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Management of Nonpalpable, Mammographically Detectable Breast Lesions

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Abstract. A series of 151 women underwent 156 preoperative localizations of nonpalpable, mammographically detected breast lesions. Indications for biopsy were (1) a cluster of more than five fine microcalcifications; (2) a solid lump found by ultrasound investigation; and (3) a radiologic abnormality of the breast parenchyma. The lesions were localized preoperatively using the hook-wire method (Frank needle), and all biopsies were performed under general anesthesia. Carcinoma was discovered in 34 (21.8%) cases; in 22 (64.7%) it was a noninvasive cancer (9 with microinvasions) and in 12 (35.3%) an invasive carcinoma with a mean tumor diameter of 0.8 cm. The highest malignancy rate was found among those with microcalcifications (21 of 81 cancers, or 25.9%). Lymph node involvement was seen in 25% of patients with invasive carcinomas. In conclusion, the needle localization of nonpalpable breast lesions is a simple, accurate method for early detection of small cancers with favorable prognosis.

Although great improvement in the management of breast cancer has been achieved over the past decades, early detection remains the best way to attain a favorable outcome. Self-breast examination and mammography are the mainstays of early diagnosis. In this context, the number of mammograms performed each year increases rapidly, leading to a respective increase in the number of diagnosed "occult" breast lesions. As a result, breast surgeons often face the problem of mammographically detected nonpalpable breast lesions. Diagnostic evaluation, indications for biopsy, and methods of localization are the main questions that arise. The purpose of our study was to present our experience in the management of nonpalpable breast lesions to elucidate the problems arising in such cases.

Patients and Methods

During the 4-year period from September 1993 to August 1997 a total of 151 women attending the Breast Unit of the 2nd Department of Propedeutic Surgery of the Athens University Medical School underwent 156 preoperative localizations of nonpalpable, mammographically detected breast lesions. Five patients underwent two separate localizations at the same time, on the same (one patient) or both (four patients) breasts. Clinical data pertaining to the type of mammographic abnormality, accuracy of localization, operative procedure employed, complications, and final histopathologic diagnosis were gathered and analyzed.

Indications for biopsy were (1) a cluster of more than five microcalcifications; (2) a nonpalpable breast lump; and (3) a radiologic abnormality of the breast parenchyma, such as an irregular opacity or areas of abnormal configuration. Lump characteristics (indication 2) dictating biopsy were an absence of benign type calcifications, an absence of the lump in previous mammograms, an increase in size compared with previous mammograms, and the solid structure of the lump in ultrasound examination.

In all of our patients the hook-wire localization procedure described by Frank et al. [1] was used. First, the exact location of the radiologic finding was judged based on lateral and craniocaudal mammography, and the Frank needle was introduced into the breast under local anesthesia. Care was taken so the entry point of the needle would allow a cosmetically acceptable incision, usually close to the areola. When the needle tip was in optimal position, the sheath was withdrawn, leaving the wire hook in place. The accuracy of the localization was checked with lateral and craniocaudal mammograms, which were then sent to the operating room with the patient. With reference to the wire, an excisional biopsy was performed under general anesthesia, and the specimen was sent to the radiology department to confirm radiologically that the lesion had been removed (specimen mammography), and then to the histopathology department for histologic examination. After obtaining the results of frozen sections, the patient either returned to the ward (benign cases) or underwent further excision, as informed consent of the patient to the operative options according to all possible diagnoses was always obtained preoperatively. Final decisions based on the pathologic report of permanent sections were made in five cases due to additional findings from those of frozen sections (two cases) and to the patient's wish for a two-step surgical procedure (three patients).

Results

In 81 of our patients (51.9%), the nonpalpable lesion that required biopsy was an area of clustered microcalcifications, in 53 cases (34.0%) it was an opacity that proved to be solid by

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ultrasound investigation, and in 22 cases (14.1%) it was a radiologic abnormality of breast parenchyma.

The accuracy of localization was determined by the distance of the wiretip from the lesion, measured on both radiographs (lateral and craniocaudal). In 41 cases (26.3%) the wiretip was on target, in 80 (51.3%) it was less than 1 cm away from the lesion, in 27 (17.3%) the distance was 1 to 2 cm, and in 8 cases (5.1%) the hook-wire was more than 2 cm off-target.

