Page 1 of 8

Original Research

Radioguided occult lesion localisation: A retrospective audit at a single tertiary academic breast unit

Authors:

Sumaya Ismail¹ ⁽¹⁾ Francois Malherbe² ⁽²⁾ Eugenio Panieri² ⁽²⁾ Lydia Cairncross² ⁽²⁾ Gaseeda Boltman³ ⁽²⁾ Florence E. Davidson¹ ⁽²⁾

Affiliations:

¹Department of Medical Imaging and Therapeutic Sciences, Faculty Health and Wellness Sciences, Cape Peninsula University of Technology, Cape Town, South Africa

²Division of Surgery, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

³Nuclear Medicine Division, Groote Schuur Hospital, Cape Town, South Africa

Corresponding author: Sumaya Ismail, sumaya.ismail01@gmail.com

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Scan this QR code with your smart phone or mobile device to read online. **Background:** The radioguided occult lesion localisation (ROLL) technique was introduced at Groote Schuur Hospital in 2003 replacing the wire-guided localisation (WGL) technique. In the case of preoperative histologically proven impalpable breast cancers, a sentinel lymph node (SLN) biopsy was done simultaneously (sentinel node [SN] with occult lesion localisation or SNOLL).

Aim: To assess the efficacy of the ROLL and SNOLL techniques for diagnostic and therapeutic excisions.

Setting: A retrospective record analysis of 190 patients who underwent a ROLL procedure for diagnostic or therapeutic excision of occult breast lesions was performed at a large tertiary hospital in the Western Cape.

Methods: Data were collected on patient and tumour characteristics, successful localisation rates, the volume of tissue removed, complete tumour resection rates, the number of re-operations performed and the proportion of SLN detection. The Pearson's chi-squared test was used to test for significance between variables at $\alpha = 0.05$.

Results: Correct radiopharmaceutical placement was achieved in 177/190 (93.2%) lesions. Histologic examination of excised specimens confirmed 115/190 (61.0%) malignant and 75/190 (39.0%) benign lesions. Involved margins were found in 37/115 (32.2%). Complete excision with adequate margins occurred in 50/70 (71.4%) of cases of invasive cancer and in 11/45 (24.4%) of ductal carcinoma in situ (DCIS). The SN was successfully identified in 30/37 (81.1%) of SNOLL cases.

Conclusion: Radioguided occult lesion localisation is an effective tool in the preoperative localisation of occult lesions for surgical biopsy as well as the removal of impalpable breast cancers. A single intratumoural injection with ^{99m}Tc nanocolloid combined with lymphoscintigraphy is a reliable method of localising the SN.

Contribution: The researchers' observations support that the ROLL and SNOLL techniques assessed in this study are practical and reliable procedures to perform.

Keywords: nonpalpable breast lesion; radioguided surgery; radioguided occult lesion localisation; wire-guided localisation; WGL; sentinel node biopsy.

Introduction

The detection of impalpable occult breast lesions worldwide has increased primarily because of the increase in screening programmes and improvements in technology and high-resolution imaging.¹ Occult breast lesions account for 25% - 35% of breast cancers in a population undergoing regular breast screening.² The early detection and management of these small early-stage breast cancer lesions has a significant effect on the treatment outcomes for the patient.³

South Africa does not have a population-based mammographic screening programme. Instead, a risk-based assessment is employed for symptomatic patients and high-risk women.^{4,5} Although a low- to middle-income country, there have been significant changes in service delivery in certain sectors of the health service in South Africa.⁶ One of these has been the establishment of specialist breast cancer centres within larger tertiary hospitals. These centres comprise multidisciplinary teams where the global gold standard of triple assessment (clinical examination, imaging and biopsy) in the diagnosis of breast cancer is employed.⁶ Although these centres are often concentrated in urban areas, they receive patients referred from primary health care facilities and district hospitals.^{4,6}

A suspicious impalpable lesion detected on imaging needs to be further investigated. Percutaneous fine needle biopsy (FNB) and core needle biopsy (CNB) are performed on these lesions to obtain cytological and histological tissue results.⁷ However, surgical excision is indicated if the needle biopsies proved nondiagnostic.⁷ More recently, vacuum-assisted core biopsy has also become available and has been shown to be useful when the initial core biopsies are inconclusive. Vacuum-assisted core biopsy can even be used to remove small lesions completely, replacing the need for performing surgical excisions. Its use as an alternative to surgery could be considered when the technology is available.⁸⁹

In order to accurately localise these lesions, several techniques have been documented, each with its own advantages and drawbacks.^{1,7,10} The wire-guided localisation (WGL) technique is the most widely used and preferred method of choice in many centres worldwide.^{11,12,13} Despite its widespread use, WGL does have many reported disadvantages such as patient discomfort, technical difficulty and risk of complications.^{7,14}

The radioguided occult lesion localisation (ROLL) is an alternative technique using a radioactive tracer injected into or close to the lesion under radiographic guidance prior to surgery, where the localisation and removal of the lesion are aided by a handheld gamma probe.⁷ An added advantage is that in the case of histologically proven impalpable breast cancers, a sentinel lymph node biopsy (SLNB) can be done simultaneously with occult lesion localisation (SNOLL) to detect axillary metastases.¹⁵

In 2003, ROLL replaced the WGL technique for occult breast lesions at the research site. While the efficacy of the ROLL technique with or without sentinel node (SN) biopsy has been well-documented internationally, to the best of our knowledge, this study is the first to document the effectiveness of ROLL in the South African context.

