



Comparison of Radio-guided Occult Lesion Localization (ROLL) and Magnetic Occult Lesion Localization (MOLL) for Non-palpable Lesions: A Phantom Model Study

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Abstract

We sought to compare radio-guided localization and magnetic tracer localization techniques by using a phantom model for excision of nonpalpable breast lesions. There was no difference between the groups in the duration of operative excision, specimen weight, or specimen volume. Magnetic occult lesion localization can be performed in clinics without the need for a nuclear medicine team and radiation safety procedures.

Background: Localization of nonpalpable breast cancers can be achieved with several techniques. We sought to compare radio-guided localization (ROLL) and magnetic tracer localization (MOLL) techniques by using a phantom model we previously developed, which can provide an accurate simulation for excision of nonpalpable breast lesions.

Materials and Methods: We designed 20 phantom models (10 MOLL, 10 ROLL group) for localization. A handheld gamma probe for the ROLL group and a manual magnetometer (SentiMag) for the MOLL group were used to test the ability of the modality to detect olives in turkey breasts. The excision time for each procedure, specimen size, and weight of the specimens removed from the turkey breasts were recorded. **Results:** Both techniques resulted in 100% retrieval of the lesions. There was no difference between the groups in the duration of operative excision, specimen weight, or specimen volume. **Conclusion:** This experimental trial found similar success rates for ROLL and MOLL in localization of occult lesions using the turkey breast phantom model. MOLL can be performed in clinics without the need for a nuclear medicine team and radiation safety procedures.

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Introduction

The detection of nonpalpable breast lesions and cancer has increased significantly owing to the implementation of widespread screening programs.¹ Approximately 20% to 30% of detected breast

cancers are nonpalpable.²⁻⁴ Image-guided localization of these lesions prior to surgical removal is necessary. Localization of nonpalpable breast cancers can be achieved with several techniques, including skin projection, carbon localization, wire-guided locali-

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zation, intraoperative ultrasound, and indocyanine green fluorescence-guided occult lesion localization, each with risks and benefits.⁵⁻⁸ Wire-guided localization (WGL), is currently the most commonly used method for excision of nonpalpable breast cancers, but it has several disadvantages, including difficulty in scheduling the surgery and the radiologic localization on the same day, discomfort of the patient, and wire displacement.^{9,10}

Radio-guided occult lesion localization (ROLL) or radio-guided seed localization (RSL) techniques became excellent alternatives to WGL methods for non-palpable breast lesions, but these radio-guided localization (RGL) techniques require involvement of a nuclear medicine team and radiation safety procedures, including safe handling of radioactive seeds.^{5,11-14}

A novel magnetic technique, which is radiation-free, was developed for sentinel node and nonpalpable lesion localization.^{15,16} A superparamagnetic iron oxide (SPIO) or magnetic seed had been used to perform the procedure.^{9,13} There are no studies that compare RGL and new magnetic tracer localization techniques. We previously described a simple RGL phantom model imitating an occult breast lesion from inexpensive supplies including a pimento olive, a green pea, and a turkey breast.¹⁷

We sought to compare RGL and magnetic tracer localization techniques by using this phantom model.

Materials and Methods

We designed a phantom model in order to compare ROLL and magnetic occult lesion localization (MOLL) techniques for detection of nonpalpable breast lesions. A total of 0.2 mL of liquid radioactive tracer (Tc-Human Serum Albumin Macroaggregate-MAA) was injected in 10 green peas in the ROLL group, and 0.2 mL of magnetic tracer (superparamagnetic iron oxide nanoparticles) was injected in 10 green peas in the MOLL group (Figure 1). Then the green peas were inserted into the pimento olives. These olives were embedded in the back of the turkey breasts with the assistance of a scalpel, and the incision was sutured closed (Figure 2). By completing these steps for 10 turkey breasts in each group, we created a model that represents occult lesions of breast tissue.

