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RESEARCH

Radioguided Occult Lesion Localisation Versus Wire-Guided Lumpectomy in the Treatment of Non-Palpable Breast Lesions

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Abstract The purpose of this study was to compare the two methods—guidewire localisation and the radioguided occult lesion localisation—used in the localisation and surgical removal of non-palpable breast tumours. This retrospective study enrolled patients diagnosed with nonpalpable malignant breast tumours. In this study either guidewire localisation (GWL, n=69) or radioguided occult lesion localisation (ROLL, n=321) was used for the detection and removal of the tumours. The two methods were compared with regards to preoperative localisation time, operating time, removed specimen volume, the pathological tumour size, the presence of positive surgical margins and postoperative complications. Furthermore, we have also investigated other factors that could have an impact on the frequency of positive resection margins. The localisation time was significantly shorter in the ROLL group, both with ultrasound guidance (5.7±1.44 min vs. 21.6±2.37 min, p=0.05) and with radiographic guidance (21.8±3.1 min vs. 41.6±3.75 min, p=0.021) as well. No significant difference was observed between the two methods in terms of operating time, removed specimen volume and pathological tumour size, or the presence of positive resection margins, or the occurrence of postoperative wound infections. The size of the tumour (ROLL, GWL grps), the presence of a multifocal tumour (ROLL grp), the presence of an extensive in situ breast carcinoma around the invasive cancer (ROLL, GWL grps) and the volume of the removed breast specimen (GWL grp) significantly increased the frequency of positive resection margins. We recommend the use of the ROLL method for the removal of nonpalpable breast tumours as it has a much shorter localisation time, and it is a simpler surgical technique as well.

Keywords Non-palpable · Breast cancer · Wire-guided localisation · Radioguided occult lesion localisation · Surgical margins

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Introduction

The extensive use of mammography for tumour screening has resulted in an increasing number of non-palpable malignant breast tumours being detected at an early stage [1]. In early stage breast cancers, radical mastectomy has been replaced in the mean time, by breast-conserving surgery, with which technique the precise surgical and oncological removal of the tumour could be achieved, and it is cosmetically more acceptable to the patients. At present, two techniques are used for the localisation and removal of non-palpable breast tumours: guidewire localisation (GWL) [2] and radioguided occult lesion localisation (ROLL) [3].

The GWL method, which has been used for decades for the localisation of non-palpable breast tumours, was described by Kopans in 1980 [2]. The ROLL technique has been widely used in clinical practice since 1996. This method has been introduced at the European Institute of Oncology in Milan, and has become since the gold standard technique in the tracking of non-palpable breast tumours. During this procedure, a small amount of radiocolloid (^{99m}Technetium-labeled colloid particles of human serum albumin) is injected directly into the centre of or close to the lesion 24 hours prior to the operation under radiographic or ultrasonographic guidance. The detection and excision of the tumour is carried out with a handheld gamma-detecting probe (taking the radiologically measured size of the tumour also into account). After the excision is made the resection margins can be checked for residual radioactivity [3, 4] as well. Although, the ROLL method has recently been preferred to the GWL method in the surgical treatment of non-palpable breast tumours, GWL is still widely used in numerous institutes.

The main requirements of the surgical removal of non-palpable lesions are using quick, accurate preoperative localisation techniques to facilitate the complete excision of the lesion, with total resection margin negativity, and at the same time to avoid excessive removal of healthy tissues. Few studies suggested that with the GWL method the positive resection margin rate is relatively high, resulting in increased risk of local recurrence and higher reoperation rates [5–10].

On this basis, the aim of the present study was to compare these two localisation methods with special attention to duration of localisation, the removed specimen volume, resection margins and postoperative complications (wound infection). Furthermore, we also investigated different factors as they could have an impact on the frequency of positive resection margins.

Patients and Methods

This retrospective study enrolled patients with non-palpable malignant or possibly malignant breast tumours. Primary surgical treatment comprised of the excision of the tumour with the use of either the GWL or the ROLL method. Between January 1997 and December 2008, we retrospectively investigated a 5-year period in the GWL group and a 7-year period in the ROLL group. During the course of the preoperative examinations, the patients underwent mammography, ultrasonographic breast examination and fine-needle aspiration cytology or core-needle biopsy.

The study protocol met the approval of the local Ethics Committee and an informed consent form was signed by all participants, in compliance with the Helsinki Declaration of 1964.