The primary objective of this study was to review the experience of the ROLL technique at a tertiary hospital and to evaluate its accuracy and effectiveness for diagnostic and therapeutic excisions. Secondary aims were to look at technical difficulties, duration of surgery and radiation dose administered.

Materials and methods

A retrospective analysis was conducted of patients who underwent ROLL and SNOLL procedures at Groote Schuur Hospital, a large tertiary hospital in Cape Town, South Africa. Inclusion criteria were patients who underwent ROLL and SNOLL procedures for radiologically suspicious nonpalpable breast lesions from January 2003 to December 2016. Excluded were patients who had incomplete or missing radiologic and histopathologic data. Data collected included patient and tumour characteristics, localisation procedures and diagnostic outcomes. The ROLL injection was administered on the day before or on the same day as scheduled theatre. 99mTc tin colloid or 99mTc hepatate was used. Doses ranging from 5 MBq to 22 MBq were dispensed in a volume of 0.1 mL. The injection was carried out with the assistance of image guidance by either ultrasonography or stereotaxis as appropriate. The radiologist positioned the tip of a 22 gauge (G) spinal needle intralesionally or, in the case of microcalcifications, in the bulk of the microcalcifications, as determined by mammographic stereotaxis. The radiopharmaceutical was injected, followed by 0.2 mL of air. For the SNOLL, a single intratumoural injection of 99mTc nanocolloid with 95% of the particle size having a diameter of ≤ 80 nm was used. A dose in the range of 70 MBq to 113 MBq was injected. Scintigraphic images were acquired on a dual-headed Siemens gamma camera. A rectangular cobalt source was used to outline the body contour, allowing correlation to the injection site. For ROLL, localised anterior and lateral static images were taken 30 min after injection or even later to localise the site of the injection and to ensure there was no migration of the radiopharmaceutical from the injection site.

For SNOLL, imaging was performed at least 30 min after injection, and static images were taken in the anterior, lateral (90°) and oblique (45°) positions. Images were repeated at 2 h and continued later if no SN were visualised at the time. When the SN was visualised, skin markings were made in relation to the position on the images. Thereafter, the gamma probe was used to locate the maximum reading to account for distortion of the position caused by imaging, and a final marking was made as a guide for optimal surgical incision of the SN. During surgery, a C-Track gamma probe was used to determine the point of highest radiation detection to guide the skin incision and to define the margins of the lesion by detecting the decrease in levels in the surgical field. Once excision of the lesion was complete, the area was surveyed to ensure that there was no residual radioactivity in the resected area, and the lesion was then X-rayed to confirm presence of the occult lesion or presence of microcalcifications. If necessary, more tissue was removed. A histological evaluation of the resected tissue was performed by a pathologist.

When SLNB was performed, an injection of 0.5 mL of methylene blue dye was administered subcutaneously peri-areolar in the quadrant of the lesion. Once the lesion was removed, the SN was located using the skin markings and gamma probe readings as a guide.

Ethical considerations

Ethical approval for the study was received from the Human Research Ethics Committee at the University of Cape Town (reference number 281/2017) as well as the Research Ethics Committee (REC) of the Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology (reference number CPUT/HW-REC 2016/H27). All patient identifiers were anonymised before statistical analysis.

Data analysis

Data were analysed using Microsoft Excel and statistical package NCSS, LLC, 2021, version 21.0.2 (Utah, United States) software package. The level of significance was set at $\alpha = 0.05$. Categorical data were presented as frequencies and percentages, and continuous variables were presented as means and median. The Pearson's chi-squared test was used for comparisons on discreet data.

Results

One hundred and ninety patient records were included in the retrospective analysis. The mean age of the patients was 56 years (range 28–85 years). The clinical and radiological characteristics of the lesions preoperatively are summarised in Table 1. Most lesions were found in the upper outer quadrant. Biopsy results could only be found for 173 of the lesions. Where the intent was therapeutic and an SLN biopsy was done, all lesions (37/190) were injected with ^{99m}Tc nanocolloid. One patient had a ROLL done with a simultaneous mastectomy performed on confirmation of malignancy by the frozen section result. One patient had bilateral occult lesions, one of which was highly suspicious, and had simultaneous ROLL and SNOLL done on the opposite breast. In this instance, two injections were given, ^{99m}Tc tin colloid for the ROLL and ^{99m}Tc nanocolloid for the SNOLL. Four other patients had simultaneous ROLL and SLNB with a mastectomy performed on the other breast. Surgery was performed on the same day or the day after injection, with recorded times of up to 29 h after radiopharmaceutical injection.

Table 2 compares the same day and day after protocols in terms of time to localisation, volume excised and margin status. There was no statistically significant difference between the time to localisation between the same-day and day-after injection protocols (p = 0.60). There was also no statistically significant difference with regards to the volume of tissue excised (p = 0.60). Margin status was also found

TABLE 1: Clinical and radiological characteristics of all lesions preoperatively.

