Radioguided localisation of non-palpable breast lesions and simultaneous sentinel lymph node mapping

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Abstract. The authors report their experience with a new strategy for radioguided breast surgery that combines radioguided occult lesion localisation (ROLL) and sentinel lymph node (SLN) mapping. The study population comprised 38 women with non-palpable breast lesions suspicious for breast cancer (BI-RADS 4–5). On the day before surgery, 0.2 ml solution containing particles of dextran labelled with approximately 15 MBq of technetium-99m was injected under stereotaxic guidance by mammography. All patients underwent open surgical biopsy guided by gamma probe, radiographic control of the surgical specimen and frozen section analysis. The rate of confirmation of lesion removal was 100% and the rate of simultaneous SLN mapping was 97.3% (37/38). Eleven cases of infiltrating carcinoma and eight of ductal carcinoma in situ (DCIS) were diagnosed intraoperatively. In the first eight invasive lesions, the SLN was biopsied and complete axillary lymph node dissection was performed; in the three other invasive lesions and in two aggressive cases of DCIS, only the SLN was dissected. The intraoperative results of SLN analysis and the definitive histopathological examinations of the SLN were always negative. It is concluded that ROLL and SLN can be employed simultaneously when dextran is used as a tracer; this technique allows frozen section diagnosis and intraoperative node analysis, and has many advantages over the conventional two-step procedure.

Keywords: Non-palpable breast lesions – Radioguided localisation – Sentinel lymph node

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Introduction

Radioguided occult lesion localisation (ROLL) is a new method (first presented by Zurrida et al. in 1998) to localise and orientate the excision of non-palpable breast lesions suspected to be malignant on the basis of mammography or ultrasonography [1]. It is a practical procedure that involves the injection of technetium-99m labelled colloids directly into the area to be excised, under guidance by ultrasonography or stereotaxic mammography. Subsequently surgical biopsy is guided by a hand-held gamma ray detection probe, this being an easy and accurate procedure.

The sentinel lymph node (SLN) is the first lymph node to receive lymphatic drainage from the primary tumour. Radioguided SLN biopsy in breast cancer entails peritumoural injection of ^{99m}Tc, lymphoscintigraphy and node identification during surgery guided by gamma probe [2]. In early-stage breast carcinoma, SLN biopsy has replaced complete axillary lymph node dissection, as analysis of the SLN accurately predicts the status of all axillary nodes in more than 95% of cases with minimal morbidity [3].

ROLL and SLN biopsy are increasingly being employed in the same patients, but always using two separate injections with different tracers at an interval of 1–3 weeks.

In this study, a new strategy for radioguided breast surgery that allows simultaneous localisation of non-palpable lesions and SLN identification was evaluated. Here we report our initial experience with combined ROLL and SLN mapping, immediately followed by frozen section of breast abnormalities, SLN biopsy when malignancy was detected and selective axillary dissection according to the intra-operative SLN analysis.

Materials and methods

Thirty-eight asymptomatic women in whom suspicious non-palpable breast lesions were detected mammographically and who were seen between February 1999 and September 2001 at the Hospital Sirio Libanês, São Paulo, Brazil, were enrolled in the study (average age 52 years, range 36–82). Twenty cases (55.5%) were classified as BI-RADS 4 and 16 (45.5%) as BI-RADS 5, according to the American College of Radiology classification for occult breast lesions [4].

The day before surgery, a 20-gauge needle was placed into the centre of the suspicious lesion (nodular opacities or clusters of microcalcifications) under stereotaxic guidance by mammography (Siemens, Mammomat), followed by a single injection of 0.2 ml solution containing particles of dextran (molecular weight 5.1 [5]; particle size 2–4 nm) labelled with approximately 15 MBq of ^{99m}Tc. A small volume (0.1 ml) of saline solution was immediately injected to avoid radiotracer reflux through the needle, as such reflux might interfere with count readings during surgery. Figure 1 shows the stereotaxic injection of the radiopharmaceutical agent.

