Radioguided occult lesion localization (ROLL) of the nonpalpable breast lesions*

J. ZGAJNAR[1], M. HOCEVAR[1], S. FRKOVIC-GRAZIO[1], K. HERTL[1], A. SCHWARZBARTL-PEVEC[1], E. SCHWEIGER[2], N. BESIC[1]

[1]Institute of Oncology Ljubljana, e-mail: jzgajnar@onko-i.si, 1000 Ljubljana, Slovenia; [2]Medical Faculty, University Ljubljana, 1000 Ljubljana, Slovenia

Received March 3, 2004

Standard localization techniques of the nonpalpable breast lesions (guide wire, carbon, skin marking) have several disadvantages. Radioguided occult lesion localization (ROLL) was recently proposed as a better alternative resulting in wider surgical margins and lower average specimen weight. The aim of our study was to compare ROLL to our previously published series of the standard guidewire localization, performed at the Institute of Oncology Ljubljana. ROLL was performed in 110 nonpalpable breast lesions. Human serum albumin macroaggregats, marked with 1.8–5.5 MBq ^{99m}Tc was injected in the nonpalpable lesion. During surgery the radioactive breast tissue was excised using hand held gamma probe. Nonpalpable breast lesions were excised in all 110 patients. The definitive histology revealed 32 invasive carcinomas, 19 DCIS, 5 LCIS in and 54 benign breast lesions. Mean specimen weight was 40 g which is less in comparison to 53 g of the guidewire series (p=0.002). Surgical margins were clear in 36/51 (70%) invasive breast cancer or DCIS patients and close or involved in 15/51 (30%) patients. Compared to the guidewire series, where 41/92 (44%) margins were clear and 51/92 (56%) were close or involved, the difference was statistically significant (p=0.005). ROLL proved to be superior to guidewire localization in our series, allowing excision of the nonpalpable breast lesion with wider surgical margins despite lower average specimen weight.

Key words: radioguided surgery, nonpalpable breast lesions

The widespread use of mammographic screening in last two decades resulted in an increased number of discovered nonpalpable breast lesions [5, 7, 10, 12]. Surgery is a frequent option in managing the nonpalpable breast lesions whether as a diagnostic or a therapeutic procedure. In order to remove surgically the nonpalpable breast lesions they have to be localized under stereotactic or ultrasonic control. Several different localization methods are in use worldwide: guide wire, carbon injection or skin marking [8, 13, 15]. As an alternative to these standard localization techniques, radioguided occult lesion localization (ROLL) was proposed as a better alternative resulting in wider surgical margins and lower average specimen weight [14].

We have recently published a series of the guidewire localization of the nonpalpable breast lesions, performed at the Institute of Oncology Ljubljana where we found an unacceptably high ratio of surgical positive margin and high average specimen weight [2]. Stimulated by the unsatisfactory results of our series we studied ROLL at our institution.

The aim of the present study was to evaluate ROLL in our series of patients and to compare ROLL to the standard guide wire localization.

Patients and methods

From February 2001 until January 2003, 110 patients were enrolled in the study. The average age of the patients was 54 years, range 34–77. The patients with nonpalpable lesions classified as BI-RADS category 4 or 5, or those in whom the fine needle biopsy (FNAB) or core biopsy was suspicious or positive for non-invasive cancer were enrolled

*This paper is a part of the Research studies No. J3-3460-0302-01 and J3-3104-0302-01 supported by the Ministry of Education, Science and Sport of Slovenia.

in the study. The patients in whom preoperative core biopsy revealed invasive cancer were excluded from the study; they were enrolled in another study of the radioguided excision of the nonpalpable breast cancer and simultaneous sentinel node biopsy.

Mammographic appearance of the lesions, the preoperative FNAB or core biopsy results and guidance of the tracer injection are presented in Table 1. A previous surgery for breast cancer was performed in four patients and a simultaneous one in two patients. In four patients a second group of microcalcifications was simultaneously removed by the guidewire localization.