Procedure	п	N	%	Mean age in years	+ s.d.	Age	Right Breast		Left breast		Combined		Р
							п	%	n	%	n	%	-
ROLL	153	190	80.5	56.02	± 11.05	28-85	-	-	-	-	-	-	-
SNOLL	37	190	19.5	56.70	± 9.07	38–72	-	-	-	-	-	-	-
Radiological Appearance													
Density/mass	119	190	62.6	-	-	-	-	-	-	-	-	-	-
Microcalcifications	67	190	35.3	-	-	-	-	-	-	-	-	-	-
Not recorded	4	190	2.1	-	-	-	-	-	-	-	-	-	-
Pre-operative histology													
Malignant	59	173	34.1	-	-	-	-	-	-	-	-	-	-
Benign	55	173	31.8	-	-	-	-	-	-	-	-	-	-
Inadequate/Indeterminate	59	173	34.1	-	-	-	-	-	-	-	-	-	-
Not recorded	-	-	17.0	-	-	-	-	-	-	-	-	-	-
Breast	-	-	-	-	-	-	94	49.5	96	50.5	190	-	0.47
Quadrant													0.013
Upper inner quadrant	-	-	-	-	-	-	11	5.8	12	13.6	23	12.1	
Upper outer quadrant	-	-	-	-	-	-	44	23.2	43	22.6	87	45.8	
Retroareolar	-	-	-	-	-	-	4	2.1	1	0.5	5	2.6	
Midline	-	-	-	-	-	-	5	2.6	5	2.6	10	5.3	
Lower inner quadrant	-	-	-	-	-	-	7	3.7	10	5.3	17	9.0	
Lower outer quadrant	-	-	-	-	-	-	7	3.7	14	7.4	21	11.1	
Not recorded	-	-	-	-	-	-	16	8.4	11	5.8	27	14.2	

ROLL, radioguided occult lesion localisation; SNOLL, sentinel node with occult lesion localisation; s.d., standard deviation.

TABLE 2: Comparison of same-day and day-after protocols.

Parameter	Same-Day Protocol				Day-After Protocol				Not recorded				p-value						
_	n	%	N	Mean	Range	IQR	n	%	N	Mean	Range	IQR	n	%	N	Mean	Range	IQR	
Number of cases	35	18.4	190	-	-	-	137	72.1	190	-	-	-	18	9.5	190	-	-	-	
Time to localisation† (min)	-	-	-	25.0	5–45	-	-	-	-	21	5–45	-	-	-	-	-	-	-	0.60
Volume excised cm ³	-	-	-	140.4	-	30–167	-	-	-	122	-	37–143	-	-	-	-	-	-	0.60
Margin Status of Malignant lesions (Total = 115)	25	-	-	-	-	-	85	-	-	-	-	-	5	-	-	-	-	-	0.70
Clear	10	40.0	-	-	-	-	43	49.0	-	-	-	-	-	-	-	-	-	-	-
Close	6	24.0	-	-	-	-	20	23.0	-	-	-	-	-	-	-	-	-	-	-
Involved	9	36.0	-	-	-	-	25	28.0	-	-	-	-	-	-	-	-	-	-	-

IQR, interquartile range.

†, Time taken from the time of incision until excision of lesion.

TABLE 3: Postoperative lesion characteristics.

Lesion in specimen	Number	%
Yes	177	93.2
No	9	4.7
Not Recorded	4	2.1
Post-operative histology		
Benign	75	39.5
Malignant	115	60.5
Invasive cancer	70	61.0
DCIS	45	39.0

TABLE 4: Margin status and type of tumour.

Variable	Clear >	> 2 mm	Close	< 2 mm	Invo	p-value	
	п	%	n	%	n	%	-
Type of Tumour							0.0004
Infiltrating cancer ($n = 70$)	42	60	8	11	20	29	
DCIS (n = 45)	11	24	17	38	17	38	
Total (n = 115)	53	46	25	22	37	32	
Radiologic Appearance							0.0044
Density/mass (n = 69)	40	58	10	15	19	28	
Microcalcifications (n = 43)	12	21	15	34	16	39	
Not recorded (n = 3)	-	-	-	-	-	-	
Position of lesion in breas	t						0.33
Lower inner quadrant (<i>n</i> = 11)	4	8	3	13	4	12	
Lower outer quadrant (<i>n</i> = 12)	8	15	1	4	3	9	
Retroareolar (n = 2)	2	4	0	-	0	-	
Midline ($n = 7$)	5	10	0	-	2	9	
Upper inner quadrant (n = 17)	7	14	7	29	3	9	
Upper outer quadrant (n = 59)	26	50	13	54	20	61	
Not recorded (n = 7)	-	-	-	-	-	-	

DCIS. ductal carcinoma in situ.

to be independent for same-day or day-after protocols (p = 0.70).

Table 3 shows the postoperative surgical characteristics of the lesions and margin status. In nine cases (4.74%), lesions or microcalcifications were not found in the specimen or found to be representative of the pathology (on confirmation of mammogram and/or histology). Six of these were repeated.

Table 4 shows the distribution of margins according to the type of tumour. There was a statistically significant difference in margin status and the type of tumour (p = 0.0004). For infiltrating cancer lesions, an adequate excision was considered when margins had no tumour cells present at the inked margin, regardless of whether margins were close (< 2 mm), whereas in the case of ductal carcinoma *in situ* (DCIS), only margins greater than 2 mm were considered an adequate excision. There was also a statistically significant difference in the margin status and the radiologic appearance of lesions (p = 0.0044).

On analysis, there was no statistically significant difference in the amount of tissue resected, based on the preoperative histology as well as the radiologic appearance on imaging before surgery (Table 5).

