Review Article

Radioguided occult lesion localization and sentinel node and occult lesion localization in breast cancer: The future beckons

ABSTRACT

Wire Guided Localisation has been the traditional technique for occult breast lesions. However, ROLL has emerged as a safer alternative to WGL approach. ROLL provides an improvement on margin positive rates and offers better pain and cosmetic advantages to the patient combined with a shorter learning curves for both radiologists and surgeons. SNOLL adds to the advantages of the procedure by combining SLNB with ROLL hence offering an economic advantage. The use of ROLL as primary modality for occult lesion localisation is bound to increase with potential to replace WGL as the primary modality for such lesions.

Key words: Breast cancer; occult breast lesion; radioguided breast surgery; radioguided occult lesion localization; sentinel node and occult lesion localization

Introduction

Breast cancer is fast becoming the most common cancer in females in India.[1] This increase in incidence has led to a heightened awareness toward screening for breast cancer and as a result, breast surgeons are often confronted with a nonpalpable, screen-detected lesion. Though the exact incidence in India is not available, we are still far away from the situation in west where up to a third, or even half of patients present with a nonpalpable breast lumps.[2,3] Wire guided localization (WGL) is the widely accepted and current standard technique for excision of these lesions. In this technique, a hooked wire is placed under ultrasound or stereotactic guidance to identify the lesion.[3] The patient is then shifted to the operation theater and the lesion is excised by estimating the tip of the wire.

The WGL technique is not without its share of disadvantages [Table 1].[2-6] Since the exact position of the tip is merely an estimate, there are higher chances of incomplete or margin-positive excisions. The incidence of margin positive excision can be as high as 14–47%.[2,3,6] Higher margin positive rate leads to increased re-explorations, increased risk of local recurrences, and increased costs. There is a risk of inaccurate positioning and a risk of wire displacement after positioning. The point of wire insertion with respect to the planned incision is also important. If the planned incision and wire position are not aligned, it can lead to a struggle during excision, which in turn can lead to wire displacement. All radiologists are also not well versed with the procedure of wire localization and wire placement, hence restricting the setups where this procedure can be done. A higher patient discomfort has also been reported with WGL.[6]

Radioguided occult lesion localization (ROLL) as an alternative to WGL arose from coffee room banter for the solution of occult lesions after the success of sentinel lymph node biopsy (SLNB). The first radioguided excision was done in May 1996

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Table 1: Comparison of ROLL and WGL techniques

	ROLL	WGL
Pros	More accurate	Standard more commonly used method
	Lesser margin positive rates	Long established technique
	Shorter learning curves for surgeons	Can be done without need for nuclear medicine facility
	Easier for radiologists	
	Shorter localization time	
	Lesser risk of displacement/migration	
	Lesser patient discomfort	
	Optimal choice of incision	
	Better cosmetic outcome	
	Provides an estimate of margins while excision	
	Can be combined with SLNB	
Cons	Newer technology	Higher chances of margin positive excisions
	Fewer surgeons experienced with the technique	Increased re-explorations, local recurrences and increased costs
	Radioisotope dependent	Risk of inaccurate positioning and wire displacement
	Requires infrastructure, i.e., Gamma probe	All radiologists are not well versed
		Higher patient discomfort
		Wire transection
		Diathermy burns

ROLL - Radioguided occult lesion localization; WGL - Wire guided localization; SLNB - Sentinel lymph node biopsy

and was termed centratura radioisotopica, which was later changed to ROLL.[7]

The occult lesion in ROLL is highlighted by injection of a liquid radioactive tracer. The tracers commonly used are 99-technetium (99Tc) labeled macro aggregate albumin (99Tc-MAA), 99Tc nanocolloid and even 99Tc sulfur colloid. Other options are injection of titanium seed with I^{131} radioiodine seed localization, (RSL) or injection of a small volume of radiocontrast along with radioactive dye, to make lesion visible on a specimen mammogram as well. The volume ranges from 0.2 ml to 0.5 ml. The injection can be done under ultrasound or stereotactic guidance and can be done either on the day of surgery or a day prior as well. The unique advantage of RSL is long half-life and hence can even be placed prior to the start of neoadjuvant chemotherapy. The dye is injected into the lesion in most of the studies; however, perilesional injections have also been used. In hard, scirrhous lesion, a perilesional injection can be given to avoid spillage. Often a small air bubble is injected trailing the dye to prevent the dye from staining the needle track. The needle can also be disconnected from syringe hub prior to removal for the same affect. The position and migration can be confirmed by imaging with a single-photon emission computed tomography-computed tomography that can show the dye with respect to lesion and dye migration if any. The lesion is then identified during surgery using a handheld gamma probe and excised.

