

Radioguided Occult Lesion Localization Versus Wire-guided Localization of Nonpalpable Breast Lesions: A Comparative Analysis

Nonpalpabl Meme Lezyonlarında Meme İşaretleme Teli ve Radyoaktif Madde ile Lezyon Lokalizasyonu Yöntemlerinin Karşılaştırılması

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ABSTRACT

Objective: Wire-guided localization (WGL) is the preoperative localization method most commonly used before the surgical excision of non-palpable breast lesions (NPBLs). Recently, radioguided occult lesion localization (ROLL) has emerged as an alternative to WGL. We sought to compare the efficacy of ROLL with that of WGL for the preoperative localization of NPBLs and to assess our experience encountered as ROLL is implemented at our institution.

Methods: We retrospectively identified reports of patients with NPBLs who underwent mammography- or ultrasonography-guided ROLL or WGL between January 2014 and March 2017. Medical records were reviewed to compare radiologic and pathologic findings, rates of accurate localization, specimen volumes, lengths of operation, creation of positive surgical margins, number of simultaneous sentinel lymph node biopsies (SLNB) performed, complication rates, and lengths of hospital stay.

Results: Our search identified 67 women (mean age, 52.7 years; range, 32-69 years) diagnosed with NPBLs during the study period. ROLL was used in 25 patients; WGL was used in 42 patients. Both methods had a high accurate localization rate (ROLL, 96%; WGL, 98%). The length of operation was longer in the ROLL group than in the WGL group ($p=0.001$), and more SLNBs were performed in the ROLL group than in the WGL group. No significant differences were seen between the groups in terms of radiologic and pathologic findings, specimen volumes, positive surgical margins, complication rates, or lengths of hospital stay.

Conclusion: ROLL is a promising alternative to WGL for preoperative localization of NPBLs. The operation time for ROLL procedures at our institution will likely decrease as clinicians become more familiar with the procedure.

Keywords: Nonpalpable breast lesion, ROLL, WGL

ÖZ

Amaç: Telle işaretleme (WGL) non-palpabl meme lezyonlarının (NPBLs) cerrahi öncesi yerinin belirlenmesinde yaygın olarak kullanılan bir yöntemdir. Son zamanlarda geliştirilen bir teknik olan radyonüklid okült lezyon lokalizasyonu (ROLL) telle işaretlemeye önemli bir alternatiftir. Çalışmadaki amacımız bu iki yöntemi karşılaştırmak ve kliniğimizde son zamanlarda uygulanmaya başlanan ROLL yöntemi ile ilgili deneyimlerimizi paylaşmaktır.

Yöntemler: NPBLs olup 2014-2017 yıllarında kliniğimizde cerrahi öncesi işaretleme yapılan hastaların raporları retrospektif olarak tarandı. Hastaların medikal kayıtları kontrol edilip, patolojik ve radyolojik bulguları, doğru lezyon lokalizasyonu, spesmen boyutu, operasyon süresi, cerrahi sinir pozitifliği, simultane sentinel lenf nodu biyopsi sayısı, komplikasyon oranları, hospitalizasyon süreleri karşılaştırıldı.

Results: NPBLs olan 67 kadın (ortalama yaş, 52,7; yaş aralığı, 32-69) çalışmaya alındı. ROLL uygulanan 25 hasta ve WGL uygulanan 42 hasta saptandı. Bu iki metodun da doğru lezyon lokalize etme oranları benzer yükseklikte bulundu (ROLL, 96%; WGL, 98%). ROLL tekniğinde operasyon süresi WGL grubuna göre daha uzun sürdü ($p=0,001$) ve sentinel lenf nod biyopsi sayısının ROLL grubunda daha fazla olduğu bulundu. Patolojik ve radyolojik bulgular, spesmen boyutu, cerrahi sinir pozitifliği, komplikasyon oranları, hospitalizasyon süreleri karşılaştırıldığında anlamlı fark bulunmadı.

Sonuç: Non-palpabl meme lezyonlarında, ROLL ile işaretleme yöntemi öğrenme aşamasında dahi verdiği sonuçlarla telle işaretleme yöntemine alternatif olabilecek umut vaadeden bir yöntemdir. ROLL ile operasyon süresi klinisyenlerin alışması ile giderek kısılacaktır.

Anahtar kelimeler: Non-palpabl meme lezyonu, ROLL, telle işaretleme

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INTRODUCTION

Breast lesions that cannot be palpated on physical examination but are found to have features suggestive of malignancy on imaging studies are known as nonpalpable breast lesions (NPBLs) (1). Over the past 20 years, the detection of NPBLs has increased (1-6); this is important, as early detection of NPBLs can substantially reduce both morbidity and mortality (7-9).

