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Original article

Radioguided occult lesion localization (ROLL) for non-palpable breast cancer: A comparison between day-before and same-day protocols

Fatih Aydogan [a], Volkan Ozben [a,*], Varol Celik [a], Cihan Uras [a], Gülgün Tahan [b], Ertugrul Gazioglu [a], Ali Cengiz [a], Mehmet Ferahman [a], Ali Cercel [a], Mehmet Halit Yilmaz [c], Metin Halac [d], Hilal Unal [a]

[a] Istanbul University, Cerrahpasa Medical School, Department of General Surgery, Istanbul, Turkey
[b] Marmara University, Institute of Gastroenterology, Istanbul, Turkey
[c] Istanbul University, Cerrahpasa Medical School, Department of Radiology, Istanbul, Turkey
[d] Istanbul University, Cerrahpasa Medical School, Department of Nuclear Medicine, Istanbul, Turkey

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ABSTRACT

Background: Although radioguided occult lesion localization (ROLL) has become a widely accepted technique, the optimal time interval between the radioisotope injection and surgery has not yet been determined.
Aim: To delineate the effects of time from the injection of the radionuclide until surgery on the ROLL success rate in a patient population diagnosed as having non-palpable breast cancer.
Methods: Between December 2004 and May 2009, 75 patients underwent ROLL procedure. The day-before protocol and same-day protocols included 50 and 25 breast cancer patients respectively.
Results: The two study groups were comparable in terms of age, localization technique, radiological findings and the type of surgical procedures ($P > 0.05$). No statistically significant difference was noticed in the pathological diagnosis, cancer size and the surgical margin clearance between the two groups ($P > 0.05$).
Conclusions: Same-day injection of the radiotracer was not superior to the day-before injection in ROLL. The day-before protocol can be scheduled for the convenience of both patients and hospital staff.

Introduction

During the last 20 years, non-palpable breast cancer is increasingly being detected due to the use of widespread breast screening programs.[1,2] Early detection of small, non-palpable breast malignancies decreases the morbidity and mortality of breast cancer patients.[3,4] Accurate preoperative localization of these lesions is necessary. For this purpose, several techniques, such as skin projection, carbon localization, wire-guided localization, intra-operative ultrasonography (US) have been described.[5–7] Wire-guided localization is currently the most commonly used localization technique for radiological marking of occult breast lesions, however, it has several disadvantages.[2–4]

Radioguided occult lesion localization (ROLL) is a relatively new method to localize and orientate the excision of non-palpable breast lesions. In ROLL, the injection of ^{99m}Tc-labeled Human Serum Albumin adjacent to the lesion is performed under ultrasonographic or stereotactic guidance within 24 h before surgery. Subsequently, surgical biopsy is guided by a hand-held gamma ray detection probe, this being a practical and accurate procedure.[8,9] In clinical practice, the radioisotope injection can be performed either on the same day of surgery,[6,10,11] or a day-before surgery.[11–14] Although ROLL has become a widely accepted technique and a standard for localizing clinically occult lesions in several breast units worldwide,[6] to the best of our knowledge, the optimal time interval between the radioisotope injection and surgery has not yet been determined. Same-day injection may cause difficulties in coordinating the schedules of the nuclear medicine and radiology departments, and the operating room. On the other hand, day-before-surgery involves the administration of an up to two-fold dose of the radioactive tracer. We therefore performed a study in a patient population consisting of patients with only non-palpable breast cancer to delineate the effects of time from the injection of the radionuclide until surgery on the ROLL success rate.

Patients and methods

The protocols for this study were approved by the Ethical Committee of The Istanbul University, Cerrahpasa Medical School.

* Corresponding author at. Istanbul Universitesi, Cerrahpasa Tip Fakultesi, Genel Cerrahi Anabilim Dali, Kursu Sekreterligi, 6. Kat. 34098 Cerrahpasa, Fatih, Istanbul, Turkey. Tel.: +90 212 414 30 00 (work), +90 534 648 46 78 (mobile), +90 212 588 08 73 (home); fax: +90 212 414 33 70.
E-mail address: volkanozben@yahoo.co.uk (V. Ozben).

