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Abstract
With the increased awareness and use of breast cancer screening programs, detection of nonpalpable lesion of breast is also increasing in incidence. Previously, wire guidance under ultrasonography was used for localization of these occult lesions, and in the second stage, sentinel node biopsy (SNB) was taken under radioactive guidance or blue dye injection. We conducted a study to combine radioactive-guided occult lesion localization (ROLL) with SNB. We concluded that ROLL is an efficient method for the detection of these occult lesions, enabling more effective planning of skin incision, precise excision of the lesion with minimal normal tissue edge excision, and ultimately better postoperative cosmetics. When combined with SNB, it effectively decreases the intraoperative time. Key words: Occult lesion, radio-guided localization, sentinel node.

Introduction
Frequency of clinically suspicious occult breast lesions has grossly increased as a result of extensive mammographic screening programs of asymptomatic women [1, 2]. Some 15%-20% of these lesions are malignant, and their removal should be heralded by a radiographically guided localization procedure [1]. Several techniques have been developed as diagnostic and therapeutic tools to guarantee an accurate and low tissue volume biopsy [3,4]. Wire-guided localization (WGL) is presently the most commonly used localization method for nonpalpable breast lesions [5,6]. However, the ideal technique involves precise localization, avoids the excessive surgical resection of healthy breast tissue, improves the rate of free margin, not discomforts the patient, and decreases the operative time. Although WGL has been shown to accurately localize the lesions, the technique has some disadvantages. The placement of the wire is difficult in dense breast tissue [7]. For surgical excision with free margins, the surgeon must follow the wire through healthy tissue until the lesion is found, and this causes the extensive removal of healthy breast tissue. Furthermore, migration or rupture of the wire leads to a small risk of pneumothorax. Discomfort to the patient and injuries for both the surgical team and the pathologist are other restrictions of the procedure [8,9].

Radio-guided occult lesion localization (ROLL) has emerged as a novel technique in surgical excision of impalpable breast lesions. In ROLL, radioisotope injection adjacent to or into the lesion is performed under ultrasonographic or stereotactic guidance preoperatively. Intraoperative tumor localization is carried out searching for the maximum radioactivity by gamma probe. In ROLL technique, 99mTc-labeled human albumin colloid with particle size large enough to retain at the site of the injection (macro albumin aggregates) is used [10,11].

In our study, we evaluated the combination of ROLL with sentinel node biopsy (SNB) using two different radioactive injections in a single stage. The advantages of the single-stage procedure include less procedure time, less hospital stay, and less overall cost of the procedure. Macro albumin aggregates are used for tumor injection as they are retained at the tumor site which results in precise surgical excision of the margins.

Materials and Methods
This study was conducted on 30 female patients in the age range of 37-52 years with a mean age of 41 years. All patients had a nonpalpable breast mass diagnosed on mammography or breast ultrasonography. All the patients were subjected to ultrasound-guided preoperative tru-cut biopsy and were diagnosed with invasive ductal carcinoma. Seventeen patients had US-detected suspicious axillary lymph nodes while rest of the patients had no suspicious axillary nodes either on mammography or breast ultrasonography. All those patients who were found to have multicentric breast lesions or distant metastasis were excluded from the study.

After following the general anesthetic and surgical preparation protocol, the patients were subjected to breast lesion localization by a nuclear medicine physician and a breast radiologist 4-8 h before surgery, after taking written informed consent. 99mTc-labeled colloidal human serum albumin was injected directly into the breast lesion, or around the lesion, with a 15-20 gauge needle.
under US guidance. 0.15 mCi (7.5 MBq) of 99mTc-labeled macro albumin aggregate in 2-3 mL of saline was used. The injection of radioisotope at the target site was confirmed by ultrasonography. And the site of the lesion was also marked at the skin for preoperative identification by the surgeon.

Now the patients were injected with 99mTc-labeled micro albumin in 1-2 mL of saline in the periareolar area for the detection of the sentinel axillary nodes. The patients were then transferred to the operating room for the excision of the lesion and SNB.

A gamma-detecting probe measuring the radioactivity in counts per second was used; the area over the skin with maximum radioactivity count corresponded to the site of the lesion. The probe was placed in a laparoscopic camera sleeve. An incision was made in the skin exactly over the area with maximum radioactivity taking due consideration of the cosmetics. The gamma probe was frequently used to confirm the location and margins of the lesion during the excision. The limit of excision was determined by frequency and intensity of the radioactivity. Following excision of the lesion, the cavity was rechecked for any residual area of activity. If the radioactivity in the cavity remained high, further surgical exploration of the margins was undertaken till no further radioactivity was detected. The excised specimen was sent to the radiology department for radiographic confirmation of the presence of the lesion. Metallic clips were placed on the four corners of the excision area, and after hemostasis, a wound closure was performed with or without a surgical drain depending on the volume of the residual cavity.

