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Original research article

Is SNOLL a good localization technique in early breast cancer treatment? A single center's experience

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ABSTRACT

Aim: The aim of this study was to evaluate the method and present one center's experience in applying the SNOLL technique to patients with non-palpable suspicious breast lesions.
Materials and methods: 371 patients with suspected malignant lesions or diagnosed non-palpable breast cancer were subjected to a preoperative SNOLL procedure. The day before the surgery, they were administered two radiotracers to localize the tumor in the breast and the sentinel node. The following day, with the help of a handheld gamma probe the breast conserving surgery was performed.
Results: All 371 patients (100%) had their suspected occult breast lesions resected. Histo-pathological examination revealed cancer in 339 patients all these patients had their sentinel nodes examined. The intraoperative tests showed the sentinel node to be metastatic in 35 patients, who were then given a simultaneous axillary lymphadenectomy. Another 7 patients were diagnosed with positive lymph nodes in the final pathology and had to undergo a second operation. Reoperations compelled by positive surgical margins were performed in 26 cases.
Conclusions: SNOLL as a good technique of intraoperative localization, enables to remove a nonpalpable breast cancer together with sentinel lymph node in a single surgical procedure. It seems to be a optional method to be used in patients treated with breast conserving therapy.

1. Introduction

Recent years have seen a considerable growth in the number of diagnosed cases of early breast cancer. This has become possible mainly because of screening assays, prevention programs, and changes in women's awareness of and approach towards the disease. Together with the development of imaging and biopsy techniques, breast lesions can now be detected at a very early stage, before becoming clinically palpable. In such cases patients are offered breast conserving therapy (BCT), an option providing them a significant improvement in quality of life.

The main issue with non-palpable breast lesions, which represent about 30% of diagnoses, is to localize them precisely enough to be able to perform a correct excision with an adequate margin of healthy tissues, while limiting the extension of the surgical procedure. Therefore, efforts are being made to develop a method to permit this kind of precise localization.[1] Radio-guided occult lesion localization (ROLL) was first proposed in 1997 at the European Institute of Oncology, Milan, Italy.[1,2] The technique makes it possible to localize non-palpable breast lesions preoperatively. Patients with early breast cancer and no suspicious lymph node status are usually candidates for sentinel lymph node biopsy (SNB).The application of both ROLL and SNB within one surgical session has given rise to the development of the SNOLL technique (sentinel node and occult lesion localization).[1,2]

This article presents our experience in the use of SNOLL in patients with non-palpable malignant breast lesions who qualified for breast conserving therapy.

2. Materials and methods

371 female patients aged 35–86 (mean age 60) were subjected to the SNOLL procedure between May 2008 and September 2012.

All the patients had been diagnosed to have single, non-palpable and suspected malignant breast lesions, as revealed by ultrasonography and/or mammography. Average size of the tumor was 10 ± 4 mm. They had been ranked 4–5 in the BI-RADS scale and classified as T1 (size $\leq$20 mm). Clinical examination had not indicated any suspected axillary lymph nodes. 254 women had been preoperatively diagnosed with early breast cancer, as based on

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Table 1
Tumor characteristics.

	Number	Percentage
Fine needle biopsy		
C 4	50	13
C 5	53	14
Not diagnostic	13	3
Core biopsy		
B5	172	46
Tumor localization		
Central	24	7
Upper lateral	200	54
Upper medial	56	15
Lower lateral	29	8
Lower medial	33	9

cytological examination (N 82) and a thick-needle biopsy (N 172). In 53 patients the cytology had recognized C4 but with a radiological indication of cancer. The characteristics of the study group are presented in Table 1. Preoperatively, 371 patients followed the SNOLL technique. Informed consent was obtained from all patients.

Statistical analysis was performed with Statistica 9.0 Softwere (StatSoft Inc.).

In our study two types of radiotracers (^{99m}Tc) were used in the SNOLL procedure:

Human albumin macro-aggregates (MAA), with particles sized 10–150 u m, were used in the ROLL procedure. This is an immobile radiotracer that remains at the site of the injection (MAASOL, GE Healthcare);

Human albumin nanocolloid (NC), with particles sized 10−80 nm, was used in the SNB procedure. This is a mobile radiotracer that migrates through lymphatic conduits from the injection point to the sentinel node, where it accumulates (Nannocol, GE Healthcare).