Incomplete and margin positive resections are the major concerns with WGL. Hence, this has been evaluated by multiple studies as the main criteria. Majority of the studies have shown either better or equal complete excision rates with ROLL as compared to WGL.[2,4,8-16] ROLL provides a continuous dynamic feedback during the excision helping the surgeon to gauge the distance from the lesion. ROLL provides the exact location of the lesion as compared to the estimation of tip of the wire, which leads to a more accurate excision. Most of these studies have reported complete excision rates to the tune of 78–99%.[8-16] Lovrics *et al*. in their systematic review considered 12 studies (5 randomized controlled trials [RCT's] and 7 nonrandomized cohorts) after assessing the quality of studies. The data were analyzed separately for RCT's and cohort studies and then as a combined group. Their meta-analysis found that radioguided localization (RGL) generated lower "close or involved" margins rates for RCT data ($P = 0.007$), cohort data (P - 0.0001) and for combined group as well. RGL also reported lower re-operation rates in RCT data (P - 0.04), cohort data ($P < 0.001$) as well as combined group data. There was no significant difference in operative time and specimen volume, but time for localization by the radiologist was significantly lesser in the RCT data.[3] The other meta-analysis included 4 RCT's with 449 patients found higher positive resection margins, longer duration for localization, and surgical excision with WGL. However, the accuracy of localization, peri-procedural complications, and reoperation rate were comparable between two techniques. The volume and weight of the excised occult breast lesion were similar in WGL and ROLL groups.[17]

ROLL as a procedure is simply an injection of small amount of radioactive tracer and hence conceptually it should be easier for the radiologist not experienced with either WGL or ROLL to adapt to this procedure. This point has also been a consistent finding in the majority of studies that have either evaluated the ease by either a subjective assessment or by time to localization. A significant difference in ease of localization and a shorter time has been reported by many studies.[4,12,18,19] Landman *et al*. compared the ease of procedure for the radiologist and surgeons by means of a Likert 1–10 scale with 1 being easy and 10 being difficult.[6] They found radiologists had a very short learning curve with ROLL and Likert score assessment was also in favor of ROLL.

ROLL carries multiple advantages for the patient as well. ROLL scored higher in subjective ease of procedure for the patients.[6] Since there is just a single fine needle injection,

patients find it to be less painful. Since the localization can be done a day before without any wire sticking out or risk of wire displacement, it allows the patient to be more comfortable. Patients reported lesser pain (2.2 for WGL versus 1.62 for ROLL on the pain scale) on the first postoperative day with ROLL.[6]

Cosmetic outcome is an important consideration for breast surgery. Most of the studies have reported the smaller volume of excisions as a surrogate for the cosmetic outcome. However, the smaller volume of excision is not a consistent finding across all the studies.[8-14] The meta-analyses found no significant difference in specimen volumes between the two techniques.[3,17] The flexibility of ROLL to allow placement of cosmetically better incisions can be a reason for an apparent cosmetic benefit. The patient-reported cosmetic outcome is also better with ROLL with a higher proportion of patients reporting "excellent" cosmetic outcome with ROLL as compared to WGL ($P < 0.001$).[6]

Early detection of breast cancer also means lesser chances of lymphatic metastases.[21-24] SLNB has replaced axillary lymph node dissection as the standard of care for node-negative, early breast cancer for the purpose of axillary staging.[23] The nodal involvement in breast cancer is considered to be in a systematic manner, and if the sentinel lymph node (SLN) is not involved, the rest of the nodal basin is also free of the disease.[24] The use of SLNB has been shown to be safe even in multifocal tumors and patients with previous breast and axillary surgeries.[23] Sentinel node and occult lesion localization (SNOLL) is a logical extension and another advantage of ROLL wherein ROLL is combined with SLNB. SNOLL provides a single step solution for identification of both the lesion and sentinel node by a single method. This offers an economic advantage as well wherein the cost of WGL and SLNB can be replaced by SNOLL. The safety and efficacy of SNOLL have been established in multiple studies and reviews. The rate of identification of SLN has ranged from 88% to 100% with most of the larger studies have an SLN identification rate of 95–100%.[25,26]

SNOLL can be done by a single injection or double injection method.[22-24] In the two-injection method, a separate superficial (subdermal/periareolar) injection of Tc nanocolloid is given for the SLNB along with the intratumoral injection of MAA and this method resembles the traditional method of SLNB identification. In single injection method, 99m-Tc nanocolloid is injected into the lesion. If the lesion is a hard schirhous tumor, a perilesion injection can also be given to avoid spillage.[6] The dye along with highlighting the primary site migrates to the draining nodes to identify the sentinel node.[20] The major dilemma with using the single injection method is whether the node is the representative SLN. The site of injection of a dye for accurate SLN identification has always been under scrutiny.[27-30] Intratumor/perilesional injections are associated with higher internal mammary (IM) identification rate whereas superficial injections very rarely highlight IM nodes.[31] Apart from the site of injection, other factors such as small breast size, medial, and inferior tumors, younger age, and lower body mass index are also associated with higher IM node identification.[31] Identification of IM chain as SLN is a controversial topic as its management and impact on clinical decisions and patient outcome is not clear.[32,33] Superficial injections were found to identify axillary SLN more accurately and hence have replaced the intratumor injections as the preferred site in traditional SLNB procedure.[24] De Cicco *et al*. in their study compared the various methods of dye injections in SNOLL and found the two-injection method to have the least SLN identification failure rate (98% vs. 89%, $P < 0.001$).[30] However, a majority of studies evaluating single injection technique have an SLN identification rate between 90% and 100%[25] and hence the site of injection remains a question of physician preference. The authors in their own practice prefer the two-injection technique.

Conclusions

ROLL has emerged as a safer alternative to traditional WGL approach. ROLL provides an improvement on margin positive rates as compared to WGL and offers pain and cosmetic advantages to the patient. It has good acceptability with shorter learning curves for both radiologists and surgeons. SNOLL adds to the advantages of the procedure by combining SLNB. The single injection technique may lead to a higher IM node identification rate, which needs more data to clear its implications.

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Conflicts of interest
There are no conflicts of interest.

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