We estimated to detect a difference in means of at least 40% more than the standard deviation in each group. Nine samples

Figure 1 Injection of Magnetic Tracer Into the Pea

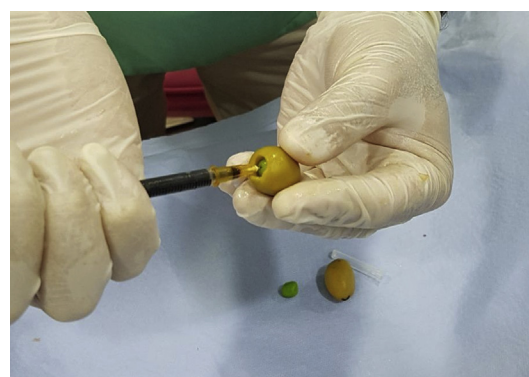
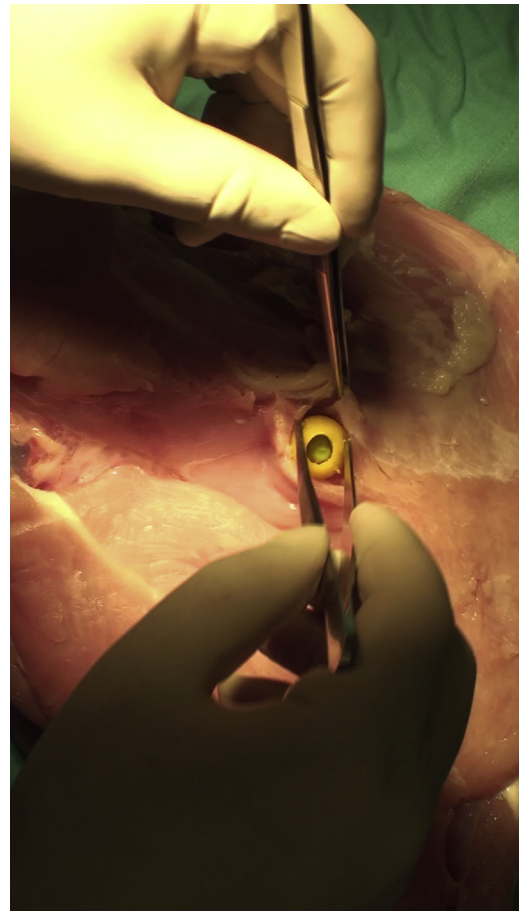


Figure 2 Embedding of the Pimento Olive in Back Side of Turkey Breast



would be enough with 80% statistical power at an alpha value of 0.05. Therefore, we used 10 samples for each group in the study.

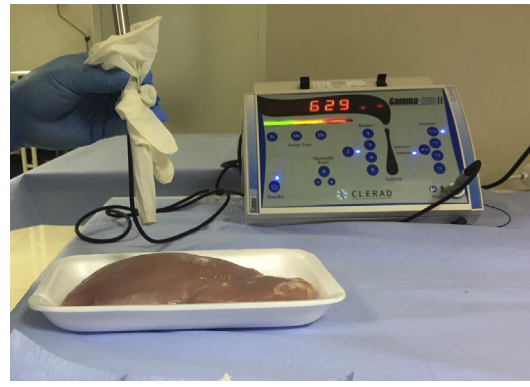
We used a handheld gamma probe for the ROLL group and a manual magnetometer (SentiMag, Endomagetics Ltd) for the MOLL group to be able to detect the olives in turkey breasts (Figure 3). The area of maximum radioactivity was used for detecting the site of incision (Figure 4). After excision of the olive, including approximately 2 mm of surrounding tissue, the cavity in the turkey breast was measured for residual radioactivity (Figure 5); all the procedures were performed by the same surgeon. We noted the excision time for each procedure, and we measured the size and the maximum diameter and weight of the specimens removed from the turkey breasts.

The superior margin (12 o'clock position) of the specimen was marked using a short suture, and the lateral margin (9 o'clock position) with a long suture to orient it correctly for the pathologist (Figure 6). These samples were sent to the pathology department for surgical margin assessment (Figure 7). Surgical margins were evaluated according to their distance to the olive. Absence of olive pieces at the margins was accepted as clear margin.