The GWL Method

During the five year period between 1st January, 1997 and 31st December, 2001 altogether 69 patients diagnosed with non-palpable malignant breast tumour were operated in our institute using the GWL method. In this method a guidewire was introduced by radiologists under radiographic or ultrasonographic guidance immediately before surgery. The correct position of the wire was then verified by mammography. During the operation, this wire serves as a guide to the surgeon to which areas were to be excised. The level of excision was to the pectoral fascia. The excised specimen was marked with orientation stitches, and then mammographic tests were performed on it. Depending on the results of the preoperative and the final postoperative histology, the procedure was supplemented—during the examined five year period—with axillary block dissection (ABD), because sentinel lymph node biopsy (SLNB) was only introduced in our institute after 2001. In the event of positive resection margins a supplementary operation (reexcision or mastectomy depending on the size of the intact breast) was performed.

The ROLL Method

Between the 1st January, 2002 and 31st December, 2008 (in the examined 7-year period) 321 patients diagnosed with non-palpable malignant breast tumour were operated in our institute using the ROLL method. The ROLL technique was supplemented with double marking SLNB [4, 11]. One day before the operation, under radiographic or ultrasonographic guidance 0.4 mL ^{99m}Tc-labeled human colloid albumin was injected into the tumour. 4 hours after the injection of the radiocolloid, a lymphoscintigraphic examination was carried out, and the projections of the sentinel lymph nodes (SLNs) were marked on the skin from two sides (sentinel lymph node mapping). The next day, 10 minutes before the operation, 2 mL of a second SLN marker substance (patent blue dye) was injected into the subareolar region of the breast. During the operation, the tumour was removed by measuring the peak of the radiocolloid activity with a gamma-detection probe, but the preoperative findings were also taken into consideration. The level of excision was to the pectoral fascia. The excised specimen was marked with orientation stitches and tested with specimen mammography. If positive resection margins were detected, a second operation (reexcision or mastectomy) was carried out on the patient, and in the cases where macro- or micrometastases were found in the SLNs, an axillary block dissection was also performed.

The radiologists recorded the time (in minutes) needed to localize the lesions either with a guidewire or with the radiocolloid substance, and the surgeons recorded the time (in minutes) required for the excisions (without axillary surgery).

Histological Methods

During the pathological examination, each surface of the excised specimen was stained with a different colour of dye: the anterior surface with black (Indian ink), the posterior surface with blue (Alcian Blue) and the superior surface with red (Cadmium Red). Then the total mass and three dimensions of the specimen (medio-lateral, supero-inferior and antero-posterior) were measured. The surgeon, when removing the lesion, made the excision in a cylindrical shape, so that the pathologist could easily calculate the specimen volume.

After the size of the tumour was measured the specimen was then divided into blocks. From these samples the pathologist could determine the distance of the tumour from each of the resection surfaces. During this procedure, at least 11 blocks were formed, with the first supero-inferior section being the macroblock. From this section the size of the tumour and its distance from the anterior, posterior, superior and inferior resection surfaces could be determined. The second block was formed from the medial part of the specimen (from the lateral side of the macroblock to the medial resection margin). With the help of this block, the tumour's distance from the medial resection margin was taken. The third block was formed from the lateral part of the specimen (from the medial side of the macroblock to the lateral resection margin), thus providing the distance of the tumour from the lateral resection margin. Besides the traditional sections, 8 extra sections (shaves) were formed, thus dividing the external surface of the removed tissue into 8 parts (superior, supero-medial, supero-lateral, medial, lateral, infero-medial, infero-lateral and inferior). By making these extra sections, our investigation of the resection margins became more precise [12].

Pathologists considered multifocality where two or more invasive cancer foci could be found in the same quadrant of the breast and where there was no contact between the invasive focuses. Extensive in situ breast cancer around the invasive focus was defined in cases where the proportion of intraductal component was at least 25 %, and intraductal focuses were present in the adjacent breast tissue as well.

When comparing the GWL and the ROLL methods, we have taken into consideration the preoperative localisation time, the operating time, the age of the patients, the size of the tumour, the volume of the removed specimen, the ratio of the tumour size and the removed specimen volume, the number of positive surgical margins, the subsequent reoperations (re-excision or mastectomy) and the postoperative complications. Furthermore, we investigated other factors, such as the presence of an extensive in situ breast carcinoma around the invasive cancer and the presence of multifocal tumours, as they could have an impact on the frequency of positive resection margins.

Statistical Analysis

For the comparison of mean values, t-test and one-way analysis of variance were used, as well as the Mann–Whitney in cases of non-normality. The normal distribution of samples was tested by using the Kolmogorov-Smirnov test. Categorical data were analyzed by using chi-square test. SPSS version 15.0 (© 2007 SPSS Inc.) was used for statistical analysis. Significance was considered at $p<0.05$.