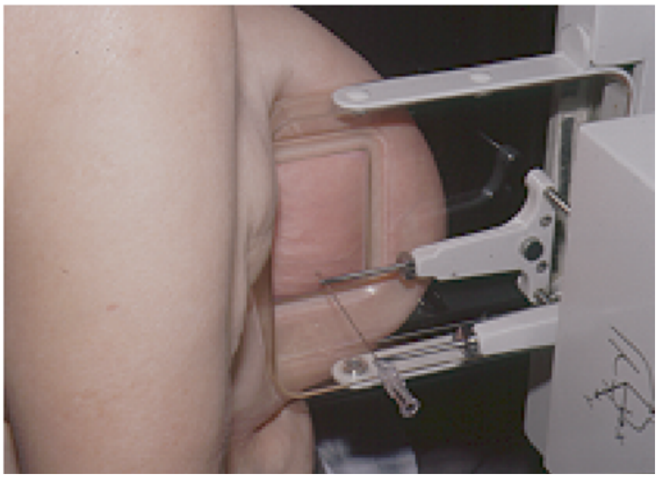

Fig. 1. Stereotaxic injection of ^{99m}Tc-dextran

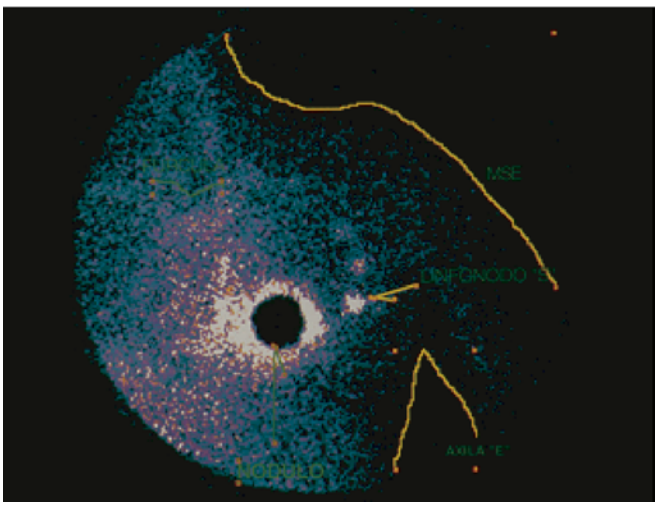

Fig. 2. Scintigraphy showing radioactivity in the suspicious area and in the axillary SLN

Lymphoscintigraphy is an integral component of the procedure. Following removal of the needle, planar scintigraphic images of the breast (in the anterior and lateral views) were obtained with a gamma camera (Siemens, Orbiter ZLC75) 30 min and 3 h after tracer administration, in order to confirm that the tracer had marked the lesion and the SLN (Fig. 2). Lymphoscintigraphy was performed with the patient in the supine position, with the arm completely abducted. Exposure time was 180 s per image, using a high-resolution collimator and an acquisition matrix of 128×128 pixels.

Open surgical biopsy of the lesion was performed on the next day, orientated by a gamma ray detecting probe (Navigator, RMD Inc., Watertown, Mass., USA) that converts radiation into acoustic and digital readout signals (Fig. 3). The frequency and intensity of the signals are directly proportional to the level of radioactivity detected.

After performing a small (3- to 4-cm) incision, just in the skin projection over the area of maximum count detection, the surgeon easily performed the biopsy by inserting the probe into the wound at different angles, under radioguidance. Extent of the resection was considered adequate when counts in the surgical bed after tissue excision fell to 10% compared with counts in the hot spot.

A 1-cm margin around the suspected lesion is recommended. Routinely surgical specimens were placed in a special square glass container and radiographed to confirm that the suspicious lesion had been excised and to orientate the pathologist in choosing tissue for analysis by imprint cytology and frozen section.

The specimen was sectioned in 3- to 4-mm slices, which were examined with a magnifying glass (10×) to identify suspected areas. Cytological imprints were collected and analysed under light microscopy. Grossly or cytologically suspicious areas greater than 5 mm were submitted to frozen section (in a cryostat or manual microtome) and histopathological analysis. For lesions measuring less than 5 mm, no frozen sections were performed in order to avoid damage to the specimen and to preserve it for definitive histopathological and histochemical examinations of paraffin-embedded tissue. In these situations, intraoperative analysis was based only on cytological features.