Figure 3 Measuring the Activity With SentiMag in the Specimen



Figure 4 The Area of Maximum Radioactivity Was Used for Detecting the Site of Incision



were achieved in 90% of the MOLLs group and 80% of the ROLLs group ($P = .53$). When compared according to width of the margins, both groups were similar ($P = .60$).

Discussion

The localization of nonpalpable breast lesions has increasingly become a prominent component in the practice of breast surgery, both benign and malignant. Several techniques have been developed to replace the traditional WGL.^{5-9,12} The clinical studies that

Figure 5 The Cavity Is Checked for Residual Activity by Using Gamma Probe



Statistical Analysis

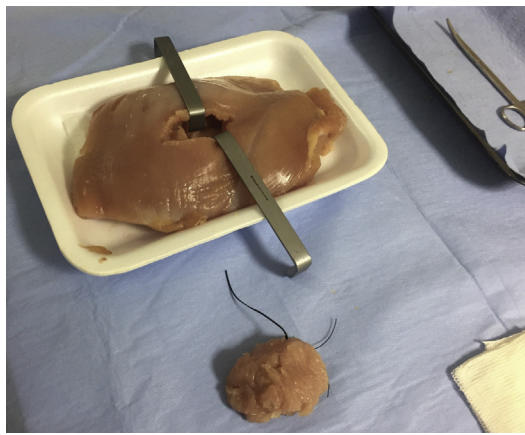
Distribution of categorical variables between the 2 groups were compared by χ^2 tests. Continuous variables are expressed as mean \pm standard deviation and compared between the 2 groups by t tests after testing for the equality of variances. P -values less than .05 were considered as statistically significant. All statistical analyses were conducted by SAS/STAT version 9.3 (SAS Institute, Inc, Cary, NC).

Results

A total of 20 phantom models (10 MOLL, 10 ROLL group) were constructed and used for localization. Both techniques resulted in 100% retrieval of the lesions. There was no difference between groups in the duration of operative excision, specimen weight, or specimen volume (Table 1). The mean time for operative excision of the lesion was 4:40 minutes (range, 3:30-5:31 minutes) for MOLL and 4:07 minutes (range, 3:12-5:00 minutes) for ROLL ($P = .23$). Specimen volume was similar in both groups, although the specimen weight was slightly smaller for ROLL ($P = .08$). Clear margins

Comparison of ROLL and MOLL

Figure 6 The Long Suture Marks the Lateral (9 O'clock Position), Whereas the Short Suture Marks the Superior (12 O'clock Position)



compare new techniques are time-consuming and expensive.¹⁸ We compared 2 localization methods by using a low-cost phantom model in a shorter period of time.

RGL techniques have some disadvantages, including the requirement of a nuclear medicine team, education of team members, radiation safety procedures, and proper licensing.^{9,19} These obstacles prompted the need for nonradioactive methods for lesion localization without nuclear regulations. On the other hand, special equipment that does not interfere with the signal are required for MOLL, and the detection performance of the manual magnetometer is limited in lesions deeper than 4 cm.²⁰

In our study, injections were made on the same day for both techniques. However, in real practice, the injection may be

Figure 7 These Samples Were Sent to the Pathology Department for Evaluation of Surgical Margins

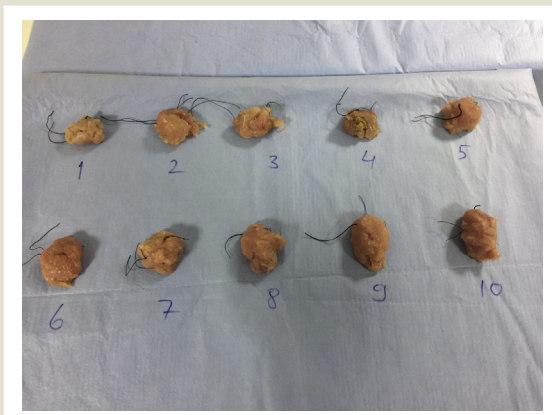


Table 1 Comparison of Procedure Time, Features of Specimen and Margins in the MOLL and ROLL Groups