Results

The final histological examination revealed 69 malignant lesions in the GWL group, and 321 malignant lesions in the ROLL group. Table 1 presents the histological results of the removed malignant breast lesions.

Ultrasonographic guidance localisation was performed in 58 cases using GWL method and in 277 cases using the ROLL method. Radiographic guidance localisation was performed in 11 cases using the GWL method and in 44 cases using the ROLL method.

The localisation time was significantly shorter in the ROLL group both with ultrasonographic guidance (5.7±1.44 min vs. 21.6±2.37 min, $p=0.05$) and with radiographic guidance (21.8±3.1 min vs. 41.6±3.75 min, $p=0.021$). It must be taken into consideration, however, that every time the GWL method was used, patients underwent mammography to verify the correct localisation of the guidewire, which of course increased the localisation time in all GWL cases. There was no significant difference in the operating time requirements (30.2±4.6 vs. 30.7±4.7). The mean age of the patients was similar in both groups (59 vs. 57.7 yrs). The removed breast

Table 1 Pathological features of the GWL and ROLL groups

Type of specimen	GWL (N=69)	ROLL (N=321)
LCIS	–	3 (0.9 %)
DCIS	5 (7.3 %)	53 (16.5 %)
Papillary in situ breast cancer	–	3 (0.9 %)
DCIS with microinvasion	4 (5.9 %)	4 (1.3 %)
Invasive ductal carcinoma	54 (78.3 %)	218 (67.9 %)
Invasive lobular carcinoma	3 (4.2 %)	20 (6.3 %)
Mucinous carcinoma	2 (2.9 %)	1 (0.3 %)
Tubular carcinoma	–	7 (2.2 %)
Papillary carcinoma	–	2 (0.6 %)
Phylloid carcinoma	–	1 (0.3 %)
Mixed carcinoma	–	9 (2.8 %)
Medullary carcinoma	1 (1.4 %)	–

GWL guidewire localisation, *ROLL* radioguided occult lesion localisation, *LCIS* lobular carcinoma in situ (of the breast), *DCIS* ductal carcinoma in situ (of the breast)

Table 2 Comparison of various factors between GWL and ROLL in malignant breast tumours

	GWL (N=69)	ROLL (N=321)	P
Duration of localisation (mean ± SD), min			
Radiographic guidance	41.6±3.75	21.8±3.1	0.021
Ultrasound guidance	21.6±2.37	5.7±1.44	0.05
Duration of surgical excision (mean ± SD), min	30.2±4.6	30.7±4.7	NS
Mean age, yr	59	57,7	NS
Removed breast specimen volume (mean ± SD), cm^3	89.5±116.3	104.1±78.6	NS
Pathological size of tumour (mean ± SD), mm	12.4±8.6	15.2±11.2	NS
Size of the tumour (cm)/specimen volume (cm^3)	0.0237±0.0258	0.0181±0.0179	NS
Involved surgical margin(s), n (%)	16 (23.2 %)	47 (14.6 %)	NS
Residual tumour, n (%)	6 (8.7 %)	25 (7.8 %)	NS
Wound infections, n (%)	2 (2.9 %)	3 (0.9 %)	NS

GWL guidewire localisation, *ROLL* radioguided occult lesion localisation, *NS* not significant

specimen volume did not differ significantly between the GWL (89.5±116.3 cm^3) and the ROLL group (104.1± 78.6 cm^3). The pathological tumour size and ratio of tumour size and removed specimen did not show any significant difference between the GWL and the ROLL groups.

The final pathological examination revealed 16 patients (23.2 %) with a positive resection margin in the GWL group (n=69). Reoperations were performed on 14 of these patients (20.3 %); 5 patients (7.2 %) underwent breast reexcision and 9 patients (13.1 %) mastectomy, and 2 patients refused consent to mastectomy. Residual tumour tissue was found by the histological examination in 6 patients (8.7 %). In the ROLL group (n=321), positive resection margins were detected by the final pathological examination in 47 of the cases (14.6 %). Reoperations were performed on 46 of these patients (14.3 %); 24 patients (7.5 %) underwent breast reexcision, and 22 patients (6.8 %) underwent mastectomy. One patient refused mastectomy. Residual tumour tissue was found by the histological examination in 25 patients (7.8 %). No significant difference was detected between the GWL and the ROLL groups in the frequency of positive resection margins. The incidence of postoperative complications did not differ significantly in the two groups (Table 2).