TABLE 5: Volume	of tissue	excised	based	on	preoperative	histology	result	and
radiologic appeara	ance.							

Variable	Mean size Tissue Excised (cm ³)	<i>p</i> -value
Preoperative histology result		0.76
Inadequate	114.4	
Indeterminate	106.0	
Benign	103.5	
Malignant	136.3	
Radiologic appearance		0.55
Microcalcification	118.8	
Density/mass	124.0	

There were four cases in which the SN was not identified, one of which was due to an increased body mass index (BMI). Two cases were repeated because of technical difficulties during the injection. In one case, there was no activity detected during theatre and the study was rescheduled. In the other case, the patient did not go to theatre as there was a significant number of lymphatic tracts seen on scintigraphy after the injection. Both these studies were repeated successfully. In the fourth case, where no SN was identified, an axillary nodal clearance was done.

Discussion Radiological appearance

In this study, lesions were categorised by their appearance on imaging as density/mass and microcalcifications. In our series, 119/190 (62.6%) lesions were classified as a density/mass, while a smaller proportion 67/190 (35.3%) were microcalcifications. Pijnappel et al. showed that microcalcifications are more likely to be associated with DCIS₂ a finding supported in the present study, where the majority of lesions were invasive cancer 70/115 (61%) and only 5/115 (39%) DCIS.⁹ This increased proportion of invasive cancers can be explained by the fact that South Africa has no population-based screening programme, leading to a later stage of presentation.^{5,16}

Preoperative histology

Fine needle aspiration biopsy and CNB are preferred over surgical excision to determine cytology and histology in breast lesions because of the low risk of complications, ease of the procedure and cost-effectiveness. The sensitivity rate of CNB in breast cancer is reported as 97.0%.8 In this study, needle biopsy reported 59/190 (31.1%) lesions as malignant, while 59/190 (31.1%) lesions were indeterminate or inadequate tissue samples. This finding is somewhat lower than the study by Pilkington et al., where insufficient material was obtained in 24/40 (60.0%) of lesions.¹⁷ But this may be explained by the lower rate of microcalcifications in the present study's series, as Pijnappel et al. found that microcalcifications are less likely to yield a definitive diagnosis on CNB.9 In the present study, 18/59 (30.5%) of indeterminate or inadequate lesions were from biopsies of microcalcifications. A total of 20/55 (36.7%) lesions classified as benign were found to be malignant on excision biopsy, and in 11 lesions, a malignant diagnosis on biopsy was found to be benign after excision. The total incorrect diagnosis on needle biopsy was therefore 31/190 (16%). In their study, Pijnappel reported FNB and CNB to have an underestimation rate of 3.0% and 8.0% - 12.0%, respectively.⁹

Successful localisation rates

Accurate lesion localisation and successful histological diagnosis were achieved in 93.2% of the lesions in this study. Results of this were comparable to those of Pilkington et al. of 95.2%.¹⁷ In this study, the histology was found to be nonrepresentative of the pathology in only nine patients (4.7%). A successful excision biopsy is therefore very useful, especially where there is discordance or indeterminate histology.

As stated by Dua et al., the properties of the localisation marker should be that it remains at the site of the lesion after placement until the commencement of surgery and should be easily identifiable by the surgeon.⁷ No migration of the radiopharmaceutical was noted or documented on scintigraphy reports, except for one where lymphatic drainage was noted. The radiopharmaceutical used thus showed the ability to remain in the lesion until surgery. This finding confirms the results of a previous study done by Aydogan et al., who showed that there was no diffusion of macroaggregates from the injection site unless the radiopharmaceutical had been introduced into milk ducts or lymphatic vessels. This allows for accurate localisation of the lesion, even after hours of delay between injection and surgery.¹⁸

Skin markings made during scintigraphy and using the gamma probe also helped to guide the surgeon to make the incision accurately. This study used particle sizes in the region of 100 nm – 600 nm because large colloid particle sizes of more than 100 nm do not drain easily and stay at the injection site.¹⁹ In this study, ultrasound and stereotactic imaging alone were relied on to confirm accurate needle placement, unlike several other studies where radio-opaque contrast was administered at the time of injection to assess the accurate placement of the injection with mammography.^{20,21,22,23}

Rates of clear margin excisions

The ROLL technique has been shown to have better margin status when compared to the WGL.^{24,25} Although the ROLL is a diagnostic procedure to determine the histology of a suspicious lesion, the removal of such a lesion with adequate margins will allow for a therapeutic resection if the histology comes back as malignant. This will therefore also negate the necessity for further re-excision of involved margins, allowing for a better cosmetic outcome.²⁶

At the research site, margin status changed over time. Initially, prior to 2015, the accepted margin for invasive cancer was > 2 mm, which subsequently changed to any margin where there were no tumour cells at the inked margin. For DCIS, a clear margin was any margin > 2 mm.