Table 1. Lesion characteristics

Lesions characteristics	Number of lesions
Mammographic appearance (110 pts)	
Solid or density distortions	54
Microcalcifications	56
Localization guidance (110 pts)	
Stereotactic	97
Ultrasound	13
FNAB (52 pts)	
Positive	6
Suspicious	16
Negative	11
Inadequate	19
Core biopsy (28 pts)	
DCIS	10
LCIS	1
Atypical ductal hyperplasia	9
Suspicious for cancer	2
Benign	2
Inadequate	4

Not more than 24 hours before surgery, human serum albumin colloid particles, ranging between 10 and 150 μm (Macrotec; NYCOMED Amersham Sorin, S.l.r. Saluggia, Italy), marked with 1.8–5.5 MBq ^{99m}Tc in 0.1 ml of saline were injected in the nonpalpable lesion under mammographic or ultrasonic guidance. In addition, 0.1 ml of the radiographic contrast medium was injected via the same needle in order to allow mammographic control of the accuracy of the injection. The accuracy of the injection was first controlled by mammography immediately after the injection. The scintigraphy was performed for further control of the accuracy of the tracer injection, to exclude any radioactivity contamination and to mark the hottest spot on the skin of the breast. Front and lateral scintigraphy images of the breast were obtained on the planar gamma camera (General Electric and MIE). The breast contour on scintigram was marked with ^{57}Co wire.

During surgery, the radioactive breast tissue was excised using a handheld γ-probe (Navigator GPS). The specimen was marked with metal clips and intraoperatively radiologically checked for the accuracy of the excision and then sent for the definitive histopathological examination. No frozen sections of the specimen were performed. In all specimens the weight was measured. Following definition of SOLIN [16] surgical margins were defined as “clear“ when at least 2 mm of normal breast tissue surrounded the carcinoma, “close“ when less than 2 mm of normal breast tissue surrounded the carcinoma, and “involved“, when carcinoma was found in surgical margins. Surgical margins were assessed in invasive carcinoma and DCIS; LCIS were excluded from margins assessment.

The data of ROLL were compared to our previously published results of guidewire localization [2]. For statistical analysis we used Mann-Whitney Rank sum test and Chi-square test (SPSS software package).

Results

All 110 localized lesions were excised. Mean specimen weight was 40 g, median 32 g, range 4–236 g. The definitive histology revealed invasive carcinoma in 32, DCIS in 19, LCIS in 5 and benign breast histology in 54 lesions, respectively. Mean invasive tumor size was 10 mm, median 9 mm; range 1–25 mm. Mean DCIS tumor size was 7 mm, median 5 mm and range 1–40 mm.

Surgical margins analysis (invasive carcinomas and DCIS only) is shown in Table 2.

Statistical analysis of specimen weight (ROLL versus guidewire) is presented in Table 3.

Statistical analysis of surgical margins (ROLL versus guidewire) is presented in Table 4.

Table 2. Surgical margins in DCIS or invasive cancer specimen

	Margins	n
Invasive carcinomas (32 pts)		
	Clear	21
	Close	4
	Involved	7
	Tumor bed reexcision performed	12
DCIS (19 pts)		
	Clear	15
	Close	1
	Involved	3
	Tumor bed reexcision performed	5

Table 3. Statistical analysis of specimen weight (ROLL versus guidewire)

	ROLL	Guidewire	Statistical analysis (p-value)
Specimen weight (g)			
Mean	40	53	0.002
Median	32	45	

Table 4. Statistical analysis of surgical margins (ROLL versus guidewire)

Margins (carcinoma only)	ROLL patients (%)	Guidewire patients (%)	Statistical analysis (p-value)
Clear	36 (70%)	41 (44%)	0.005
Close or involved	15 (30%)	51 (56%)	0.005
Tumor bed reexcision	17 (30%)	43 (47%)	NS (0.16)

Discussion

Radioguided surgery of the nonpalpable breast lesion was first published by the investigators from the European Institute of Oncology (EIO) showing its superiority in comparison to the guidewire localization [14]. Larger series of the same group (647 and 812 patients) confirmed the first finding [4, 9]. Several different methods of radioguided surgery for nonpalpable breast lesions, showing favorable results, were reported by other groups [3, 6, 11, 17]; the Amsterdam group used beside the radioguidance also the guidewire [17]. Our series represents to our knowledge the first series outside EIO who were treated by the originally proposed method of ROLL using low dose ^{99m}Tc labeled macroalbumin.