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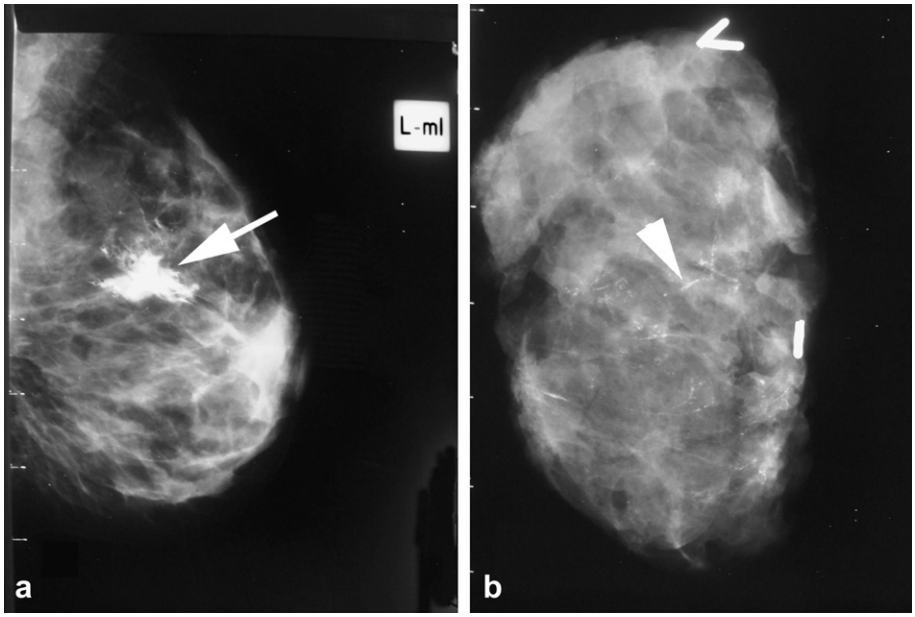

Fig. 1. Arrow shows the radiotracer with contrast medium covering the suspected lesion on preoperative check mammography (a), and arrowhead shows the microcalcifications on intra-operative specimen graphy (b).

Between December 2004 and May 2009, 75 patients who underwent ROLL procedures due to radiologically suspected non-palpable breast lesions and diagnosed as having breast cancer on histopathological examination postoperatively were included in this retrospective study. Patients with multicentric breast cancers were excluded. Written informed consent was taken from each patient after the patients were informed of the details of the ROLL procedure. The patients' information was entered prospectively into a computer database.

Lesion localization

^{99m}Tc-Human Serum Albümin Makroaggregate (MAA) in 0.2–0.5 cc serum saline was injected intralesionally in all patients. For the same-day protocol, 1 mCi of ^{99m}Tc (37 MBq), and for the day-before protocol, 2 mCi of ^{99m}Tc (74 MBq) was administered. The intralesional placement of a 22 G spinal needle under local anesthesia followed by the injection of radionuclide was performed by experienced radiologists. Image guidance was done either by ultrasonography or stereotaxis depending on the diagnostic modality which was utilized previously to detect the lesion at the time of patients' admission. Correct localization of the injected radionuclide was confirmed either by checking the mammography with the help of 0.2 cc water-soluble non-ionic iodinated contrast medium covering the suspected lesion (Fig. 1), or by ultrasonography with the help of the change in echogenecity caused by the radiotracer (Fig. 2). Ultrasonography was utilized in the case of both ultrasonography and mammography-detected lesions.