There was a statistically significant difference between margins and the type of tumour (p = 0.0004). Sixty percent of invasive cancers had clear margin status, while only 20.75% of DCIS margins were found to be clear. This was in concurrence with Dillon et al., who found that DCIS was associated with a higher incidence of involved margins in patients undergoing breast conservation surgery (BCS).²⁷ This could be due to the multifocal nature of DCIS and the presence of microcalcifications, which could be difficult to localise in its entirety.^{27,28,29} Other factors that have been cited as influencing involved margin rates are an initial underestimation of the size of the lesion before surgery, inaccuracy of the localisation, too little tissue excised and the injection not being placed centrally into the lesion.¹¹

In the SNOLL group, four re-excisions because of involved margins were identified and three of those were found to have no residual disease upon re-excision. This is in line with the findings of Landheer et al., who reported that often histology of these re-excised specimens is found to be negative.²⁶

Volume of excised tissue

The amount of tissue excised has a direct impact on the cosmesis of the procedure. The aim of BCS in early stage cancer is to remove as little healthy tissue as possible while still achieving the desired outcome.² In their systematic review, Ahmed and Douek alluded to the fact that perhaps a bigger dose of radioisotope could result in a bigger excised volume because of radioisotope diffusion.¹⁵ They explained this by the fact that Postma et al. reported a statistical difference in volume size when comparing it to the WGL in their study, while Giacalone et al. (using a smaller dose) reported smaller volume sizes, comparing it to WGL in their study.^{30,31}

In this study, when comparing administered doses for ROLL and SNOLL group, where the dose is much higher in the SNOLL group (range of 71 MBq – 113 MBq vs 5 MBq – 22 MBq), the mean excised volume for SNOLL was 148.71 cm³ while ROLL was 105.61 cm³ which, although larger, was not statistically significant (p = 0.54).

The mean excised volume was 114.02 cm³ regardless of the surgical intent. For the SNOLL group to achieve clear margins, a bigger volume was removed with a mean of 148.17 cm³. Excision volumes in this study are bigger in comparison to other studies (Table 6). The larger excised volumes in this study could be due to surgical technique or due to the treatment of larger lesions at presentation.

TABLE 6: Volume of tissue excised.

Study (reference)	Mean size tissue excised ROLL	Mean size tissue excised SNOLL
Giacalone et al.31	-	96.3 cm ³
Adamczyk et al.32	81.6 cm ³	79.55 cm ³
Postma et al.30	64 cm ³	-
Ismail (current study)	105.61 cm ³	148.17 cm ³

 $\mathsf{ROLL},$ radioguided occult lesion localisation; $\mathsf{SNOLL},$ sentinel node with occult lesion localisation.

However, because of the retrospective nature of this study, complete records could not be found with regards to actual lesion size to compare whether the bigger excision volumes were due to the size of the lesion.

Effectiveness of the sentinel node with occult lesion localisation as a therapeutic tool

Excision margins and re-excisions

Clear excision margins in reviewed studies were reported to be between 86.5% and 94.8%.30,31,33,34,35 Thind et al. had the highest complete excision rate.35 They used the dual radiopharmaceutical technique with 99mTc macroaggregated albumin (MAA) and 99mTc nanocolloid. Giacalone et al. used a subdermal injection of colloid for SLNB.³¹ In the present study, clear margins for invasive cancers were the absence of tumour cells at the inked margin. A clear margin rate was achieved for all invasive cancers of 71.4%. In the SNOLL group, the margin was clear in 19/32 (59.3%) of cases. There were only four DCIS lesions in this group and three of them had involved margins. This result shows that extra caution should be exercised when removing DCIS lesions because of the higher probability of incomplete excision. All lesions were identified on the first attempt 37/37 (100.0%). Therefore, no re-excisions were done because of intraoperative lesion localisation failure.

Sentinel lymph node detection

Different factors have been shown to influence SN detection, namely, the size of the radiopharmaceutical used, the type of injection method and the use of blue dye during theatre.^{15,20,35,36} In this study, the single intratumoural injection of 99mTc nanocolloid was used to perform lesion localisation with simultaneous SNB. The smaller size of the particles facilitates drainage to and uptake by lymphatic channels.37,38 Other studies used the same method.^{20,30,33} Giacalone et al. used the dual radiopharmaceutical technique with an intratumoural injection and a subdermal injection for SN detection.31 SN detection rate in the present study was 30/37 (81%). In their study to evaluate different injection techniques for SN detection, De Cicco et al. showed a significant difference in SN detection rate among the different methods favouring a subdermal injection method.³⁶ However, in the large groups of Van Rijk et al. and Postma et al. with study groups of 293 and 100 patients, respectively, they were able to demonstrate 98% and 100% SN detection rate, respectively, while using the single intratumoural method.^{30,33} Factors that can influence the drainage from the breast include the size of the breast, previous surgery to the axilla or breast and the location of the tumour within the breast.33 In one patient in this study where the SN was not located, it was reported that the patient had an increased BMI. Some of the procedures were also performed on patients that had had previous surgery in the area.

The use of blue dye has been used to help identify and locate the SN during surgery. In their study, Van Rijk et al. used

http://www.sajo.org.za

patent blue dye.³³ In the present study, the surgeon injected methylene blue in theatre to help identify the SN. Sufficient data could not be found to assess how many of the SNs removed were stained blue.

A total number of 55 SNs were identified and examined. Only three patients had positive SN. All SNs were in the axilla, except for one which was found in the intramammary region. In one patient, no SN was identified on scintigraphy or in theatre.

Operating time and ease of the procedure

The ease of procedure from the view of the surgeon was not assessed in this study. However, there was no additional training for the surgeons performing the ROLL and SNOLL procedure, as they were already familiar with the SNB procedure performed for breast cancer patients at the site.