A second wire was required in three cases where the distance of the first wiretip from the lesion was unacceptable. In another patient the wire was inserted into the pectoralis major muscle, and in seven cases the wire hook was broken during the biopsy procedure. In all of these cases the hook was localized intraoperatively and removed without additional mammograms and with no further complications.

The lesion was successfully excised at the first attempt in 136 cases (87.2%). In 14 cases (9.0%), a wider excision followed as the radiologic lesion was not seen in the specimen mammography. In five cases (3.1%) three attempts were required, and in one patient (< 1%) the lesion was excised only after the fourth attempt.

All of our patients underwent mammography 6 months after the operation. In two of them the lesion (solid lump) proved to be still in place. In both of these patients the specimen radiograph was falsely positive, as it wrongly confirmed successful excision of an area of abnormal breast architectural configuration.

Pathologic examination revealed carcinoma in 34 (21.8%) of the 156 needle localized breast biopsy specimens. In the rest [122 (78.2%)], benign breast disease was diagnosed, among which adenosis (61 cases, 39.1%) and fibroadenoma (26 cases, 16.7%) were the most common findings (Table 1).

The relation between breast cancer and mammographic findings is shown in Table 2. Lesions with microcalcifications carried a greater risk of malignant disease (25.9%) than those without microcalcifications (17.3%).

Analysis of the results according to patient age showed that as age increased the percentage of hook-wire-directed biopsies in which cancer was found also increased (Tables 1, 2).

Among the 34 cancers, 22 (64.7%) were in situ; three (13.6%) of them were lobular carcinomas in situ (LCIS) and 19 (86.4%) ductal (DCIS). In 9 cases of DCIS microinvasions were present. The rest (12, 35.3%) of the 34 cancers were invasive, ranging in tumor diameter from 0.5 to 1.6 cm (mean ± SD = 0.8 ± 0.29). There was one patient with synchronous bilateral DCIS, and in one case two carcinomas in different quadrants of the same breast were detected by performing two localizations.

Surgical procedures performed following a positive frozen section or final histologic report indicating malignancy included 10 modified radical mastectomies (MRMs) and 23 wide local excisions (WLEs). Among the 10 patients undergoing MRM, 4 had invasive cancers and 6 DCIS. Indications of MRM were the large size of the cancer in four cases, the multifocal character of the cancer in four cases, the presence of two synchronous cancers in different quadrants of the same breast in one patient, and the patient's wishes in one case. All of our patients with LCIS (three cases) were treated with WLE only. WLE with or without lymph node dissection was also performed in 7 of the 12 patients with invasive tumors and in 13 of the 19 with DCIS.

Axillary lymph node dissection was performed in 22 (66.6%) patients: in the 10 patients who underwent mastectomy and in 12 of the 23 who underwent WLE (8 patients with invasive tumors and 4 patients with DCIS). Invasive cancers, irrespective of size, were always treated by axillary lymph node dissection whether a mastectomy or a WLE had preceded it. Axillary lymph node dissection was also performed in cases of DCIS, when frozen sections showed multiple microinvasions, a comedo-type cancer, or a large tumor. Positive lymph nodes were found in 3 (13.6%) patients, all of which had invasive tumors; only one lymph node was involved by the disease in each patient. Lymph node involvement was seen in 25% of patients with invasive carcinoma; the tumor diameters in those patients were 0.7, 0.8, and 1.0 cm, respectively.

All of the patients with invasive tumors who underwent WLE were submitted to postoperative radiotherapy of the breast only. Radiotherapy after WLE was also applied to five patients with DCIS with microinvasions. Postmenopausal women with estrogen receptor (ER)-positive tumors (14 patients) received adjuvant therapy with tamoxifen at a dosage of 10 mg orally twice a day. Premenopausal women with invasive tumors and positive axillary lymph nodes (two patients) received adjuvant chemotherapy (the CMF standard regimen).

Table 1. Histology of 156 lesions and classification of the results according to patient age.