The second stage of the surgery, namely, SNB started again with the use of the gamma probe in the axilla. The sentinel nodes were detected as the area of high radioactivity. A small skin incision was made, and the axillary node was removed using radioactivity count as guidance. Immediately after retrieval of the nodes, the specimen was sent for frozen section. Depending on the result of the frozen section, patients with positive nodes were subjected to complete axillary dissection while in patients with negative results, no further dissection was done and wound closure was performed.

**Results**

All patients in our study presented with nonpalpable mass (17 patients) and microcalcification (13 patients) diagnosed on mammography and/or breast ultrasonography. All patients had US-guided tru-cut biopsy of the lesion, and only patients with invasive carcinoma (ducal carcinoma in 28 patients and lobular in two patients) were included in the study. Only those patients who preferred breast conservative surgery after providing informed consent were included in this study.

Preoperatively, the lesion localization was done by US-guided injection of 99mTc-labeled colloidal human serum albumin directly into the lesion. The mean localization time in our study was 13 min.

Twenty-nine patients had complete excision of the lesion confirmed by the specimen mammogram, but one patient had to undergo reexcision of the margins under gamma probe guidance in the same sitting. After retrieval of the specimen (confirmed by specimen mammogram), the residual cavity showed no significant radioactivity in all patients.

Operative time for complete excision of the lesion was 27 min with a range of 16 min to 129 min. This excluded the patients who had to go for complete axillary dissection.

Sentinel lymph nodes were sent for frozen section biopsy which came out to be positive for malignancy in five patients who had to undergo complete axillary dissection in the same sitting. Histopathology of the specimen revealed invasive ductal carcinoma in 28 patients and invasive lobular carcinoma in two patients. The specimen was subjected to hormone receptor expression such as estrogen (ER), progesterone (PR), and Her-2. Seventeen patients had ER- and PR-positive status, five patients had Her-2 positive, while five had all receptors positive and the rest of the three had all receptors negative. All patients had clear margins with a mean width of 2.2 mm (range of 1.3-4.7 mm). Three patients had seroma and one patient had hematoma, which was managed conservatively without any surgical intervention. Postoperatively, all patients were referred to an oncologist for assessment of the adjuvant chemo radiation.

We followed all patients for 1 year, except one patient who lost follow-up after 1 month postoperatively. Patients were followed up at 3, 6, and 12 months postoperatively with computed tomography chest and abdomen at 6 and 12 months. No procedural complications and/or any recurrence was found in any patient during the follow-up period.

**Discussion**

The increasing frequency of nonpalpable breast lesions, characterized by a low risk of metastatic lymph nodes at diagnosis, requires an approach aimed at both accurate intraoperative localization of occult neoplastic lesions and reliable SLN identification. As a matter of fact, several imaging techniques are used to detect metastasis from different types of cancers [12].

Radio-guided occult lesion localization (ROLL) is a new method for the localization and resection of nonpalpable breast lesions [14,15]. It has emerged as a novel technique in the surgery of impalpable breast lesions implementing practically the same technique of detecting sentinel nodes, namely detection of radioactivity by gamma probe [11]. The approach involves the intratumoral injection of a small amount of nuclear radiotracer under guidance by ultrasonography or stereotactic mammography. Radioactivity allows for the radiolabeling of the lesion and subsequent surgical excision guided by a handheld gamma ray detection probe. ROLL has gained immense popularity on account of several advantages associated with a reduced excision volume, more accurate centricity of a lesion within the surgical specimen, better cosmetic results, and a higher percentage of tumor-free margins [16-18]. In addition, in recent studies investigating the feasibility of ROLL for lesion localization, the method was shown to be a simple, fast, and accurate technique [19]. The technique was pioneered by Dodd, et al. in 1996 at the European Union of Oncology, Milan, applying an intratumoral injection of 99mTc-labeled human albumin colloid, with particle size large enough to retain at the injection site (macro aggregates) [20]. The centering of the tumor with the handheld gamma probe under radioactive guidance helps the removal of the lesion with an adequate free margin of the healthy tissue. The tumor edges are easily controlled using a gamma probe while the radioactivity clearly decreases outside the tumor. Further, it is easy to check residual tumor activity in the wound to ensure that the
tumor is removed completely, but this procedure does not affect mortality of breast cancer when compared with other excision methods.

Following the mammographic or ultrasonic identification of a suspicious breast lesion, typically as a cluster of microcalcifications, opaque spot, or parenchymal distortion, use of ROLL facilitates the diagnostic and therapeutic process, which can be summarized as follows: 1. Precise localization of the lesion with minimal invasion and better patient comfort as compared to WGL 2. Less operative time (27 min average) as compared to WGL 3 (37 min average) [21].

Precise excision of the lesion with an adequate margin of healthy tissue, with less distortion of cosmetics, postoperatively.

References