As well, ROLL has been found to have shorter surgical times when compared to the WGL.^{14,30} The mean duration of operation times reported in other studies ranged from 22 min to 31 min.^{22,39,40,41} In this study, the time taken to excision was recorded rather than the time taken for the entire surgery. This time was calculated from the time the initial incision was made until the lesion was excised. The mean time to excision was 16.67 min with times ranging from 5 min to 45 min. The use of the gamma probe to constantly guide the surgeon in terms of an audible alarm allowed for easier localisation.

Radiation dose

A dose in the range of 71 MBq – 113 MBq was administered to patients undergoing a SNOLL procedure. The doses used in this study allowed for an extra time delay after radiopharmaceutical administration to optimise the time of accumulation in the SN. Several studies have reported using doses in the range of 74 MBq – 123 MBq.^{15,30,31,33} An average dose of around 130 MBq will result in a dose of about 10 MBq at 17 h.²⁰ These higher doses do not carry with them an added radiation exposure risk.³

Limitations and strengths of the study

Because of the retrospective nature of this study, there were limitations encountered in terms of retrieving and finding all histology, radiology and nuclear medicine reports. These were in terms of analysing data because of missing data such as histology reports, doses administered, lesion location, time to excision and reasons for re-excision. Furthermore, the format of histology reporting was not the same between different pathologists, and while some reported on specimen weights or lesion dimensions, others did not. The surgical reports indicating the identification of SLN and whether it was stained blue were limited, and this made it impossible to comment on any benefits of using methylene blue dye. In addition, not all histology reports could be retrieved. Records at the study site were only kept for a period of six years, and therefore manual retrieval of data that were not found on databases was not always possible. A cost analysis was not performed in this study. The cost factor as well as availability and/or acquisition of a gamma probe would be an important factor, especially in the South African setting.

The strengths of the study are that this was the first study to investigate the efficacy of ROLL and SNOLL in a tertiary hospital in the Western Cape, South Africa. Furthermore, the sample size in this study was bigger than most other reviewed studies included in this analysis, with only two studies having bigger sample sizes, namely, Monti et al. (n = 959) and De Cicco et al. (n = 812).^{20,21,25,36,41,42,43}

Recommendations

A further study could be done to investigate the rate of local recurrence after SNOLL, as local recurrence rates were out of the scope of this study as this would require a longer followup. The results of this study could be used to compare the ROLL technique with the Magseed localisation method currently being used at the study site.

Conclusion

The researchers' experience with the ROLL and SNOLL procedure confirms those of previous studies proposing it as a practical and easy procedure to perform. The majority of lesions were successfully located, and the technique was especially useful in cases where needle biopsies were inconclusive. There was a high rate in involved margins where the procedure was done as a therapeutic outcome, especially in patients with DCIS. The researchers' observations on imaging confirmed the current literature. Once injected, the radiopharmaceutical did not diffuse into the surrounding tissue, except where it had been introduced into lymphatic vessels or ducts.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

S.I. was responsible for study design, data collection, analysis, interpretation and manuscript writing. F.M. was responsible for data analysis and interpretation, revision for important intellectual content, editing and approval of final draft. F.E.D. was responsible for responsible for data analysis and interpretation, revision for important intellectual content, editing and approval of final draft. E.P. was responsible for conception and design, revision for important intellectual content and approval of final draft. L.C. was responsible for conception and design, revision for important intellectual content and approval of final draft. G.B. was responsible for conception and design, revision for important intellectual content and approval of final draft.

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Data availability

The data sets generated during and/or analysed during the current study are available from the corresponding author, S.I., on request.

Disclaimer

The views and opinions expressed in this research article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