NPBLs must be accurately localized before surgical excision is attempted (1). The main aim of localization is to allow for total excision of the lesion with minimal tissue loss. Wire-guided localization (WGL) is the most commonly used technique for lesion localization (10). However, this method can be complicated by the breakdown of the wire, difficulties with insertion, and wire dislodgement and migration, which can lead to pain and pneumothorax (11-13).

The radioguided occult lesion localization (ROLL) method is increasingly being used as an alternative to WGL (14) and was just recently introduced at our institution. With the ROLL technique, a radionuclide is injected into the lesion under imaging guidance and the lesion is then surgically excised, with a gamma probe used for intraoperative localization. The ROLL technique has several advantages over the WGL method, including a shorter procedure time, smaller volume of tissue removed, cleaner surgical margins, and less pain and improved comfort for the patient (13,15). Additionally, when ROLL is used, a sentinel lymph node biopsy (SLNB) can be performed simultaneously (16). Although recent studies have showed ROLL is a good method to assess the NPBLs (17-21), there is lack of information regarding the assessment of this method at the learning curve period, when implementing the ROLL technique at an institution. The aim of this study was to compare the efficacy of the ROLL method with that of the WGL technique in localizing NPBLs before surgery and to assess our experience encountered as ROLL is implemented at our institution.

METHODS

Ethics committee approval was received for this study from the ethics committee of University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital (approval number: 2017/29). Ethics committee approval and waiver of individual consent of participants were obtained for this retrospective study. Eligible patients were those who had an NPBL <2 cm in diameter with features suggestive of malignancy on mammography and ultrasound [Breast Imaging Reporting and Data System (BI-RADS) score of 4 or 5] and who underwent mammography or breast ultrasonography with breast marking and surgical excision between January 2014 and March 2017. Patients who were pregnant or breastfeeding were not eligible for inclusion. Patients who had been treated with neoadjuvant chemotherapy and clips were also not included in the study. Patients were divided into 2 groups based on the method used for lesion localization (ROLL vs WGL).

The method used for breast marking was chosen by the radiologist. Microcalcification, parenchymal distortion, and asymmetric density were marked with mammography; irregularly shaped, spiculated, solid, and complex cystic lesions were identified with ultrasonography.

In mammography-guided WGL, the radiologist used a Selenia DS mammography device (Hologic, Bedford, MA, USA) and a 20 G/10 cm Hawkins needle (Angiotech Breast Localization Needle; National-Standard Medical Products, Gainesville, FL, USA) to perform breast marking before surgery. First, lateral and craniocaudal images of the mammary gland were obtained. With the patient seated, the breast tissue was exposed to pressure, and the closest distance between the lesion and the skin was determined. The x- and y-coordinates of this area were identified on a perforated plate. Once the desired depth of the lesion was reached with a wire, control graphics were taken from 2 different positions. A wire in the form of a hook was fixed inside the localization needle, and a control chart was used to determine whether the wire was in the lesion. Specimen graphy was also obtained to determine whether the lesion could be surgically excised.

In ultrasonography-guided WGL, an Aplio 500 system (Toshiba Medical Systems Corp., Tokyo, Japan) was used for breast marking. With the patient in the supine position, a local anesthetic was applied to the area near the lesion. Using ultrasonographic guidance, the radiologist advanced the marking needle and then the wire into the lesion, and surgical excision was performed.

The technique used for mammography-guided ROLL was similar to that used for mammography-guided WGL. With ROLL, however, marking was performed via the intrathecal injection of radioactive material through a 20 G needle. The radiologist injected 0.5 mCi Tc-99m-macroaggregate albumin (MAA) in a volume of 0.2 to 0.3 mL. Subsequently, 0.2 mL of water-soluble nonionic contrast material was injected to determine whether the lesion had been accurately localized, and mammography was performed to determine whether the area of suspicion could be surgically excised.

The technique used for ultrasonography-guided ROLL was also similar to that used for ultrasonography-guided WGL. The only difference was that lesions were localized with ultrasonography while the radionuclide was injected to ensure that increased echogenicity in the lesion was seen. For surgical excision with ROLL, general anesthesia was administered to patients in the operating room, and radioactivity was measured as a hot spot with an intraoperative gamma probe (Crystal Probe System SG04; Crystal Photonics, Berlin, Germany). The highest hot spot was then selected for excision on skin that was marked with a marking pen, and this region was excised. Radioactivity control of the excised area was assessed with a gamma probe to ensure that no radioactive tissue remained.