When malignancy was detected, adequate local surgical treatment was performed immediately. In infiltrating carcinomas and in certain cases of ductal carcinoma in situ (comedo and high nuclear grade), SLNs were dissected with probe monitoring. In our

Fig. 3. Surgical biopsy guided by gamma probe

initial cases, complete axillary lymph node dissection was always performed even after SLN biopsy, but as we acquired more experience, the axilla was only dissected if the SLN was involved.

Results

In all cases, mammography of the excised tissue confirmed that the suspicious lesions were included in the specimen. The lesion removal rate was thus 100%.

In 37 of the 38 cases (97.3%), the first draining node was mapped by lymphoscintigraphy and it was also possible to identify it by placing the gamma probe over the skin. These first draining nodes were localised exclusively in the axilla in 32 cases (84.2%), exclusively in the internal mammary chain in three (7.8%) and concomitantly in the axilla and internal mammary chain in two (5.2%) (Table 1). Recognition of the first draining node did not automatically lead to its dissection; rather this was performed only after diagnosis of malignancy.

Frozen section analysis of non-palpable breast lesions revealed infiltrative carcinoma in 11 (28.9%) cases, ductal carcinoma in situ in 8 (21.0%), atypical hyperplasia in 5 (13.1%) and benign alterations in 14 (36.8%). In all 19 cases of malignancy, SLNs were mapped. Their localisations were as follows: axilla 17 (89.4%), internal mammary chain 1 (5.2%) and both axilla and internal mammary chain 1 (5.2%) (Table 2).

There was concordance between frozen sections and definitive histopathological analysis in 35 of the 38 cases (92.1%). There were no false positive results of frozen section analysis, but there were three false negative results: three cases of atypical hyperplasia were later re-diagnosed as micro-invasive ductal carcinoma (two cases) or ductal carcinoma in situ (one case) on the basis of routine paraffin section analysis (Table 3).

All the 11 infiltrating carcinomas diagnosed by frozen section were treated by segmental resection. In the first eight cases, complete axillary lymph node dissection was performed, and though axillary SLNs were identified, they were analysed only by special paraffin section, with one slice every 50 μm. Each of the SLNs was free of involvement, as were all other dissected lymph nodes (average of 22.5 per case).

In three infiltrating carcinomas and two aggressive ductal carcinomas in situ (comedo and high nuclear grade), the SLN was the single node dissected and it was immediately analysed by imprint cytology. Provided the SLN did not show neoplastic involvement, other axillary nodes were not removed. The definitive histopathological analysis of the SLN confirmed the results of the intra-operative cytological examination in all five of these cases.

Among the patients with SLN localisation in the internal mammary chain, histopathological examination of the breast lesions revealed benign alterations in three. In the other two, infiltrating carcinomas were diagnosed, and these patients received internal mammary chain radiotherapy without local node biopsy.

Table 1. Localisation of first draining nodes in 37 non-palpable lesions

	No.	%
Axilla	32	84.2
Internal mammary chain	3	7.8
Axilla and internal mammary chain	2	5.2

Table 2. Localisation of SLNs in 19 cases of malignancy

	No.	%
Axilla	17	89.4
Internal mammary chain	1	5.2
Axilla and internal mammary chain	1	5.2

Table 3. Comparison between frozen section and paffin section analysis in non-palpable breast lesions

	Frozen section		Paraffin section	
	No.	%	No.	%
Infiltrating carcinoma	11	28.9	13	34.2
Ductal carcinoma in situ	8	21.0	9	23.6
Atypical hyperplasia	5[a]	13.1	2	5.2
Benign alterations	14	36.8	14	36.8

[a] Three false negatives: 2 infiltrating carcinomas, 1 ductal carcinoma in situ

Discussion

Mammographic breast cancer screening has increased the diagnosis of non-palpable breast lesions and, in consequence, improved the early detection of breast carcinomas.

Various methods have been proposed to guide the surgical excision of the suspicious area and ensure exact lesion excision. The more frequently used method is guided wire localisation, introduced by Kopans in 1980 [5]. In comparison with the hook wire method, ROLL has two main advantages, namely a reduced excision volume and better lesion centering within the specimen [6]. In addition, ROLL is better accepted by patients and there is no risk of inadvertent wire section during surgery or wire hook migration. Nevertheless, radiography of the specimen is always mandatory to confirm lesion excision.