- Green M, Vidya R. Techniques used to localize occult breast lesions: An update. Clin Breast Cancer. 2018;18(3):e281–e283. https://doi.org/10.1016/j.clbc.2018.01.001
- Lovrics PJ, Cornacchi SD, Vora R, Goldsmith CH, Kahnamoui K. Systematic review of radioguided surgery for non-palpable breast cancer. Eur J Surg Oncol. 2011;37(5):388–397. https://doi.org/10.1016/j.ejso.2011.01.018
- Aydogan F, Ozben V, Celik V, et al. Radioguided occult lesion localization (ROLL) for non-palpable breast cancer: A comparison between day-before and same-day protocols. Breast. 2010;19(3):226–230. https://doi.org/10.1016/j.breast.2010.01.017
- Moodley J, Cairncross L, Naiker T, Momberg M. Understanding pathways to breast cancer diagnosis among women in the Western Cape province, South Africa: A qualitative study. BMJ Open. 2016;6(1):e009905. https://doi.org/10.1136/ bmjopen-2015-009905
- Mutebi M, Simonds H, Cairncross L, Panieri E. Breast ductal carcinoma in situ in an unscreened population: Presentation, diagnosis and management at a single tertiary centre. S Afr J Surg [serial online]. 2017;55(1):4–9.
- Lince-Deroche N, Rayne S, Van Rensburg C, Benn C, Masuku S, Holele P. Breast cancer in South Africa: developing an affordable and achievable plan to improve detection and survival. South African Health Review. 2017 Dec 1;2017(1):181–8
- Dua SM, Gray RJ, Keshtgar M. Strategies for localisation of impalpable breast lesions. Breast. 2011;20(3):246–253. https://doi.org/10.1016/j.breast.2011.01.007
- Verkooijen HM, Peeters PHM, Buskens E, et al. Diagnostic accuracy of large-core needle biopsy for nonpalpable breast disease: A meta-analysis. Br J Cancer. 2000;82(5):1017–1021. https://doi.org/10.1054/bjoc.1999.1036
- Pijnappel RM, Van Den Donk M, Holland R, et al. Diagnostic accuracy for different strategies of image-guided breast intervention in cases of nonpalpable breast lesions. Br J Cancer. 2004;90(3):595–600. https://doi.org/10.1038/sj.bjc.6601559
- Obeng-Gyasi S, Grimm LJ, Hwang ES, Klimberg VS, Bland KI. Indications and techniques for biopsy. In: The breast [homepage on the Internet]. 5th ed. Elsevier, 2018; p. 377.e2–385.e2. https://doi.org/10.1016/B978-0-323-35955-9.00028-3
- Garzotto F, Comoretto RI, Michieletto S, et al. Preoperative non-palpable breast lesion localization, innovative techniques and clinical outcomes in surgical practice: A systematic review and meta-analysis. Breast. 2021;58:93–105. https:// doi.org/10.1016/j.breast.2021.04.007
- Norman C, Lafaurie G, Uhercik M, Kasem A, Sinha P. Novel wire-free techniques for localization of impalpable breast lesions-A review of current options. Breast J. 2021;27(2):141–148. https://doi.org/10.1111/tbj.14146
- Kiruparan N, Kiruparan P, Debnath D. Use of wire-guided and radio-guided occult lesion localization for non-palpable breast lesions: A systematic literature review and meta-analysis of current evidence. Asian J Surg. 2022;45(1):79–88. https:// doi.org/10.1016/j.asjsur.2021.06.055
- Sajid MS, Parampalli U, Haider Z, Bonomi R. Comparison of radioguided occult lesion localization (ROLL) and wire localization for non-palpable breast cancers: A metaanalysis. J Surg Oncol. 2012;105(8):852–858. https://doi.org/10.1002/jso.23016
- Ahmed M, Douek M. Sentinel node and occult lesion localization (SNOLL): A systematic review. Breast. 2013;22(6):1034–1040. https://doi.org/10.1016/j. breast.2013.09.007
- Kruger W, Apffelstaedt J. Young breast cancer patients in the developing world: Incidence, choice of surgical treatment and genetic factors. S Afr Fam Pract. 2007;49(9):18–24. https://doi.org/10.1080/20786204.2007.10873634
- Woll JPP, Romera MC, Vicente AMG, et al. Impact of radioguided occult lesion localization on the correct excision of malignant breast lesions: Effect of histology and tumor size. Ann Nucl Med. 2011;25(3):197–203. https://doi.org/10.1007/ s12149-010-0453-z

- Aydogan F, Ozben V, Yilmaz MH, et al. Simultaneous excision of ipsilateral nonpalpable multiple breast lesions using radioguided occult lesion localization. Breast. 2011;20(3):241–245. https://doi.org/10.1016/j.breast.2011.01.008
- Paganelli G, Luini A, Sansovini M, Caroli P, Matteucci F. Development of sentinel node localization and ROLL in breast cancer in Europe. Clin Transl Imaging. 2015;3(3):171–178. https://doi.org/10.1007/s40336-015-0118-y
- Feggi L, Basaglia E, Corcione S, et al. An original approach in the diagnosis of early breast cancer: Use of the same radiopharmaceutical for both non-palpable lesions and sentinel node localisation. Eur J Nucl Med. 2001;28(11):1589–1596. https://doi.org/10.1007/s002590100601
- Rampaul RS, Bagnall M, Burrell H, Pinder SE, Evans AJ, Macmillan RD. Randomized clinical trial comparing radioisotope occult lesion localization and wire-guided excision for biopsy of occult breast lesions. Br J Surg. 2004;91(12):1575–1577. https://doi.org/10.1002/bjs.4801
- Moreno M, Wiltgen JE, Bodanese B, Schmitt RL, Gutfilen B, Da Fonseca LMB. Radioguided breast surgery for occult lesion localization – Correlation between two methods. J Exp Clin Cancer Res. 2008;27(1):29. https://doi. org/10.1186/1756-9966-27-29
- Patel A, Pain SJ, Britton P, et al. Radioguided occult lesion localisation (ROLL) and sentinel node biopsy for impalpable invasive breast cancer. Eur J Surg Oncol. 2004;30(9):918–923. https://doi.org/10.1016/S0748-7983(04)00174-X
- Nadeem R, Chagla LS, Harris O, et al. Occult breast lesions: A comparison between radioguided occult lesion localisation (ROLL) vs. wire-guided lumpectomy (WGL). Breast. 2005;14(4):283–289. https://doi.org/10.1016/j.breast.2005. 04.002
- Thind CR, Desmond S, Harris O, Nadeem R, Chagla LS, Audisio RA. Radio-guided localization of clinically occult breast lesions (ROLL): A DGH experience. Clin Radiol. 2005;60(6):681–686. https://doi.org/10.1016/j.crad.2004.12.004
- Landheer MLEA, Klinkenbijl JHG, Pasker-De Jong PCM, Wobbes T. Residual disease after excision of non-palpable breast tumours: Analysis of tumour characteristics. Eur J Surg Oncol. 2004;30(8):824–828. https://doi.org/10.1016/S0748-7983(04) 00144-1
- Dillon MF, Maguire AA, McDermott EW, et al. Needle core biopsy characteristics identify patients at risk of compromised margins in breast conservation surgery. Mod Pathol. 2008;21(1):39–45. https://doi.org/10.1038/modpathol.3800975
- Atkins J, Mushawah FA, Appleton CM, et al. Positive margin rates following breastconserving surgery for stage I–III breast cancer: Palpable versus nonpalpable tumors. J Surg Res. 2012;177(1):109–115. https://doi.org/10.1016/j.jss.2012. 03.045
- Marinovich ML, Azizi L, Macaskill P, et al. The Association of surgical margins and local recurrence in women with ductal carcinoma in situ treated with breastconserving therapy: A meta-analysis. Ann Surg Oncol. 2016;23:3811–3821. https://doi.org/10.1245/s10434-016-5446-2
- Postma EL, Verkooijen HM, Van Esser S, et al. Efficacy of 'radioguided occult lesion localisation' (ROLL) versus 'wire-guided localisation' (WGL) in breast conserving surgery for non-palpable breast cancer: A randomised controlled multicentre trial. Breast Cancer Res Treat. 2012;136(2):469–478. https://doi.org/10.1007/ s10549-012-2225-z