The ROLL and WGL groups were compared in terms of radiologic and pathologic findings, rates of accurate localization, specimen

volumes, lengths of operation, creation of positive surgical margins, number of SLNBs performed, complication rates, and lengths of hospital stay.

Evaluation of Lesion Localization Success

For patients undergoing mammography-guided ROLL, successful lesion localization was defined as observation of the radioactive contrast material near the lesion in question. For patients undergoing ultrasonography-guided ROLL, successful localization was defined as an increase in echogenicity in the lesion when radioactive material was administered (Figure 1). Before the surgery, scintigraphic control could be performed to ensure that the radionuclide had not spread (Figure 2); in this study, only one patient had such a scintigraphic image available. In terms of the specimen, lesions localized with mammography were examined by specimen graphy to determine whether the marked lesion was removed during surgery (Figure 3). Lesions localized with

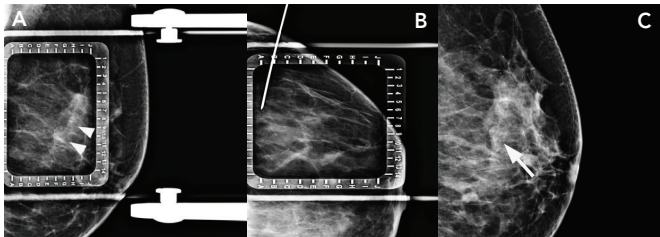


Figure 1. Radioguided occult lesion localization performed with mammographic guidance. **A.** Microcalcifications (arrowheads) can be seen. **B.** Needle can be seen entering the suspected area. **C.** After injection of contrast, increased density can be seen (arrow)

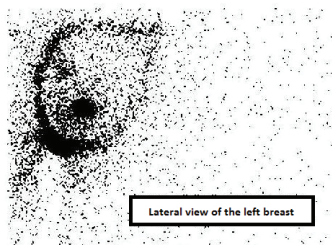
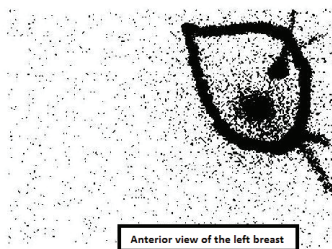


Figure 2. Scintigraphic graphy of lesion obtained using radioguided occult lesion localization under ultrasonographic guidance before surgical excision

ultrasonography were assessed with a gamma probe while the radionuclide was injected to ensure that increased echogenicity in the lesion was seen (Figure 4).

For patients undergoing mammography-guided WGL, successful lesion localization was defined as the presence of the wire tip near the lesion in question (<1 cm). For those undergoing ultrasonography-guided WGL, successful lesion localization was defined as the presence of echogenicity of the wire in the lesion. For patients who underwent mammography-guided WGL, observation of the suspicious lesion on specimen control graphy was considered indicative of successful lesion removal (Figure 5).

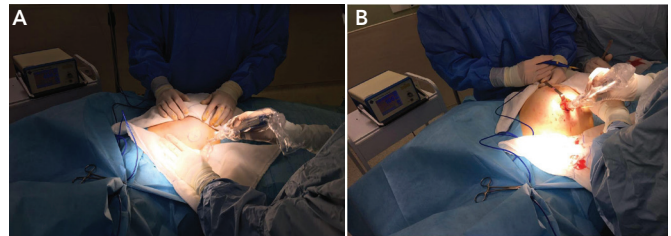


Figure 3. Use of a gamma probe **(A)** before surgical excision to localize the lesion and **(B)** after lesion removal to assess the cavity for evidence of residual lesion tissue

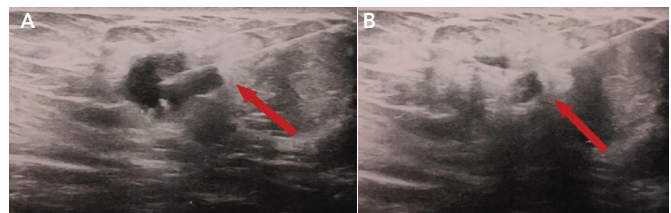


Figure 4. Radioguided occult lesion localization performed with ultrasonographic guidance. **A.** The needle can be seen inside the lesion (red arrow). **B.** After radionuclide injection, there is increased echogenicity in the lesion (red arrow)