Introduction of the ROLL to our institution followed the unsatisfactory results of the nonpalpable breast lesions treatment, as showed by our recent analysis [2]. In the present study we found the ROLL superior to the to standard guidewire localization in several aspects (Tab. 3 and 4). The mean specimen weight was statistically significantly lower in ROLL (p=0.002) compared to the guidewire localization. Thus, better cosmetic result could be achieved. Furthermore, margin assessment in the subgroup of patients in whom carcinoma (invasive or non-invasive) was found on the histopathological analysis, showed significantly higher proportion of clear surgical margins in the ROLL group compared to the guidewire group (p=0.005). In the ROLL group there were also less tumor bed reexcisions performed (30% vs. 47%), although the difference was not statistically significant.

Revision of 15 patients with close or involved margins showed that in eight cases the inappropriate surgical procedures might have been avoided. Preoperative core biopsy in four of these cases could have changed the treatment plan to more radical approach. In another two cases the lesion was not localized accurratelly (>1 cm distant from the lesion). Another two cases could be attributed to the poor surgical technique; in these two patients the disease was unicentrical, mammographically limited (<3 cm) with the localization was performed accurately. Despite that, the surgeon failed to excise the cancer with sufficient clear margins. Sometimes, however, involved surgical margins cannot be avoided; this is the case if preoperative diagnostics could not provide a diagnosis in patients with mammographically extensive disease (>3 cm of microcalcifications). In these patients the surgical biopsy is performed only with the diagnostic intent. If the histopathological report later revealed carcinoma, the patient would be in second operation usually treated by a mastectomy. This was the case in three of our patients.

When comparing our results to other published series attention must be paid to substantial studies differences. First, the patient selection was different. In our series, the patients with preoperatively confirmed invasive cancer were not included. Namely, 17 patients in whom preoperative core biopsy confirmed invasive cancer were treated by our institutional method of radioguided excision of the cancer and the simultaneous sentinel node biopsy with the use of a single intralesional injection of the nanocolloid and the blue die, as recently described [18]. In contrast, the EIO studies included the patients in whom suspected breast lesions were detected by imaging techniques alone, without performing further non-surgical diagnostic procedures (biopsies) [4, 9, 14]. GRAY et al included in their series of patients, besides those with benign lesions, also those with preoperatively confirmed invasive cancers [11]. FEGGI et al and TANIS et al included the patients with invasive and noninvasive cancers only [6, 17]. BUONUOMO et al included also the patients with palpable cancers [3]. Therefore, our results cannot be directly compared to the other published series. To our view, preoperative patient selection radically changes the surgical approach. When cancer is preoperatively confirmed, the surgeon can be more radical when excising the lesion, which results in higher specimen weights and consequently higher proportion of surgical clear margins. Furthermore, axillary lymphnode staging needs to be performed in invasive carcinoma whether as a sentinel node biopsy or axillary lympnode dissection (ALND).