- Giacalone PL, Bourdon A, Trinh PD, et al. Radioguided occult lesion localization plus sentinel node biopsy (SNOLL) versus wire-guided localization plus sentinel node detection: A case control study of 129 unifocal pure invasive non-palpable breast cancers. Eur J Surg Oncol. 2012;38(3):222–229. https://doi.org/10.1016/j. ejso.2011.12.003
- Adamczyk B, Dawid M, Karol P, Arkadiusz S, Piotr N, Paweł M. Preliminary experience in sentinel node and occult lesion localization (SNOLL) technique – One center study. Rep Pract Oncol Radiother. 2011;16(6):221–226. https://doi. org/10.1016/j.rpor.2011.08.004
- Van Rijk MC, Tanis PJ, Nieweg OE, et al. Sentinel node biopsy and concomitant probe-guided tumor excision of nonpalpable breast cancer. Ann Surg Oncol. 2007;14(2):627–632. https://doi.org/10.1245/s10434-006-9070-4
- Mariscal Martínez A, Solà M, Pérez De Tudela A, et al. Radioguided localization of nonpalpable breast cancer lesions: Randomized comparison with wire localization in patients undergoing conservative surgery and sentinel node biopsy. Am J Roentgenol. 2009;193(4):1001–1009. https://doi.org/10.2214/AJR.08.2005
- Thind CR, Tan S, Desmond S, et al. SNOLL. Sentinel node and occult (impalpable) lesion localization in breast cancer. Clin Radiol. 2011;66(9):833–839. https://doi. org/10.1016/j.crad.2011.02.017
- De Cicco C, Trifirò G, Intra M, et al. Optimised nuclear medicine method for tumour marking and sentinel node detection in occult primary breast lesions. Eur J Nucl Med Mol Imaging. 2004;31(3):349–354. https://doi.org/10.1007/s00259-003-1390-z
- Núñez EGF, Faintuch BL, Teodoro R, et al. Influence of colloid particle profile on sentinel lymph node uptake. Nucl Med Biol. 2009;36(7):741–747. https://doi. org/10.1016/j.nucmedbio.2009.04.009
- Yararbas U, Argon AM, Yeniay L, Zengel B, Kapkaç M. The effect of radiocolloid preference on major parameters in sentinel lymph node biopsy practice in breast cancer. Nucl Med Biol. 2010;37(7):805–810. https://doi.org/10.1016/j. nucmedbio.2010.03.012
- Rampaul RS, Dudley NJ, Thompson JZ, et al. Radioisotope for occult lesion localisation (ROLL) of the breast does not require extra radiation protection procedures. Breast. 2003;12(2):150–152. https://doi.org/10.1016/S0960-9776(02)00265-5
- Medina-Franco H, Abarca-Pérez L, García-Alvarez MN, Ulloa-Gómez JL, Romero-Trejo C, Sepúlveda-Méndez J. Radioguided occult lesion localization (ROLL) versus wire-guided lumpectomy for non-palpable breast lesions: A randomized prospective evaluation. J Surg Oncol. 2008;97(2):108–111. https://doi.org/10.1002/jso.20880
- 41. Sarlos D, Frey LD, Haueisen H, Landmann G, Kots LA, Schaer G. Radioguided occult lesion localization (ROLL) for treatment and diagnosis of malignant and premalignant breast lesions combined with sentinel node biopsy: A prospective clinical trial with 100 patients. Eur J Surg Oncol. 2009;35(4):403–408. https://doi. org/10.1016/j.ejso.2008.06.016
- Monti S, Galimberti V, Trifiro G, et al. Occult breast lesion localization plus sentinel node biopsy (SNOLL): Experience with 959 patients at the European Institute Of Oncology. Ann Surg Oncol. 2007;14(10):2928–2931. https://doi.org/10.1245/ s10434-007-9452-2
- De Cicco C, Pizzamiglio M, Trifirò G, et al. Radioguided occult lesion localisation (ROLL) and surgical biopsy in breast cancer. Technical aspects. Q J Nucl Med [serial online]. 2002;46(2):145–151.