Radiotracers were prepared by the Nuclear Medicine Department in single doses of ^{99m}Tc-MAA of 15–20 MBq diluted in 0.2 mL saline and ^{99m}Tc-NC of 37 MBq diluted in 0.5−0.7 ml saline (volume depending on the size of the breast). Tracers were inserted one day before the planned surgery under ultra-sound guidance (line probe of 7.5–10 MHz) in cooperation with a radiologist responsible for mapping the breast lesion. First, an intra-tumoral 99mTc-MAA injection was made (Fig. 1), followed by an intra-cutaneous 99mTc-NC injection at a site located above the tumor. After the injections, each patient was submitted to a lymphoscintigraphy, which indicated the "hot spots" and the number of sentinel nodes (Fig. 2). The following day the surgery was performed. During quadrantectomy, a breast incision was made above the "hot spot" area corresponding to the point of the radiotracers' injections, as was indicated by a handheld gamma probe (Neoprobe 2000, Neoprobe Corporation, Dublin, Ohio, USA).This detector was used during the operation to localize both the non-palpable breast lesion and the sentinel node, as well as to guide the excision. The specimen thus received was evaluated intra-operatively by means of a radiogram and histopathologic examination (type of tumor, size of cancer-free margins). When a pathologist reported the margin to be uncertain or too small, the surgeon responded immediately by radicalizing the concerned area of the breast. To be deemed sufficient, the margin had to be at least 0.5 cm wide or clear from the side of the breast muscle and/or skin. Patients with confirmed breast cancer were additionally treated with a sentinel node biopsy. Resected specimens of the sentinel node were also subjected to intraoperative histopathologic assessment. If metastasis was found, the patient underwent a concurrent lymphadenectomy.

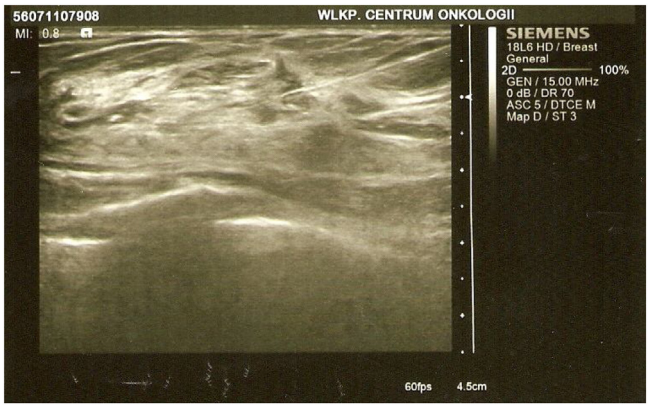

Fig. 1. ROLL (USG imaging)—the needle with radiotracer into the tumor.

3. Results

Non-palpable breast tumors were successfully localized intraoperatively and fully resected in all 371 patients.

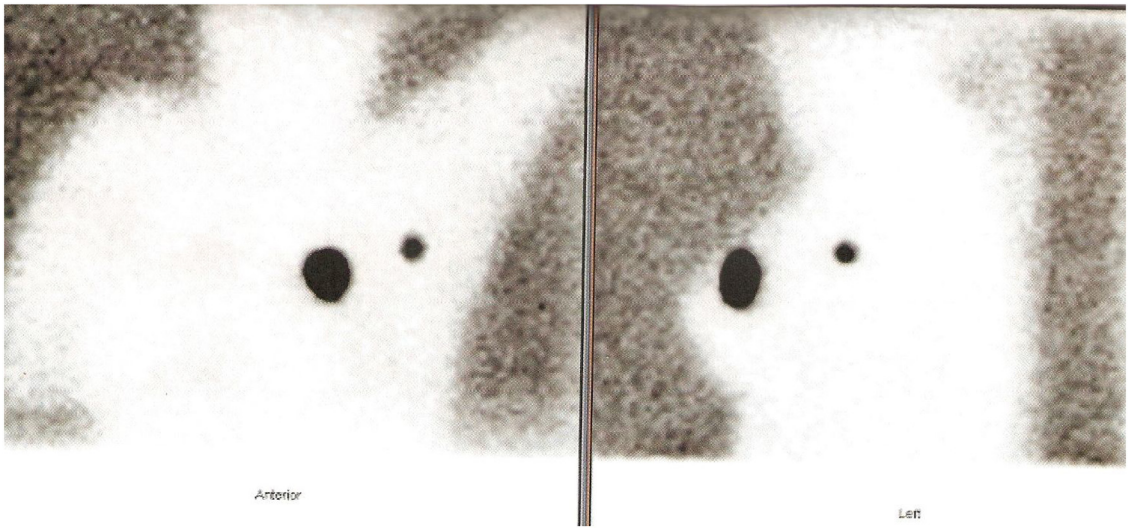

Fig. 2. Preoperative lymphoscintigraphy.

