

The value of mammographic examination of the excised sample after open biopsy for the estimation of the surgical margins

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Introduction. Breast cancer is the most common malignant tumour in women. In the case of non-palpable breast cancer, open surgical biopsy is one of the available methods for diagnosing patients in whom mammography results strongly suggest the presence of a malignancy.

Material and methods. The study group consisted of 70 women undergoing pre-operative localisation of the mammographic lesions performed with a localisation needle. Results of histopathological examination were indicative of breast cancer in all the patients. Localisation needles were placed with mammographic guidance. The excised tissue samples were sent for mammographic examination. The specimen material was then imaged and a radiologist determined whether the lesion had been actually removed and what was the status of the margins in the vicinity of the tumour. The material was then relayed to the Department of Pathology in the Institute of Oncology in Cracow. A pathologist determined the size and type of the tumour as well as the smallest possible margin in its vicinity. The examination of the specimen material was followed by single-factor analysis. The correlation between the mammographic and histopathologic margin was described by linear regression. The statistical significance level was set at $\alpha=0.05$.

Results. We compared the mammographic and histopathologic margins of the excised tissue samples. The material was collected from a group of 70 women patients who had undergone surgery for nonpalpable breast cancer. No mammographic margin was reported in 13 women, which was later confirmed by histopathologic diagnosis. In the remaining cases the margins in the mammography examination ranged from 1 to 30 mm. In the histopathological examination a lack of margins was reported in 6 cases, in the remaining cases the margins varied from 1 to 15 mm.

Conclusions. Surgical biopsy of a lesion localised with a needle should always be accompanied by mammographic examination of the breast tissue.

1. Mammographic examination allows to determine the surgical margins.
2. Recent studies reveal that the absence of mammographic margins always implies the absence of margins on histopathological examination.
3. The mammographic margin exceeds the histopathological margin by approx. 3.3 mm.

Wartość badania mammograficznego preparatu po biopsji operacyjnej w ocenie marginesów chirurgicznych

Wstęp. Rak piersi jest najczęściej występującym nowotworem złośliwym u kobiet. W przypadku niebadalnego klinicznie raka piersi jedną z metod, pozwalającą zdiagnozować zmianę podejrzaną widoczną w badaniu mammograficznym, jest otwarta biopsja chirurgiczna.

Materiał i metoda. Materiał obejmuje 70 kobiet, u których wykonano przedoperacyjną lokalizację zmiany podejranej w badaniu mammograficznym igłą lokalizacyjną. W badaniu histopatologicznym u wszystkich tych kobiet stwierdzono raka piersi. Igły lokalizacyjne zakładane były pod kontrolą mammografii. Usunięty fragment gruczołu piersiowego przesyłany był do pracowni mammograficznej. Wykonywano zdjęcie preparatu operacyjnego i lekarz radiolog oceniał, czy zmiana została usunięta i jaki był margines w otoczeniu guza. Następnie materiał operacyjny przesyłany był do Zakładu Patologii Nowotworów Instytutu Onkologii w Krakowie. Patolog oceniał wielkość i charakter guza, jak również najmniejszy margines w otoczeniu guza. Po dokonaniu przeglądu materiału zastosowano analizę jednoczynnikową. Związek pomiędzy marginesem stwierdzanym w badaniu mammograficznym i histopatologicznym opisano przy pomocy regresji liniowej. Jako poziom istotności statystycznej w analizach przyjęto $\alpha = 0,05$.

Wyniki. U 70 chorych operowanych z powodu raka piersi, niewyczuwalnego w badaniu klinicznym, oceniono margines w badaniu mammograficznym usuniętego preparatu i porównano z marginesem w badaniu histopatologicznym. W badaniu mammograficznym brak marginesu stwierdzono u 13 kobiet, co również zostało potwierdzone badaniem histopatologicznym. W badaniu mammograficznym margines wynosił od 1 do 30 mm, natomiast w badaniu histopatologicznym brak marginesu stwierdzono u sześciu z tej grupy kobiet, a pozostałe kobiety miały margines od 1 mm do 15 mm.

Key words: mammography, open surgical biopsy, surgical margin

Słowa kluczowe: mammografia, preparat chirurgiczny, margines

Introduction

Breast cancer is the most common malignant tumour in women all over the world, accounting for nearly 19% of cancer incidence. Polish statistics (1992) report that breast cancer is now the most common cancer among women in Poland, accounting for 17% of cancer incidence and for 14% of deaths. According to the Institute of Epidemiology in Poland an estimated 10 000 people are diagnosed with cancer each year, and this number tends to increase [1].