Second, the radioisotopes and dosages used were different. In original ROLL macroalbumin labeled with 3.7 MBq of ^{99m}Tc was used [14]; recently the same investigators have reported the use of higher 7–11 MBq dose [4]. The standard dose used in our institution is 3.7–5.5 MBq. In a subset of patients we used even lower dose (1.8 MBq) in order to further minimize the exposure to radiation. This ultra-low dose was used in 24 patients when the radioisotope was injected 2–4 hours before surgery. Some investigators used the ^{99m}Tc labeled nannocoloid, injected into nonpalpable breast cancer for the lymphatic mapping, also to guide the excision of the cancer [3, 6, 17]. We find this approach very attractive and we have developed our own protocol for the nonpalpable invasive cancer and simultaneous sentinel node biopsy [18]. We believe however, that the macroalbumin labeled with low dose ^{99m}Tc, as originally proposed, enables more accurate excision of the nonpalpable lesion, while reducing unnecessary exposure to the radiation. Another approach was described by GRAY et al by using radioactive iodine contained in a titanium seeds [11]. The titanium seed technique is very elegant but to our view several factors might prevent its wider use. New expensive investments in equipment (titanium seeds, probe for the pathologists) are necessary. Although the overall radioactivity dose used is small, the placement of the seed several days before surgery might not be acceptable for all institutions. Finally, no advantage over the ^{99m}Tc labeled macroalbumin has been proven.

In the first report the EIO authors proved better centricity of the lesion in the specimen in ROLL compared to the guidewire [14]. The data were however reported only for the first 30 patients of their series and the specimen size was assessed indirectly by measuring the centricity of the lesion [4]. In our study specimen size was measured in grams (g); in contrast to our study GRAY et al measured the specimen volume in milliliters (ml) [11]. The studies are nevertheless comparable if we consider 1 ml of the breast tissue approximately the same as 1 g of it. Mean specimen size in GRAY's study was 55 ml in radioguided localization group and 73.5 ml in the guidewire group [11]. The specimens were therefore slightly larger than in our series, 40 g in the ROLL group and 53 g in the guidewire group, the differences however can be attributed to the fact that they included also preoperatively confirmed invasive cancers in their series. Two other series reported data in preoperatively proven cancers only (invasive and DCIS), both showing larger specimen compared to our results. In the Amsterdam group series the mean specimen weight was 63 g, range 22–168 [17]. FEGGI et al reported the average specimen volume as high as 264 cm^3 [6]! Larger specimen in these two series, to our view, are due to the preoperative diagnosis of the breast cancer and the use of nanocolloid marked with high dose of radioactivity; the Amsterdam group used 100–159 MBq, while FEGGI et al [6] used 130 MBq of radioactivity, respectively. Both groups performed the simultaneous sentinel node biopsy. BOUNOMO et al reported no specimen size or margins data [3].

We used the definition of SOLIN (2 mm cut-off) to define clear surgical margins in order to be able to compare the results with those of our guidewire series. Two other studies used 1mm cut-off for the clear surgical margin [11, 17]. GRAY et al found 74% clear surgical margins in radioguided surgery group and only 43% in the guidewire group; strikingly similar result to our series in which 70% of patients in the ROLL group had clear margins and 44% in the guidewire group [11]. In the Amsterdam series 87% of patients had clear margins [17]. This proves that all three radioisotope localization techniques are very effective; of note, in our series the mean specimen size was the lowest and the clear margin cut-off wider.

In conclusion, ROLL allows the surgeon to excise the nonpalpable breast lesion with wider surgical margins despite the lower average specimen weight in comparison to guidewire localization. This in turn should allow the surgeon to achieve better breast cosmesis. Based on these results ROLL became the standard localization technique at our institution.

References

[1] AMERICAN COLLEGE OF RADIOLOGY. "Breast Imaging reporting and data System (BIRADSTM)." American College of Radiology, 1998.

[2] BESIC N, ZGAJNAR J, HOCEVAR M, RENER M, FRKOVIC-GRAZIO S et al. Breast biopsy with wire localization: factors influencing complete excision of nonpalpable carcinoma. Eur Radiol 2002; 12: 2684–2689.

[3] BUONOMO O, CABASSI A, GUADAGNI F, PIAZZA A, FELICI A et al. Radioguided-surgery of early breast lesions. Anticancer Res 2001; 21: 2091–2097.