Table 2
Postoperative histopathological outcomes.

Breast tumor		
Benign lesions	**32**	**8**
Cancer	**339**	**92**
Non-invasive		
DCIS	57	17
LCIS	1	0.3
Invasive		
Ductal	144	42
Ductal and in situ	81	24
Lobular	11	3
Lobular and in situ	9	2.7
Other	36	11
Grading		
G1	110	32
G2	118	35
G3	53	16
Gx	13	4
Margins of breast resection		
>10 mm (clear)	150	46
5–10 mm	120	36
1–4 mm (small)	51	16
0 mm (involved)	8	2
Sentinel node status assessment		
Average number of SN		
1	155	50
2	107	34
≥3	51	16
SN metastatic	42	19
Intraoperatively	35	83
In final pathology	7	17
SN non-metastatic	299	81
Lymphadenectomy		
Simultaneous	35	83
Second surgery	7	17

The final histopathologic examination revealed cancer in 339 patients and benign lesions in 32 patients. The histological findings and data concerning the sentinel node are shown in Table 2.

The average size of a ROLL-localized tumor was 12 mm (5–40 mm) and the average volume of resected tissues during quadrantectomy was 42 cm^3 (3–169 cm^3). In 92% of cases malignant breast lesions were removed with negative surgical margins. 26 patients had to undergo another breast surgery (re-excision, mastectomy) because of non-radical primary resection, as evaluated in final pathology.

Table 3 shows the reoperations of patients with SNOLL in terms of tumor size as well.

Sentinel node biopsies were given to all 339 patients with diagnosed breast cancer. In 5 cases the SN was not identified and these patients were treated with immediate axillary lymphadenectomy. An average of 1.76 sentinel nodes were resected. In 35 invasive cancer patients metastasis to the sentinel node was recognized during intraoperative examination. These patients were treated with axillary lymphadenectomy within the same surgical session. The final post-surgery histopathologic examination revealed neoplastic cells in the sentinel node in further 7 patients who had undergone a second operation.

4. Discussion

Recent years have seen a growth in the number of diagnosed early breast cancers due to the increased availability of imaging examinations and disease prevention programs. Now, it is necessary to develop a reliable, safe and patient-friendly method of localizing non-palpable tumors. The SNOLL, as a procedure enables the intraoperative localization of occult lesions and has already been recognized as an important component of breast conserving therapy.[1–3]

Treatment of occult breast cancer aims primarily at its precise resection together with an appropriate margin of surrounding tissues. Increasing emphasis is being put on preventing unnecessary removal of healthy tissues and on improvement of the post-operative cosmetic effect. There are several methods that are currently in use for this purpose, e.g. skin marking with USG, intra-operative US, carbon localization or, most commonly applied, wire-guided localization (WGL). Most of these methods, however, are characterized by insufficient accuracy.[3] The ROLL method is a way to avoid all the disadvantages of the standard wire-guided procedure, while providing the benefits of precise localization and access to the center of an occult breast lesion. It is a low-invasive, fast and thus patient-friendly, method of tracer implantation. If offers a larger rate of clear margins of resected specimens, resulting in a lower rate of reoperation, as well as more convenience of use as well as the resection special control offered by a handheld gamma probe.[4] Finally, the lower volume of resected breast gland means a significant improvement in the cosmetic effect.[5] Many comparative studies of the needle method and the ROLL technique have been conducted in recent years. Results clearly indicate the superiority of the latter and confirm the radio-guided method to be more beneficial.[3,5,6,7,8–10]

We have adopted the original SNOLL method[11] developed in 1997 by the European Institute of Oncology, Milan, which combines the ROLL technique with a sentinel node biopsy and employs two types of Technetium Tc99m carriers. But there are also studies published in recent years that have shown comparable effects of applying the SNOLL method using a single radiotracer. This is certainly a way to facilitate the procedure while reducing the time and costs needed to perform it.[12,13,14]

In our study some patients (mostly within the period of 2008–2010) were qualified for SNOLL based on cytology results of C4. We recognized this as the most probable cancer diagnosis, which was not verified preoperatively in the core biopsy because of timing and organizational reasons. We assumed that injection of a radiotracer for SN localization in these patients is a less invasive and expensive procedure compared to further hospitalization and a second surgery. The last two years have brought a significant improvement in preoperative diagnosis in our institution. Nowadays, it is based mostly on histological findings of the specimens obtained in a core or vacuum assisted biopsy. This results in

Table 3
Reoperations in SNOLL patients.