Variables	MOLL (n = 10) Mean (± SD)	ROLL (n = 10) Mean (± SD)	P
Procedure time, min	4.40 (±0.67)	4.07 (±0.54)	.23
Specimen weight, gr	39.6 (±5.32)	33.4 (±9.02)	.08
Specimen volume	67.62 (±9.47)	78.67(±31.80)	.31
Margins, %			
Clear	90	80	.53
Involved	10	20	
Width of margin, %			
≤2 mm	20	30	.60
>2 mm	80	70	

Abbreviations: MOLL = magnetic occult lesion localization; ROLL = radio-guided occult lesion localization.

performed within 24 hours prior to the procedure in ROLL, 5 days in RSL, and 7 days for MOLL. A seed form of the magnetic and radioactive tracers, which are called MagSeed and radioactive seed, could also be used instead of a liquid. These seeds can be placed up to 30 days prior to surgery. We used the same size materials, and equal volumes (0.2 mL) of injected liquid in both groups to eliminate any bias. The mean time for operative excision of the lesion and specimen volume were similar in both groups.

Occult breast cancers require localization-guided surgery and axillary staging using sentinel lymph node biopsy (SLNB). The intratumoral injection of the magnetic tracer, both for tumor localization and SLNB have been described.²¹ Intratumoral injection of magnetic tracer demonstrated an inferior sentinel lymph node identification rate compared with the standard dual technique.²¹ Alternatively, lymphatic mapping agents, such as technetium sulfur colloid, isosulphan blue, and methylene blue, can be used as a second technique to increase the success of the SLNB procedure.

The other nonradioactive novel method, SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, CA) is a localization device that uses a radar reflector activated with infrared light.²² The surgeon uses a dedicated intraoperative probe that emits infrared light to identify and excise the target area.²³ There are no studies that compare SAVI SCOUT and magnetic tracer localization techniques.

Although clear margin rates were similar in both groups, the evaluation of margin status may not reflect real practice owing to the easily damaged quality of turkey tissue. This model is time-efficient and easily prepared with inexpensive materials. It offers surgeons and trainees a safe learning environment prior to real practice, and it can be used as a simulation model for introducing a new technique to institutions.

Our study has some limitations. The first is the representation of actual breast tissue, although it has been the most ideal method of simulation for breast procedures. The second is the inaccurate evaluation of surgical margins owing to the fragility of turkey breast tissue. Third is the limited evaluation of cosmetic results in our model.

Conclusion

This study found similar success rates for ROLL and MOLL in localization of occult lesions using the phantom model of turkey breast. MOLL can be performed in clinics without the need for a nuclear medicine team and radiation safety procedures. This technique can be an alternative to RGL with the support of further clinical studies.

Clinical Practice Points

- Localization of nonpalpable breast cancers can be achieved with several techniques including WGL, intraoperative ultrasound, and ROLL; each with risks and benefits.
- A novel magnetic technique (MOLL), which is radiation-free, was developed for sentinel node and nonpalpable lesion localization.
- ROLL and MOLL techniques both resulted in 100% retrieval of the lesions. There was no difference between the groups in the duration of operative excision and specimen features.
- MOLL can be performed in clinics without the need for a Nuclear Medicine team and radiation safety procedures.

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Disclosure

The authors have stated that they have no conflicts of interest.