Surgical procedure

In the operating room, before the induction of general anesthesia, the surgeon used a hand-held gamma probe (Europrobe®, Strasbourg, France) to identify and mark the site of the lesion by locating the area of maximal radioactivity allowing an appropriate location of the incision over the breast lesion. An incision was made and the probe was used to define the margins of resections. The primary lesion was excised with the surrounding tissue. After the

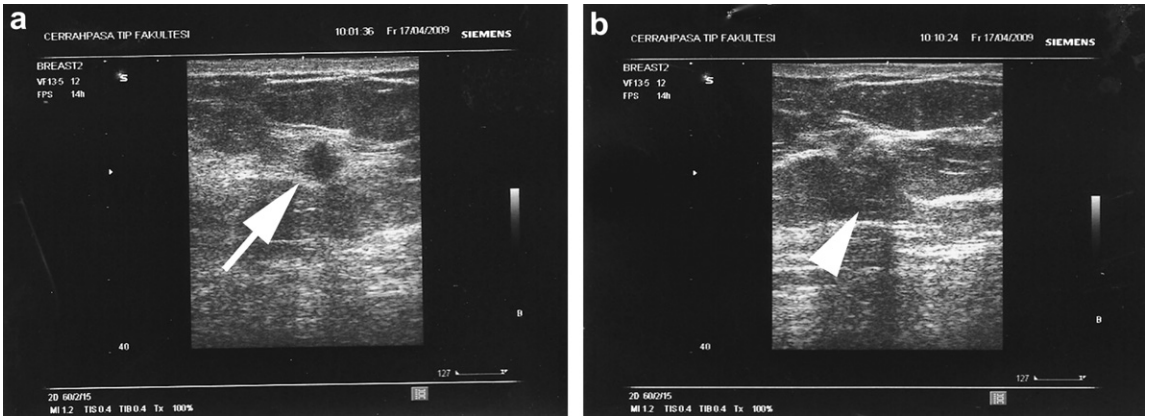

Fig. 2. Arrow indicates the ultrasonographic appearance of clinically occult breast cancer (a), and arrowhead indicates the change in the echogenecity of tumor caused by the radiotracer (b).

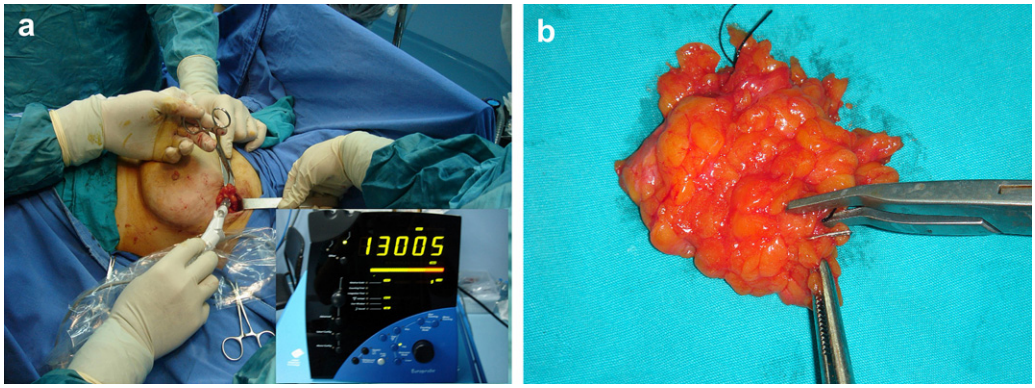

Fig. 3. Radioguided excision of tumor foci (a). Silk sutures and metallic clips were placed to the surgical margins of the excised specimen for anatomical orientation (b).

specimen was excised, the probe was then used to examine the resection bed to verify that there were no residual areas of high radioactivity. Further surgical exploration was performed if the count in the resection bed remained high. Silk sutures and metallic clips were placed to the margins of the excised specimen for anatomical orientation (Fig. 3). The specimen was returned to the radiology department for radiographic confirmation of the presence of the lesion. If the margins were involved with the lesion, further re-excisions were performed to obtain radiologically clear margins. Clearance margin ≥2 mm and near-margin between 0.1 and 2 mm were accepted on histopathologic evaluation.