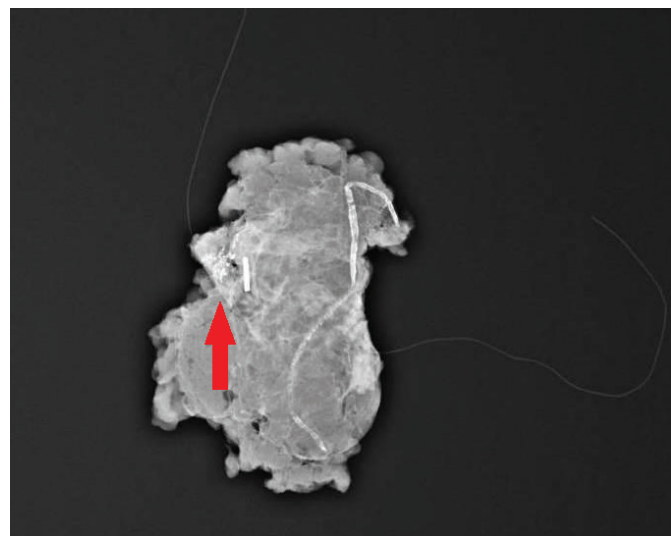


Figure 5. The control graphy for a specimen obtained using wire-guided localization shows the wire in the area of the calcification (red arrow)

No radiologic examinations of the specimens were performed for patients who underwent ultrasonography-guided WGL.

Statistical Analysis

Mean, standard deviation, and median values for continuous variables and frequency and percentage values for categorical variables were calculated. A chi-square test, Fisher's exact test, and the Fisher-Freeman-Halton exact test were used to assess categorical interrelationships. Normal distribution was assessed with the Kolmogorov-Smirnov test. An independent-samples t-test was used when normal distribution was observed for continuous variables, whereas a Mann-Whitney U-test was used when normal distribution was not observed. For all statistical tests, $p < 0.05$ was considered statistically significant.

RESULTS

Our search identified 67 women (mean age, 52.7 years; range, 32-69 years) who had been diagnosed with NPBL with features suggestive of malignancy during the study period. ROLL was used in 25 patients (26 lesions, including 2 separate foci in 1 patient), and WGL was used in 42 patients (44 lesions, with 2 separate foci in 2 patients) (Table 1). There was no significant difference between the groups in terms of age ($p=0.09$) or in terms of lesion location in the right or left breast ($p=0.378$). Nine of the patients in the ROLL group (36%) and 34 of the patients in the WGL group (81%) underwent mammography-guided breast marking; 16 of the patients in the ROLL group (64%) and 8 (19%) of the patients in the WGL group underwent ultrasonography-guided breast marking. Simultaneous SLNB was performed in 13 patients in the ROLL group and in 4 patients in the WGL group.

Images obtained before ROLL or WGL was performed demonstrated evidence of microcalcifications in 34 patients (79%) in the WGL group and in 9 patients (20%) in the ROLL group; a mass was observed in 8 patients (33%) in the WGL group and in 16 patients (66%) in the ROLL group. Pathologic analysis demonstrated that in the WGL group, 15 of 39 BI-RADS 4 lesions and 2 of 5 BI-RADS 5 lesions were malignant; in the ROLL group, 4 of 11 BI-RADS 4 lesions and 13 of 15 BI-RADS 5 lesions were malignant.

In the ROLL group, the lesion was accurately localized in 24 of 25 patients (96%). The one patient in the ROLL group without accurate localization demonstrated diffuse increased echogenicity

on ultrasonography after Tc-99m-MAA injection; this finding was further evaluated on intraoperative ultrasonography, and the lesion was found and excised. In the WGL group, the lesion was accurately localized in 41 of 42 patients (98%). In the one patient without accurate localization, the wire was dislodged out of the lesion.

No significant difference was observed between the groups in terms of the median specimen volume ($p=0.202$). There were also no significant differences between the groups in terms of complication rates, lengths of hospital stay, and creation of positive surgical margins. The length of operation was significantly longer in the ROLL group than in the WGL group (ROLL: 96.40 ± 37.54 minutes; WGL: 60.21 ± 20.21 minutes) ($p=0.0001$).

DISCUSSION

In this study, we found that ROLL was as effective as WGL in preoperatively localizing NPBLs. This accurate preoperative localization should lead to improved success rates for the surgical excision of NPBLs.

The WGL method of lesion localization has been used successfully for many years. In this study, we assessed whether the ROLL technique, just recently introduced at our institution, could provide safe and effective lesion localization, and we found that ROLL accurately localized NPBLs in 96% of patients, a rate similar to that seen with WGL (98%). These rates are also comparable to the localization rates of 89% to 100% reported in previous studies (17-22).