We have also taken further factors into consideration that influenced the frequency of positive resection margins. In the GWL group, 2 of the 69 patients (2.9 %) had multifocal breast tumour, and another 4 patients (5.8 %) had extensive in situ tumour components around the invasive cancer. In the ROLL group 22 of the 321 patients (6.8 %) had multifocal breast tumours, and 37 of the 321 patients (11.5 %) had extensive in situ tumour components around the invasive cancer.

The results of the histological analysis of the patients in the ROLL group indicated, that the size of the malignant lesion (p=0.021), the presence of a multifocal tumour (p= 0.035), and the presence of an extensive in situ breast carcinoma around the invasive cancer (p=0.01) significantly increased the frequency of positive resection margins (Table 3).

In the GWL group the size of the tumour (p=0.05), the presence of an extensive in situ breast carcinoma around the invasive cancer (p=0.05) and the volume of the removed breast specimen (p=0.002) influenced the occurrence of unclear margins considerably. The frequency of reexcision was also higher for smaller specimens (Table 4).

Discussion

The extensive use of mammography has resulted in the increased detection rate of early-stage non-palpable

Table 3 Investigated features and surgical margin status in the ROLL group

	ROLL N=321 (100 %)		p
	Involved surgical margins	Clear margins	
Patients, n	47 (14.6 %)	274 (85.4 %)	
Mean age, yr	55.6	58.1	NS
Specimen volume (mean ± SD),cm^3	119.9±104.7	111.7±73.4	NS
Tumour size (mean ± SD), mm	22.8±19.5	13.9±8.5	0.021
Extensive DCIS present around the invasive cancer	12 (25.5 %)	25 (9.1 %)	0.01
Multifocal lesion	8 (17 %)	14 (5.1 %)	0.035

ROLL radioguided occult lesion localisation, *DCIS* ductal carcinoma in situ (of the breast), *NS* not significant

Table 4 Investigated features and surgical margin status in the GWL group

	GWL n=69 (100 %)		P
	Involved surgical margins	Clear margins	
Patients, n	16 (23.2 %)	53 (76.8 %)	
Mean age, yr	58.4	60.6	NS
Specimen volume (mean ± SD), cm^3	66.4±40.3	96±127.1	0.002
Tumour size (mean ± SD), mm	17±11.6	11.2±7.4	0.05
Extensive DCIS present around the invasive cancer	2 (12.5 %)	2 (3.8 %)	0.05
Multifocal lesion	1 (6.3 %)	1 (1.9 %)	NS

GWL guidewire localisation, *DCIS* ductal carcinoma in situ (of the breast), *NS* not significant

malignant breast tumours. Both the GWL and the ROLL methods are widely applied in surgical therapy to reveal and to remove non-palpable breast tumours. However, the GWL method is the more widespread technique in use today. Though it has some well-known disadvantages: [1] radiologically the guidewire placement is a difficult procedure to carry out; spontaneous wire displacement, and inability to reposition can occur as well. [2] The procedure is traumatic, causing discomfort and pain to the patient; furthermore, the wire must remain in place until the operation. [3] The surgical excision of a wire-located lesion with clear margins is a technically difficult procedure. There is obvious interference with the incision line and the surgical approach, and the wire can be accidentally transected as well.

The ROLL method was developed to overcome some of the disadvantages of the GWL technique. Its reported advantages include precise localisation, accurate surgical removal, higher rate of clear margins, reduced size of the excised specimen, better concentricity of the lesion, less patient discomfort, shorter operating time, and reduced numbers of reoperations, with an accompanying reduction in costs.

Despite the fact that the radioisotope localisation technique has been available for more than 10 years now, only a few studies have been published about it. The GWL and the ROLL techniques have been compared only in 11 clinical studies and subjects were randomized only in 4 studies [5–10, 13–16].

Altogether 6 trials have described a significant difference regarding the clear resection margins in favour of the ROLL technique [5–10]. 3 studies have found that the excised specimen volume/weight ratio was lower in the ROLL group than in the GWL group [5, 9, 16]. Several studies have confirmed the well-known advantages of the ROLL method, such as better cosmetic results, less perioperative pain [8, 9, 16] and shorter localisation time [8–10, 14, 17]. The newest systematic review demonstrated that radioguided localisation techniques (including ROLL and radioguided seed localisation (RSL) methods) produce lower positive resection margin rates and consequently fewer reoperations. However, this review was limited by its small size and the quality of the randomized controlled trials [18].