	Total		≤ 50 Years old		> 50 Years old	
Pathologic finding	No.	%	No.	%	No.	%
Adenosis	61	39.1	42	46.6	19	28.8
Cancer	34	21.8	12	13.3	22	33.3
Fibroadenoma	26	16.6	19	21.1	7	10.6
Cyst	10	6.4	9	10.0	1	1.5
Papilloma	9	5.8	3	3.3	6	9.1
Duct ectasia	5	3.2	1	1.1	4	6.1
Fibrosis	5	3.2	3	3.3	2	3.0
Fat tissue necrosis	2	1.3	—		2	3.0
Radial scar	2	1.3	1	1.1	1	1.5
Lymph node	2	1.3	—		2	3.0
Total	156		90		66	

Discussion

Increasing numbers of women undergoing screening mammography and the improvement in mammographic technique have led to an increasing number of nonpalpable breast lesions being detected. Excising such a lesion without a localizing procedure could lead to resection of an excessive amount of breast tissue or to an unsuccessful intraoperative localization and excision. Preoperative needle localization offers an opportunity to make a quick, accurate excision with minimal trauma and less tissue disruption [2–4]. The cosmetic result assumes great importance considering that about 75% of these lesions are benign.

The best method available nowadays for preoperative localization of nonpalpable breast lesions is the hook-wire localization technique described by Frank et al. [1], which we have used in our study. The lesion is localized by a two-dimensional technique using a self-retaining hook-wire, which gives precise guidance to the site of the lesion and facilitates removal of a minimum amount of breast tissue. There is also the possibility of three-dimensional stereotactic positioning of the hook-wire using a stereotactic device (e.g., Mammomat stereo system; Siemens Corp. Erlanden, Germany) [5], but it has certain limitations, such as difficulty localizing lesions close to the chest wall.

Table 2. Malignancy rate related to mammographic findings and distribution of results by patient age.

	Total			≤ 50 Years old			> 50 Years old		
Mammographic finding	No. of cases	Cancer rate	%	No. of cases	Cancer rate	%	No. of cases	Cancer rate	%
Microcalcifications	81	21	25.9	42	8	19.0	39	13	33.3
Radiologic abnormality	22	4	18.2	12	1	8.3	10	3	30.0
Solid lump	53	9	17.0	36	3	8.3	17	6	35.3
Total	156	34	21.8	90	12	13.3	66	22	33.3

Table 3. Malignancy rate, proportion of in situ cancers, and positive axillary lymph nodes in nonpalpable breast cancer.

		Total cancers		In situ cancers		
First author	No. of biopsies performed	No.	%	No.	%	Node positive *(%)*[a]
Schwartz [12]	3752	1175	31.3	376/1130	33.3	27.1
Silverstein [13]	1805	395	22	202	51	
Wilhelm [14]	1464	264	18	178	67	21
Franceschi [9]	1144	269	24	66	25	
Lein [15]	809	219	27	37	17	18
Symmonds [3]	500	72	14	13	18	11
Papatestas [6]	475	149	31	60	40	21
Mokbel [16]	317	151	48	87	58	
Griffen [17]	279	38	13.6	16	42	
Bigelow [2]	150	24	16	6	25	14
Tresadern [10]	130	46	35	24	52	20
Sickle-Santanello [18]	107	22	20.5	5	22.7	

[a]Patients with invasive carcinoma.

Controversy exists about what we consider successful preoperative localization. Generally, the goal is to traverse the lesion and place the tip of the wire just under it, but distances between the hook-wire and the lesion of < 1 cm are also considered "successful" localization and distances of 1 to 2 cm are considered "acceptable" [5]. With 78% to 92% of the hooks being within 1 cm of the target and $> 95\%$ within 2 cm, the surgeon can successfully excise the lesion in 84.0% to 98.5% of cases [2, 4, 5].

Specimen mammography can almost always verify the success (or not) of the biopsy. False-positive results are rarely encountered [2, 6], and areas of concern are architectural abnormalities or lumps. Microcalcifications are more easily identified on the specimen radiograph and can be compared to those seen on the mammogram. Having in mind the small but existing possibility of false-positive results of specimen radiography, it is prudent to perform a follow-up mammogram a few months after the biopsy. These mammograms, while aiding in the exclusion of residual abnormalities, also serve as a baseline for future reference.