Our current mature technique of SLNB which was described in detail previously involves the injection of 1–2 mCi (17.5–37 MBq) of ^{99m}Tc tin colloid around the periareolar area, the confirmation of SLN location by the lymphoscintigraphic images, and the intraoperative injection of 3–5 cc of methylene blue dye into the subareolar area to mark the sentinel lymph node(s) of the involved axillary region.[15]

Statistical analysis

Microsoft Excel and Statistical Package for the Social Sciences™ (SPSS 12, Inc., Chicago, IL) were used to store and analyse the data. Numerical data were reported as means ± standard deviation (SD). Chi-square and Fisher tests were used to compare the variables between the two ROLL protocols. Values were considered as significant when $P < 0.05$.

Results

The mean age of the 75 patients was 54.05 years. Of all the breast cancer patients, we identified 50 patients (66%) who had had the day-before injection, and the remainder had had the same-day injection. The comparison between the day-before and the same-day protocols were summarized in Table 1.

The two study groups were comparable in terms of age, localization technique, radiological findings and the type of surgical

Table 1
Comparison of same-day and day-before protocols in patients localized with ROLL.

Parameter	Same-day protocol		Day-before protocol		
	Number	Mean ± SD (Range)	Number	Mean ± SD (Range)	*P* value
Total number of patients	25		50		
Age in years		53.08 ± 6.44 (42–71)		55.02 ± 7.52 (41–70)	0.2
Localization technique					
Stereotactic	13		17		0.2
Ultrasonography	12		33		0.2
Radiological findings					
Asymetrical density	1		2		0.9
Mass	10		28		0.2
Microcalcifications	11		15		0.2
Mass + Microcal.	2		5		0.8
Type of surgical procedures					
Lumpectomy	20 (80%)		42 (84%)		0.7
Mastectomy	5		8		0.7
Plus axillary dissection	4		7		
Sentinel node biopsy					
Involved	1		2		0.9
Clear	17		35		0.5
Pathological diagnosis					
DCIS	9		14		0.4
Invasive ductal	15		35		0.4
Mixed	1		1		1.0
Tumor size (mm)					
DCIS		24.89 ± 15.21 (5–50)		28.67 ± 16.12 (7–50)	0.5
Invasive		9.65 ± 6.29(2–22)		11.97 ± 5.32 (4–25)	0.1
Margins					
Clear (≥2 mm)	15 (60%)		37 (74%)		0.2
Near (0.1–2 mm)	3		2		0.1
Involved	7		11		0.7
Second operation	10 (40%)		13 (26%)		0.2

procedures. Thirteen patients in the same-day protocol group were localized by stereotactic technique, and 12 with US; this compares to 17 and 33, respectively, in the day-before protocol group ($P > 0.05$). No statistically significant difference was noticed in the radiological findings and the type of surgical procedures between the two groups ($P > 0.05$). The majority of patients in both groups underwent lumpectomy procedure.

No statistical significance was identified in the pathological diagnosis, cancer size and the surgical margin clearance. Furthermore, when only patients with involved margins and margins near the tumor are considered, 40% of patients in the same-day protocol group and 26% in the day-before protocol group had to be re-operated due to incomplete excisions.

Discussion

Precise localization is the most important factor in the accurate surgical removal of non-palpable breast lesions, minimizing the amount of healthy breast tissue unnecessarily excised, while preserving safe tissue margins.[6,9] Since its first description in 1996 at the European Institute of Oncology in Milan,[16] ROLL has allowed easier, more accurate, and more rapid removal of non-palpable breast lesions compared with the conventional localization techniques.[17] Other advantages are a reduction in the tissue damage within the final pathological specimen, an improved rate of clear margins, the reduced size of the excised specimen, better concentricity of the lesion, increased patient comfort, and the reduced rate of re-do surgery which in turn reducing costs.[2,6,12] We adopted the ROLL technique in December 2004 in the Istanbul University, Cerrahpasa Medical School, Breast Unit and since then we have routinely employed this technique in our clinical practice in a total number of 320 patients.