Accurate lesion localization and early surgical excision of NPBLs are important, as NPBLs are malignant in 10% to 30% of patients. BI-RADS 4 and 5 lesions carry the highest risk of malignancy (16,23,24). In this study of patients with BI-RADS 4 or 5 lesions, BI-RADS 4 lesions demonstrated heterogeneous distribution of malignancy risk in both the ROLL and WGL groups. The American College of Radiology states that the BI-RADS subgroups of 4a, 4b, and 4c have malignancy risks of 6%, 15%, and 53%, respectively (25), but the radiologic reports for lesions in this study did not include BI-RADS 4 subclassifications. For patients with BI-RADS 5 lesions, the malignancy rates in both the ROLL and WGL groups were consistent with rates previously reported (25).

We observed no difference between the groups in the creation of positive surgical margins and in the size of specimens obtained. In previous studies, the ROLL procedure was associated with less involved margins and smaller surgical specimens than the WGL technique (20,25-29). Because the surgeons at our institution have just begun using ROLL, a larger excision than usual may have been made, leading to larger specimen sizes. The size of the margins created is also dependent on lesion size and histologic grade; more involved margins are seen more frequently with cases of large ductal carcinoma in situ and lobular carcinoma in situ (28,30). The suggested protocol for creating surgical margins in patients with NPBLs is to use a gamma probe to trace the radioactivity in the center of the lesion and then assess the excision site to

Table 1. Image guidance for non-palpable breast lesions localization in the radioguided occult lesion localization and wire-guided localization groups

	Guidance techniques for localization	
	Mammography	Ultrasound
	n (*)	n (*)
ROLL	9	16
WGL	34	8

*Number of patients, ROLL: radioguided occult lesion localization, WGL: wire-guided localization

ensure that no residual lesion tissue remains (15,17,18,31,32), as we did in this study. However, some authors recommend excising an additional 1 to 2 cm of tissue around the maximal radioactive site (20,33).

The length of the operation was longer with ROLL than with WGL in our study. These results again contrast with those of previous studies, which reported shorter surgery times with ROLL than with WGL (17,18,27,32). This difference may again be partly explained by the learning curve required when implementing the ROLL technique. Additionally, more patients in the ROLL group than in the WGL group underwent SLNB, which may have added to the procedure time.

Complication rates and lengths of hospital stay were similar for the 2 groups and were similar to results from previous studies (17). Complications such as breakdown of the markers, syncope, pain, and pneumothorax have previously been reported with WGL (10-12), but a meta-analysis found that no major complications have been reported with either WGL or ROLL (27).

In this study, most of the ROLL procedures were guided by ultrasonography; this choice was determined by the radiologist. In general, the choice of imaging guidance depends on the availability of the technique and on the lesion characteristics. Mammography is recommended for assessing microcalcifications, whereas ultrasonography is recommended for evaluating solid and cystic lesions (18). Additionally, the choice of imaging used for guidance should be based on the type of imaging that first demonstrated the lesion (34).

In both the WGL and ROLL groups, SLNB was performed in only certain patients. However, more patients in the ROLL group underwent SLNB, perhaps because benign lesions were more common in the WGL group and lesions in the ROLL group were more likely to be mass-like. Histopathologic analysis of SLNB results was not included in this study.

Our study had several limitations. The main limitation of this study was that it was a retrospective study with small sample size, which limited our ability to include more lesions. Prospective data are needed to confirm these findings. On the other hand, study patients were treated by various radiologists and surgeons who had different degrees of experience with the procedures involved. These variations may have affected our analysis regarding accurate localization of lesions. Nuclear medicine at our institution has been a promising department which has provided us radionuclide material for ROLL. Collaboration of the departments of radiology and nuclear medicine has given us more chance to implement this new technique in our institution. This study was our first experience of this collaboration with some difficulties including low number of scintigraphic controls after ROLL procedures. Another limitation was that we could not evaluate the patient's comfort because of the retrospective design of the study.

CONCLUSION

In conclusion, this study demonstrated that the ROLL technique is a safe and effective method for preoperatively localizing NPBLs,

thus allowing accurate surgical excision of potentially malignant lesions. The ROLL technique may therefore serve as an alternative to WGL for the localization of NPBLs, as this technique is simple to perform (even for inexperienced operators) and provides satisfactory results.

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Informed Consent: Informed consent was not taken from patients due to the retrospective nature of the study.

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