Most authors perform needle-localized biopsies on an ambulatory basis under local anesthesia [2–4, 7, 8], do not send the specimen for a frozen section examination [7, 9], and postpone definitive surgery until the pathologic report on the permanent sections is available [3, 7–10]. Our policy is to perform the biopsies under general anesthesia and proceed to definitive surgery at the same time, based on the results of the frozen section examination. The comparison between frozen section and permanent paraffin section diagnoses justified our strategy, proving that the frozen section examination was accurate in all of our cases in terms of positivity for malignancy. Reports in the literature verify our findings, documenting the accuracy and reliability of frozen section diagnosis in nonpalpable breast lesions [11].

Several large series of needle localized breast lesions have been reported, with varying proportions of biopsy specimens that proved to be malignant (Table 3). In general, malignancy rates reported in the literature range from 8.7% to 48.0% [1–10, 12–26]. The differences are probably due to patient selection criteria, which reflect the unanimity about the degree of suspicion required for a lesion to be excised rather than be observed periodically with follow-up mammograms. It has been reported that mammographic lesions interpreted by an experienced radiologist as highly suspicious proved to be malignant in 64% to 67% of instances, whereas lesions interpreted as probably benign were malignant in only 4.5% to 11.0% of instances [2, 10].

Another factor influencing the malignancy rate reported in different series is the proportion of patients who underwent biopsy because of suspicious calcifications. It has been shown that lesions with microcalcifications carry a higher risk of malignancy (20–27%) than do lumps or areas of architectural abnormalities (7.3–12.0%) [2, 3, 6, 10, 26]. Our findings of a 25.9% malignancy rate among patients with clusters of microcalcifications and 17.3% among patients without microcalcifications are in accordance with these reports.

The age of the patient is another factor related to the malignancy rate found in hook-wire-directed biopsies [2, 3, 15, 26]. In our series the malignancy rate found among women > 50 years of age was much higher than that in women ≤ 50 years old (33.3% and 13.3%, respectively).

Most beneficial for the patient is the fact that 17% to 67% of the nonpalpable cancers being detected are noninvasive [2–4, 7–10, 14–16, 18, 21–26] (Table 3). This point is important because subclinical, mammographically detected DCIS is virtually never accompanied by axillary node metastases [3, 7, 25, 26]. However, it is our policy to treat DCIS of large size, comedo type, or with

multiple microinvasions in the same manner as any invasive cancer of the same size.

Our malignancy rate of 21.8% is consistent with that in previous reports, but our 64.7% rate of noninvasive tumors is on the high side compared with reports in the literature. The belief that nonpalpable DCIS is almost never accompanied by axillary node metastases is confirmed by our study, where axillary lymph node dissection was performed in nine patients with DCIS, yielding a negative result in all of them.

Among the 12 patients with invasive tumors who underwent axillary lymph node dissection, only 3 (25.0%) had axillary node metastases. This number is similar to those reported in other series (5.3–27.0%) [3, 4, 6–8, 10, 14, 15, 17, 23, 25–27] and much lower than the overall 40% to 50% incidence of axillary metastases for women with breast cancer [2, 15, 28]. The beneficial effect of the latter on the patients' survival is obvious. However, a nonpalpable cancer should not be considered a priori as an "early" cancer because of its small size. It has been shown that the incidence of axillary lymph node metastases is significant, even for cancers < 1 cm [7, 14], which was also noted in our series. That is why the term "minimal breast cancer," describing both noninvasive carcinomas and invasive carcinomas < 5 mm in diameter, has been challenged [3, 7, 8, 14]. The status of the axillary lymph nodes is more important than tumor size. Nevertheless, it is an indisputable fact that the smaller the primary cancer the lower is the incidence of positive axillary lymph nodes [27]. In this context, the ability of screening mammography in combination with needle-localization surgical procedures to detect a high percentage of breast cancers when they are still in situ or of small size—and thus without axillary lymph node metastases—justifies its use.

We therefore believe that the benefits of early diagnosis of breast cancer in about 25% of patients undergoing needle localized breast biopsy greatly outweighs the physical and psychological costs of benign breast biopsy in most patients (about 75%).

