Yes	SLNB
60	4	2	No	AL
63	3	2	Yes	AL
70	1.3	3	Yes	SLNB
71	2.4	3	Yes	AL
77	4	2	No	AL
81	2.5	1	Yes	AL

Legend: cm = centimeter; SLN = sentinel lymph node; AL = axillary lymphadenectomy; SLNB = sentinel lymph node biopsy.

Intraoperative identification of the SLN with *gamma-probe* was achieved in 100% of the cases in which there was migration of the radiopharmaceutical to the axillary lymphatic chain. With the aid of *gamma-probe*, 369 SLN were identified, varying from 1 to 6, with an average of 1.6 SLN per patient. At frozen-section, the SLN was involved with tumor in 22.7% (51/225) of the cases, which were submitted to AL. In 37.2% (19/51) of these cases, the SLN was the only axillary lymph node involved.

Only 31.6% (72/228) of the patients underwent AL. In eighteen of these cases, although the SLN was negative, AL was performed. All these cases were within the learning curve of this new method by the surgeons and pathologists, which can be justified by the technique learning curve.

A total of 995 lymph nodes were dissected, excluding the SLN, ranging between 7 and 31, with an average of 13.8 lymph nodes per patient. 68.4% (156/228) of the patients benefited from SLNB. They had their axillas preserved and were

not subjected to AL and its subsequent complications.

There was agreement between the frozen-section exam and the definitive exam with HE in 96,6% (168/174) of the cases and the false-negative rate was 3.4% (6/174), with these patients undergoing reoperation to perform radical AL. Of these, 33.3% (2/6) had involvement limited to the SLN; thus they did not benefit from the procedure; nevertheless, this is the standard approach in the setting of a positive SLN.

The rate of SLN identification was 98.6% and the agreement between the intraoperative exam and the HE was 96.6%. AL was avoided in 68.4% of the patients. Hence, SLNB stands as a safe alternative to AL, with the ability to predict axillary lymphonodal involvement and the low incidence of sequelae.

## RESUMO

A biópsia do linfonodo sentinela (BLNS), primeiro linfonodo a receber a drenagem linfática do tumor primário, é capaz de prever o *status* linfonodal axilar e, quando negativa, evitar a linfadenectomia axilar (LA). O objetivo deste estudo é, mediante análise de uma série de casos, verificar a localização do LNS no câncer de mama através da linfocintilografia pré-operatória e do *gama-probe* intra-operatório, bem como demonstrar os benefícios de tais técnicas na prevenção das complicações da LA. Analisou-se, retrospectivamente, 228 prontuários de pacientes portadoras de carcinoma de mama, que foram submetidas à localização do LNS e, posteriormente, à cirurgia radioguiada, no período de março de 2005 a dezembro de 2007. Coletaram-se dados referentes à idade, característica do tumor, mama acometida, tipo de cirurgia, padrão de drenagem do radiofármaco, abordagem axilar (BLNS ou LA) e número de linfonodos dissecados. Pôde-se constatar que a cirurgia radioguiada é um método seletivo de abordagem axilar no câncer de mama, o que faz dessa técnica uma alternativa segura à abordagem radical de dissecação completa dos linfonodos axilares e suas complicações posteriores.

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