The possibility of combining ROLL and radioguided SLN biopsy is quite attractive, but prior to this study, these techniques have never been employed at the same time. One reason for this is the assumption that different colloidal particles are needed for ROLL and for SLN identification. Moreover, most pathologists consider it axiomatic that frozen sections should not be carried out on non-palpable small nodules or microcalcifications since the results are not considered accurate and since there is a possibility of causing loss of tissue required for definitive examination by paraffin section [7].

On the other hand, however, some institutions, including our own, routinely perform frozen sections for non-palpable breast lesions. Bianchi et al. reported that frozen-section diagnosis is feasible and reliable in non-palpable breast lesions. They found the procedure to be easier and more reliable in cases excised because of a mammographic opacity identifiable on gross examination of the surgical specimen, but also found it to be valid in patients in whom microcalcifications were the only one alteration. Diagnosis of benignity or malignancy was accurate in 623 of 650 cases (95.8%) [8].

In another large case study, Ferreiro et al., at the Mayo Clinic, reviewed 1,490 consecutive wire-localised breast biopsies of 1,439 patients with non-palpable mammographic abnormalities (microcalcifications, nodules and architectural distortions) examined by frozen section [9]. The accuracy of the intra-operative diagnosis was 97.7%. In 77 cases (5.2%) the diagnosis was deferred to permanent sections. There were no false-positive results and false-negative diagnoses were obtained in only 0.5% of cases. The authors concluded that intraoperative frozen section of mammographically directed breast biopsies provides accurate and reliable diagnosis.

In the first publications on ROLL it was proposed that human serum albumin should be used as a radiotracer, with large particles ranging from 10 to 150 μm in diameter [1, 6]. For radioguided localisation of non-palpable breast lesions it is preferable that radiotracers do not migrate rapidly by lymphatic channels, in order to allow lesion identification by the surgeon using the probe. For this reason, it is recommended that larger ^{99m}Tc-labelled colloid particles of albumin should be used than are employed for SLN identification, for which small particles from 200 to 1,000 nm are preferred. Other small particles, such as sulphur colloid, which are used in most services in the United States, flow quickly to the axillary lymph nodes and are often trapped in several nodes. This can be rather frustrating, given that the ideal goal is identification of only one lymph node.

^{99m}Tc-labelled dextran was first used in lymphoscintigraphy by Henze et al. in 1982 [10]. More recently, in 1998, Ofodile et al. [11] demonstrated its usefulness in SLN mapping in breast carcinoma, achieving successful identification of the SLN in 98% of cases. In their study the sensitivity of SLN biopsy in predicting axillary node status was 100%, with no false-negative results. Another argument in favour of dextran is its low cost: it is much less expensive than human albumin. Unfortunately dextran is not yet licensed for this specific use in some countries, limiting its clinical application.

Our results show that the use of dextran particles (of 2–4 nm in size) allows ROLL and SLN identification with just one injection, either by lymphoscintigraphy or by gamma probe detection. Simultaneous use of ROLL and SLN biopsy in early breast carcinoma is a step-by-step, radioguided surgical technique, the use of which should be encouraged especially in services where frozen section of non-palpable lesions is performed.

In our opinion for SLN identification it is preferable to use only the isotope technique. For surgeons well trained in radioguided procedures, combination with blue dye injection offers no significant advantages.

It is now well known that SLN biopsy can accurately predict the presence or absence of axillary lymph node metastases in patients with early infiltrating breast cancer. An accuracy of 100% was obtained by Veronesi et al. [12] and Noguchi et al. [13] in tumours less than 1.5 cm in diameter and in clinically negative axillary lymph nodes. It is worth mentioning that SLN biopsy in these situations showed involvement in up to 15% of cases according to these authors.

Considering all these arguments it is reasonable to propose that the ideal patients for SLN biopsy are women with circumscribed non-palpable lesions. In such patients ROLL has many advantages over wire hook guidance. The combination of ROLL, frozen section and SLN biopsy when malignancy is detected represents a new and very practical form of management that often requires only a 1-day stay in the hospital. The usefulness of this approach should be validated in larger multicentre series of patients.

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