Résumé

Dans cette série de 151 femmes, on a analysé les données de 156 localisations préopératoires de lésions du sein détectées par mammographie mais non palpables. Les indications de la biopsie comprenaient: a) des microcalcifications fines au nombre minimal de 5, b) une tuméfaction «pleine» aux ultrasons et c) une anomalie radiologique du parenchyme mammaire. Les lésions ont été localisées en préopératoire par la méthode dite "du crochet" (aiguille de Frank) et toutes les biopsies ont été effectuées sous anesthésie générale. Un cancer a été découvert dans 34 (21.8%) cas; non-invasif dans 22 (64.7%) (9 avec des microinvasions) et invasif chez 12 (35.3%) patientes pour lesquelles le diamètre moyen était de 0.8 cm. Les lésions les plus malignes ont été trouvées parmi les cas avec microcalcifications (21 cancers des 81 ou 25.9%). 25% des patientes avec cancer invasif avaient un envahissement ganglionnaire. En conclusion, la localisation à l'aiguille des lésions du sein non-palpables est une méthode simple et précise pour la détection de petits cancers ayant un pronostic favorable.

Resumen

151 mujeres con tumores no palpables de mama, detectados mediante mamografía, fueron sometidas a 156 pruebas diagnósticas preoperatorias de localización. Las indicaciones para biopsia fueron: a) existencia de grupos de más de 5 microcalcificaciones; b) masa tumoral sólida en el estudio ecográfico; c) anormalidad radiológica del parénquima mamario. La lesiones fueron localizadas preoperatoriamente mediante el método del anzuelo (utilizando la aguja de Frank); todas las biopsia fueron realizadas bajo anestesia general. Se descubrieron 34 carcinomas (21,8% de los casos); en 22 (64,7%) se trataba de cánceres no invasivos (9 con microinvasión) y en 12 pacientes (35,3%) se constató la existencia de carcinomas infiltrantes, con un diámetro medio tumoral de 0,8 cm. La mayor tasa de malignidad se observó en aquellos casos que presentaron microcalcificaciones (21 cánceres de 81 casos), lo que representó el 25,9%. El porcentaje de metástasis ganglionares entre pacientes con cánceres infiltrantes fue del 25%. Conclusión: En lesiones tumorales no palpables de mama, la localización mediante el método del anzuelo, constituye una técnica simple y precisa para la detección precoz de pequeños cánceres de mama, de pronóstico favorable.

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Invited Commentary

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This article shows that biopsy under needle localization for nonpalpable lesion increases the detection rate of minimally invasive or noninvasive breast cancers. Especially, it is not necessary to add axillary dissection if the pathologic diagnosis is confirmed as noninvasive breast cancer.

The method applied in this study is quite simple and useful in the standard mammography setting. Three-dimensional positioning of the hook-wire using a stereotactic device has been gradually accepted because it is more accurate to place the hook-wire at the aimed area [1]. The stereotactic device has been increasingly used under digital imaging. It enables us to obtain a real-time image and to confirm the position of needle quickly in the same setting. It also makes it possible to obtain core-biopsy specimens, which can provide a pathologic diagnosis. Newer techniques, such as the 14G vacuum-assisted core biopsy system or minimally invasive stereotactic excisional biopsy system, give us enough material to ensure the accuracy of the pathologic diagnosis [2, 3].

This series showed that 21.8% of all biopsies are diagnosed as cancer. The open biopsy for benign lesions must be avoided if possible. Our institution has performed Gd-enhanced magnetic resonance imaging (MRI) for 38 patients with clustered microcalcifications seen by mammography. Among 11 patients whose MRI showed the enhanced area (the site of clustered microcalcifications), 9 of the 11 lesions (81.8%) were diagnosed as cancer by stereotactic biopsy. In contrast, no cancer has been detected by periodic follow-up using mammography or ultrasonography in 27 patients with no enhanced area (median follow-up 15 months). Therefore the indications of open biopsy for the clustered microcalcifications can be properly decreased by Gd-enhanced MRI.

In this article the accuracy and reliability of frozen section is the same as for paraffin sections. Papillary lesions are often said to be difficult to differentiate regardless of whether they are judged to be papillary cancer by frozen section. Therefore, even if the material can be obtained correctly, the definitive procedure may be added after the permanent pathologic diagnosis has been reported. Large-core biopsy for permanent sections decreases the amount of surgery [4].

Nowadays, even if the permanent section shows DCIS with minimal invasion, the idea of sentinel node biopsy with blue dye and/or sulfur-colloid can decrease the unnecessary dissections of axillary lymph nodes [5]. Finally, early detection and minimally invasive treatment with improved survival benefit is a desirable goal for breast cancer patients in the near future.

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