A recently published multicentered, randomized, controlled trial compared the RSL method to a standard

Table 5 Comparison of international results on the complete excision rates with the ROLL and the GWL techniques

Authors	Year	Patients, n		Involved surgical margins %		p
		ROLL	GWL	ROLL	GWL	
Luini et al. [13]	1999	30	30	0	0	NS
Rampaul et al.® [14]	2004	48	47	NA	NA	NA
Ronka et al. [5]	2004	64	14	8.5	28.6	0.03
Gallegos-Hernandez et al. [6]	2004	65	67	16.9	35.8	0.014
Zgajnar et al. [7]	2005	51	92	29.4	55.2	0.005
Nadeem et al. [8]	2005	65	65	17	43	0.001
Thind et al. [9]	2005	70	70	16.2	40	0.002
Strnad et al. [15]	2006	21	12	NA	NA	NA
Moreno et al.® [16]	2008	61	59	10	12.5	NS
Medina-Franco et al.® [10]	2008	50	50	11.1	37.5	0.04
Martinez et al. ® [17]	2009	66	68	10.6	17.6	NS
Present study	2012	321	69	14.6	23.2	NS

ROLL radioguided occult lesion localisation, *GWL* guidewire localisation, ® randomized trial, *NS* not significant, *NA* data not available

guidewire localisation technique in the detection of non-palpable invasive and in situ breast carcinomas [19]. In contrast to other trials the positive resection margins and the reoperation rates were similar in both techniques. However, for the RSL method the operating time requirements were shorter, and the technique was also preferred by the surgeons, making it a more acceptable method for localisation. It is important to know, that in the RSL method a radio-opaque titanium seed containing an ^{125}I-isotope was used, therefore it is not exactly equivalent to the classic ROLL method.

In the present study, we did not find any significant differences between the two compared methods in respect of the proportion of the average volume of the removed specimen, the proportion of positive surgical margins, the incidence of residual tumours (removed during a second operation), or the frequency of postoperative wound infections. Preoperative localisation time was significantly lower in the ROLL group, but there was no significant difference in the duration of surgical excision. Nevertheless, our surgeons found the ROLL method technically easier. International study results suggest a higher rate of successful primary tumour excision (clear resection margins) with the use of the ROLL method (Table 5).

Higher clear resection margin rates were also found in the ROLL group in our study as well, but the difference was not significant statistically (85.4 % vs. 76.8 %). Although the average removed specimen volume and the pathological tumour size was higher in the ROLL group than in the GWL group, but was not significantly different. We did not find any significant difference in the ratio of the tumour size and the removed specimen volume. This indicates that a relatively smaller specimen can be removed safely using the ROLL method for the same tumour size. Another important advantage of the ROLL technique is that it allows concomitant removal of the invasive breast lesion and the sentinel lymph node(s).

Furthermore, our investigation revealed that by applying the ROLL method the involved surgical margin was influenced by the tumour size, by the existence of a multifocal tumour, and by the presence of an extensive in situ breast cancer around the invasive tumour. In the case of the GWL technique, the frequency of positive resection margins was influenced by the tumour size, by the presence of an extensive in situ breast cancer around the invasive tumour and by a lower specimen volume. It is important to emphasize, that the size of the tumour was bigger and the specimen volume was lower in the GWL group with positive resection margins. Therefore the ratio of the tumour size and the removed specimen volume is a more indicative factor of the occurrence of a positive resection margin, than just the size of the tumour or the removed specimen volume itself alone.

Several studies have proved that the frequency of a positive resection margin is significantly increased by the size of the tumour [20, 21], by the presence of an extensive in situ tumour around the invasive tumour [20, 22], by the presence of multifocal tumours [20, 23] and by the volume of the removed specimen [20, 23]. Considering these facts, it is noteworthy, that the most important predictive factor of a local tumour recurrence in breast-conservation surgery is a positive resection margin [19–22, 24–26]. If the final surgical margins are negative, the 5-year risk of local failure is 2–7 %, whereas with positive margins, this risk can rise up to 22 % or even higher [27–30]. In addition to the surgical margin status, factors such as young age, large tumour size, the presence of DCIS, the presence of an extensive intraductal component and positive ALNs are all significant independent predictors of loco-regional recurrence [26, 29, 31].

International results show that both the GWL and the ROLL methods are suitable for the localisation and subsequent removal of non-palpable breast tumours. We have come to the same conclusion in our study. However, the ROLL method has more advantages, such as shorter localisation time, more accurate surgical excisions and less discomfort to the patient.

We recommend that the ROLL method should be used for the localisation of non-palpable breast tumours if preoperative examinations prove the presence of an invasive breast cancer and SLNB is also to be considered. We would recommend the use of the GWL technique in cases with extensive microcalcifications and when SLNB is not going to be performed (pure DCIS, radial scar, etc.) [32, 33].

Conflict of Interest The authors declare no competing financial interests.

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