Tumor size (pT)	No of patients	Breast reoperation	Axillary lymph nodes reoperations	Total no of patients with second operation
pTmic	4	0	0	0 (0%)
pTis	56	6	0	6 (11%)
pT1a	12	1	0	1 (8%)
pT 1b	107	11	1	12 (11%)
pT 1c	134	6	5	11(8%)
pT 2	18	1	1	2 (11%)
pTx	8	1	0	1 (13%)

objectively smaller numbers of intraoperative examinations of suspicious breast lesions. Nevertheless, there are still some patients in whom the final histology differs from preoperative diagnosis. These could result from the imperfection of pathological examination.

Another contentious issue with regard to SNOLL is determining the best location for injecting the radiotracer to achieve the best possible identification of the sentinel node. Studies concerning sentinel node localization have proposed a large variety of possible locations for injecting Tc99 nanocolloid. The most frequently described are: intratumoral, peritumoral, subdermal/intradermal and periareolar/subareolar injections.[15]

In our study, we followed the experience of the European Institute of Oncology by administering a tracer intradermally with a typical bubble on the skin right above the tumor, at a point marked by the radiologist with a felt-tip pen. We did not apply additional patent-blue staining, relying instead on our own long experience in sentinel node biopsy so as to avoid possible tattoos that clearly deteriorate the post-operative cosmetic effect. Utilizing this method, we achieved 98% sentinel node identification. Barros et al. confirm in their study that a combination of two tracers - radioisotope and patent-blau - in a medical center having extensive experience in the application of radioisotope techniques does not produce significant benefits with respect to sentinel lymph node identification.[16] It has to be assumed that in a certain number of cases the sentinel node simply cannot be localized. The reasons for this may be the variable anatomy and size of the breast, blockage of a lymph vessel, massive invasion of neoplastic cells into the lymph node, or even incorrect preparation of radiotracers or an inadequate time interval between the tracer injection and the surgery. With some of these possible factors being beyond control, the sentinel node remains undetectable in a small percentage of patients despite proper implementation of the method.[15] In our study in 5 patients the SN was not identified and an axillary limphadenectomy had to be performed. Out of many possible nanocolloid injection sites proposed by multiple studies,[2,13] the periphery of the tumor seems to be the most convincing location. Further research in this area is necessary though, as findings regarding sentinel node identification in the SNOLL method vary across centers.

Significant development of mammographic screening programs in Poland has taken place only in the past 10 years. That is why, before that time the number of patients with early breast cancer detection was rather low. Before introducing any precise technique of tumor localization, the most popular method was preoperative ultrasound examination with skin marking above the non-palpable lesion performed by a radiologist. Routinely, the specimen after partial breast resection was examined by an intraoperative radiogram. The main surgeon's concern was the presence (or absence) of the pathological lesions in the excised part of the gland. Usually, the tumor centralization or resection margins were not evaluated before the final pathology. Therefore, second operations to radicalize excisions seemed to be required more often. This statement is based on rough estimate data, but any detailed analysis was not made for this study.

In our hospital the wire-guided localization technique has not been introduced into everyday practice. That is why we cannot compare the present SNOLL method with any other equivalent to it. The use of SNOLL in our department resulted in decreasing numbers of re-excisions during second operations on breast cancer patients. The reoperations were performed mostly because of the multifocality of the disease or additional "in situ" components that were not detected preoperatively in the breast or because of metastatic sentinel lymph nodes diagnosed in final pathology. Introducing the SNOLL method has forced the surgeons to pay more attention to precise excision with minimally necessary margins. On the other hand, oncoplastic techniques demand in some cases wide breast resections. In such situations, the primary application of ROLL, as a method enabling resection of no-npalpable cancer with minimally acceptable margins, will possibly change in the nearest future.

In conclusion, our study confirms that the SNOLL technique allows an exact intraoperative localization of clinically occult breast cancer and the sentinel node within a single surgical session. The method enables a precise and fast excision of a breast tumor with a minimum necessary margin of healthy tissue. Reoperations forced by positive margins had to be performed in only 8% of patients. This simultaneous intraoperative performance of a sentinel node biopsy and sentinel node status assessment in patients with confirmed cancer has also largely contributed to the reduction of necessary reoperations. The results of this study have encouraged us to use SNOLL in our department's everyday practice as a good method of effective therapy for early non-palpable breast cancer.

Conflict of interest

None declared.

Financial disclosure

None declared.

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