References

1. Autier P, Boniol M. Mammography screening: a major issue in medicine. *Eur J Cancer* 2018; 90:34-62.
2. Ernster VL, Ballard-Barbash R, Barlow WE, et al. Detection of ductal carcinoma in situ in women undergoing screening mammography. *J Natl Cancer Inst* 2002; 94:1546-54.
3. Lyng E, Ponti A, James T, et al. ICSN DCIS Working group. Variation in detection of ductal carcinoma in situ during screening mammography: a survey within the International Cancer Screening Network. *Eur J Cancer* 2014; 50:185-92.
4. Breast Cancer Surveillance Consortium. Cancers for 2,061,691 screening mammography examinations from 2004-2008. Available at: <http://www.bcs-research.org/statistics/benchmarks/screening/2009/table4.html>. Accessed: March 12, 2019.
5. Aydogan F, Velidedeoglu M, Kilic F, Yilmaz H. Radio-guided localization of clinically occult breast lesions: current modalities and future directions. *Expert Rev Med Devices* 2014; 11:53-63.
6. Canavese G, Catturich A, Vecchio C, et al. Pre-operative localization of non-palpable lesions in breast cancer by charcoal suspension. *Eur J Surg Oncol* 1995; 21:47-9.
7. Aydogan F, Ozben V, Aytac E, Yilmaz H, Cercel A, Celik V. Excision of non-palpable breast cancer with indocyanine green fluorescence-guided occult lesion localization (IFOLL). *Breast Care (Basel)* 2012; 7:48-51.
8. Chan BK, Wiseberg-Firtell JA, Jois RH, Jensen K, Audisio RA. Localization techniques for guided surgical excision of non-palpable breast lesions. *Cochrane Database Syst Rev* 2015; 12:CD04.
9. Jeffries DO, Dossett LA, Jorns JM. Localization for breast surgery: the next generation. *Arch Pathol Lab Med* 2017; 141:1324-9.
10. Ahmed M, Rubio IT, Klaase JM, Douek M. Surgical treatment of nonpalpable primary invasive and in situ breast cancer. *Nat Rev Clin Oncol* 2015; 12:645-63.
11. Ahmed M, Douek M. Radioactive seed localisation (RSL) in the treatment of non-palpable breast cancers: systematic review and meta-analysis. *Breast* 2013; 22:383-8.
12. Luini A, Zurrida S, Galimberti V, Paganelli G. Radioguided surgery of occult breast lesions. *Eur J Cancer* 1998; 34:204-5.
13. Intra M, de Cicco C, Gentilini O, Luini A, Paganelli G. Radioguided localisation (ROLL) of non-palpable breast lesions and simultaneous sentinel lymph node biopsy (SNOLL): the experience of the European Institute of Oncology. *Eur J Nucl Med Mol Imaging* 2007; 34:957-8.
14. Zgajnar J, Hocevar M, Frkovic-Grazio S, Hertl K, Schweiger E, Besic N. Radio-guided occult lesion localization (ROLL) of the nonpalpable breast lesions. *Neoplasma* 2004; 51:385-9.
15. Ahmed M, Usiskin SI, Hall-Craggs MA, Douek M. Is imaging the future of axillary staging in breast cancer? *Eur Radiol* 2014; 24:288-93.
16. Aksakal N, Ozturk A, Tural F, et al. Magnetic probe-guided excision of non-palpable neck lesions. *Surg Innov* 2017; 24:42-8.
17. Aydogan F, Mallory MA, Tukenmez M, et al. A low cost training phantom model for radio-guided localization techniques in occult breast lesions. *J Surg Oncol* 2015; 112:449-51.
18. James S, Rao SV, Granger CB. Registry-based randomized clinical trials—a new clinical trial paradigm. *Nat Rev Cardiol* 2015; 12:312-6.
19. Jakub J, Gray R. Starting a radioactive seed localization program. *Ann Surg Oncol* 2015; 22:3197-202.
20. Pouw JJ, Bastiaan DM, Klaase JM, Ten Haken B. Phantom study quantifying the depth performance of a handheld magnetometer for sentinel lymph node biopsy. *Phys Med* 2016; 32:926-31.
21. Ahmed M, Anninga B, Goyal S, Young P, Pankhurst QA, Douek M. MagSNOLL Trialists Group. Magnetic sentinel node and occult lesion localization in breast cancer (MagSNOLL Trial). *Br J Surg* 2015; 102:646-52.
22. Cox CE, Garcia-Henriquez N, Glancy MJ, et al. Pilot study of a new nonradioactive surgical guidance technology for locating nonpalpable breast lesions. *Ann Surg Oncol* 2016; 23:1824-30.
23. Hayes MK. Update on preoperative breast localization. *Radiol Clin North Am* 2017; 55:591-603.