[4] DE CICCO C, PIZZAMIGLIO M, TRIFIRO G, LUINI A, FERRARI M et al. Radioguided occult lesion localisation (ROLL) and surgical biopsy in breast cancer. Technical aspects. Q J Nucl Med 2002; 46: 145–151.

[5] DERSHAW DD. Mammographic detection of breast cancer and preoperative needle localization. Semin Surg Oncol 1991; 7: 247–252.

[6] FEGGI L, BASAGLIA E, CORCIONE S, QUERZOLI P, SOLIANI G et al. An original approach in the diagnosis of early breast cancer: use of the same radiopharmaceutical for both nonpalpable lesions and sentinel node localisation. Eur J Nucl Med 2001; 28: 1589–1596.

[7] FRANCESCHI D, CROWE J, ZOLLINGER R, DUCHESNEAU R, SHENK R et al. Biopsy of the breast for mammographically detected lesions. Surg Gynecol Obstet 1990; 171: 449–455.

[8] FRANK HA, HALL FM, STEER ML. Preoperative localization of nonpalpable breast lesions demonstrated by mammography. N Engl J Med 1976; 295: 259–260.

[9] GENNARI R, GALIMBERTI V, DE CICCO C, ZURRIDA S, ZERWES F et al. Use of technetium99m-labeled colloid albumin for preoperative and intraoperative localization of nonpalpable breast lesions. J Am Coll Surg 2000; 190: 692–698.

[10] GOEDDE TA, FRYKBERG ER, CRUMP JM, LAY SF, TURETSKY DB, LINDEN SS. The impact of mammography on breast biopsy. Am Surg 1992; 58: 661–666.

[11] GRAY RJ, SALUD C, NGUYEN K, DAUWAY E, FRIEDLAND J et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. Ann Surg Oncol 2001; 8: 711–715.

[12] HASSELGREN O, HUMMEL RP, FIELER MA. Breast biopsy with needle localization: influence of age and mammographic feature on the rate of malignancy in 350 nonpalpable breast lesions. Surgery 1991; 110: 623–627.

[13] HERMANN G, JANUS G, LESNICK GJ. Percutaneous Localisation of non palpable breast lesions. Breast 1983; 9: 4–6.

[14] LUINI A, ZURRIDA S, PAGANELLI G, GALIMBERTI V, SACCHINI V et al. Comparison of radioguided excision with wire localization of occult breast lesions. Br J Surg 1999; 86: 522–525.

[15] SILVERSTEIN MJ, GAMAGAMI P, ROSSER RJ, GIERSON ED, COLBURN WJ et al. Hooked-wire-directed breast biopsy and overpenetrated mammography. Cancer 1987; 59: 715–722.

[16] SOLIN LJ, YEH IT, KURTZ J, FOURQUET A, RECHT A et al. Ductal carcinoma in situ (intraductal carcinoma) of the breast treated with breast-conserving surgery and definitive irradiation. Correlation of pathologic parameters with outcome of treatment. Cancer 1993; 71: 2532–2542.

[17] TANIS PJ, DEURLOO EE, VALDES OLMOS RA, RUTGERS EJ, NIEWEG OE et al. Single intralesional tracer dose for radioguided excision of clinically occult breast cancer and sentinel node. Ann Surg Oncol 2001; 8: 850–855.

[18] ZGAJNAR J, BESIC N, FRKOVIC-GRAZIO S, HOCEVAR M, VIDERGAR B et al. Radioguided excision of the nonpalpable breast cancer and simultaneous sentinel lymphnode biopsy using a single radiopharmaceutical: an original approach to accurate administration of the blue dye. J Surg Oncol 2003; 83: 48–50.

[19] ZGAJNAR J, BESIC N, HOCEVAR M et al. Radioguided occult lesion localisation (ROLL) of the nonpalpable breast lesions using reduced dose (1,8 MBq) of radioactivity. The Breast 2003; 12 Suplement 1. Primary Therapy of Early Breast Cancer Treatment; 8th International Conference, St Gallen. 15-3-2003.