Although ROLL has become a widely accepted technique in localizing clinically occult breast lesions, the optimal interval between the radioisotope injection and surgery has not yet been determined. Most published studies compared the 1-day (on the day of the surgery) and the 2-day (on the day-before surgery) protocols for the detection of SLN in patients with breast cancer. Because the 2-day protocol allows for an adequate amount of time to perform the lymphoscintigraphy, it is reported to be a more useful protocol.[18–20] Our study, inspired by the results of these published papers, was conducted to compare the results of same-day and day-before ROLL procedures. We selected only patients who were diagnosed as having breast cancer postoperatively on histopathological examination to determine the success rate of ROLL.

The results obtained in our series showed that the two comparative groups had no significant difference in the radiological findings, type of surgical procedures, pathological diagnosis, cancer size, surgical margin clearance, and second operation rate. We believe that, of all these parameters, margin clearance itself is a very important factor which can reveal the success rate of each protocol. Forty percent of the patients in the same-day protocol, and 26% in the day-before protocol had inadequate excisions due to unclear surgical margins; being either near the tumor or involved. None of the pathology results documented invasive cancer at the margins of the resected specimens. All these patients later underwent second operations; either re-excision of the primary tumor bed or mastectomy. In the literature, the rate of unclear surgical margins reported to be 11–30% in different series.[2,14,21,22] We can explain this relatively high number of second operations by 2 factors; (1) involvement of more than one surgical margins with multifocal or diffuse DCIS, and (2) learning curve artefacts during our early experiences in the ROLL technique. Of note, the radioactive tracer was positioned correctly in all of the patients.

Several studies showed that ROLL is safe for both patients and medical staff in terms of radiation exposure because of the low levels of the injected activity and the optimal characteristics of ^{99m}Tc (short half-life of 6 h, gamma-emitter, ease of labeling). The dose absorbed from the inoculated area is negligible and concentrated within the removed tissue. The lack of contamination from radioactive waste indicates that no additional radiation protection measures are required.[13,23] Our day-before protocol required a larger dose of the isotope, 2 mCi, as opposed to 1 mCi for the same-day group. Although one might argue that an increase from 1 to 2 mCi raises issues of radiation safety, 2 mCi is only 8% of that given for a standard bone scan (25 mCi), for which no isolation procedures are required.[19]

Based on our experience, the day-before ROLL protocol had several advantages; the patients underwent the procedure in a calmer setting, they did not have to be nil per oral, and they could avoid waiting between same-day injection and surgery. It provided the optimal time frame for nuclear medicine physicians to prepare the radiotracer and send it to the radiology department where it was injected into the patient's breast, and for radiologists to interpret the radiological findings on check mammography and ultrasonography more accurately. Surgeons could schedule their ROLL procedures as the first case on the following day. Difficulty of coordinating the schedules of the nuclear medicine, the radiology department and the operating room and the increasing frustrations caused by delays were found to be more prominent in the same-day surgery protocol.

Conclusion

The results of our study indicated that same-day injection of radiotracer was not superior to the day-before injection in patients with breast cancer localized with ROLL. We recommend the day-before protocol be scheduled for the convenience of both patients and hospital staff without compromising the success of the ROLL procedure.

Authorship

All authors except Gulgun Tahan, Mehmet Halit Yilmaz, Metin Halac were involved in the operations, in the postoperative care and follow-up of the patients. Fatih Aydogan and Volkan Ozben provided conception and design of the manuscript. Gulgun Tahan, Metin Hallac, Hilal Unal were involved in the analysis and the interpretation of the data. Mehmet Halit Yilmaz and Metin Halac were involved in the critical revision of the manuscript and provided the illustrations of the manuscript. All authors approved this final version of the manuscript.

Conflict of interest statement

There are no financial conflicts of interest, employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations and grants or funding to report.

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