Diagnostic procedures involve clinical testing, mammography, fine-needle or core needle aspiration biopsy [2]. Another method, which allows a mammographic lesion to be accurately diagnosed is known as the open surgical biopsy [2, 3]. The needle localisation for the surgical biopsy is performed by placing a needle in the breast with mammographic or ultrasonographic guidance. A wire is inserted in the lesion detected in imaging procedures. The wire remains in position during the entire surgical procedure and the lesion can be wholly removed. The needle localisation has to be followed by mammography of the whole breast in the lateral and craniocaudal positions to verify the localisation precision and to determine the required range of excision leaving a margin of 1-2 cm. After the lesion is removed the specimen is imaged to determine whether the mammographic abnormality has been entirely removed and to establish the "wire to focus" ratio [3, 4]. The decision to stop the surgical biopsy is based on the evaluation of the mammographic image of the tissue specimen, as the radiologist determines also the surgical margin and informs the surgeon how radical the biopsy ought to be. Pathological examinations reveal that only a fraction of mammographically suspicious lesions are cancers. The literature on the subject reports that only 21-36% of lesions suspicious at mammography prove to be cancers [5].

A surgeon removing the lesion ought to consider two vital issues:

1. Should the removed lesion prove to be cancer, utmost care must be taken to leave the required surgical margin.
2. Should the removed lesion prove to be benign, the breast tissue section has to be removed in such a manner that the breast shape is retained [5].

Breast cancer detected in the early, pre-clinical stage can be effectively cured in more than 90% patients after

the tumour and the tissue margin is removed. In most cases the breast shape can be retained as well [2, 5, 6].

Material and method

The preoperative localisation of suspicious abnormalities was performed in 70 women. Histopathologic diagnosis confirmed breast cancer in all cases.

Following the radiological and surgical consultations, the patients were qualified for surgery. The localisation wires were placed with mammographic guidance. All women underwent surgery in the operating room, under general anaesthesia. In all cases the lesions considered suspicious at mammography were removed with a 1-2 cm margin of macroscopically unchanged tissue, *en block* with the skin over the tumor projection and all the way down to the pectoral fascia (Figure 1). The removed breast tissue specimen was sent to the mammography room together with the localisation needle. The tissue specimen would be then imaged and a radiologist would

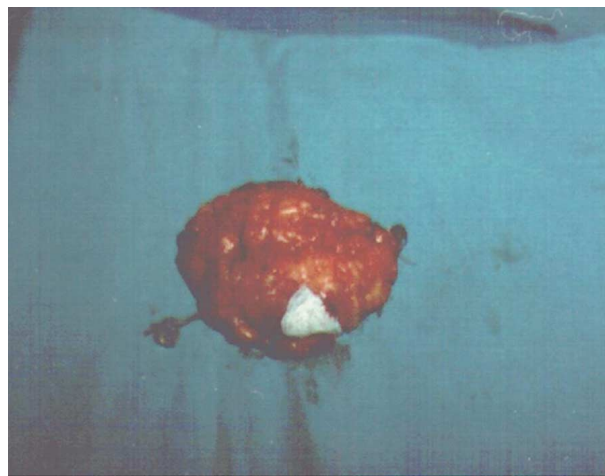


Figure 1. Excised tissue sample

determine if the lesion was wholly removed and what was the lateral surgical margin in the vicinity of the tumour (Figure 2). The margins discerned in the mammographic examination were divided into the following groups:

- a) absence of margin,
- b) margin of 1-5 mm,
- c) margin of 6-10 mm,
- d) margin of 10 mm or more.

After radiological evaluation the tissue specimen was relayed to the Department of Pathology in the Institute of Oncology in Cracow where a pathologist determined the tumour size and the smallest possible margin in the vicinity of the tumour in accordance with similar criteria as those applied in the mammographic examination (Figure 3). The margins discerned in the histopathological examination were divided into the following groups:

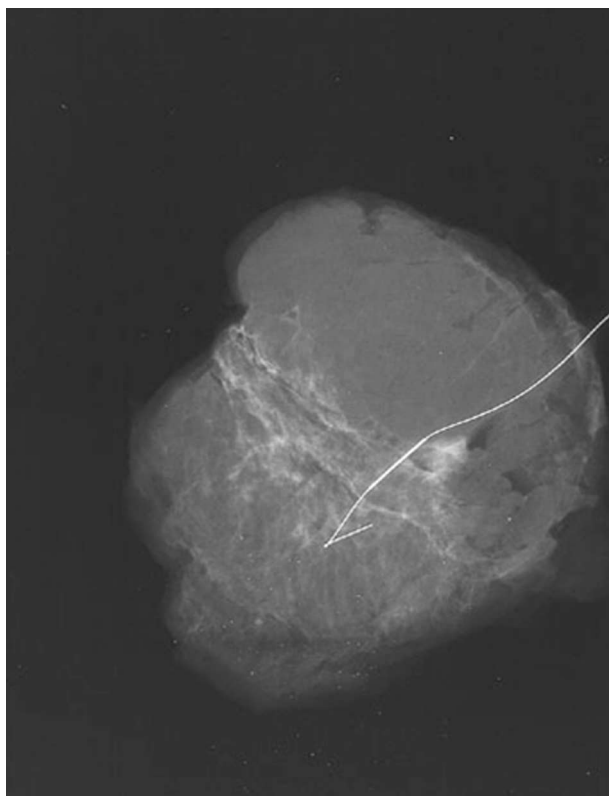


Figure 2. Mammography of the excised tissue sample

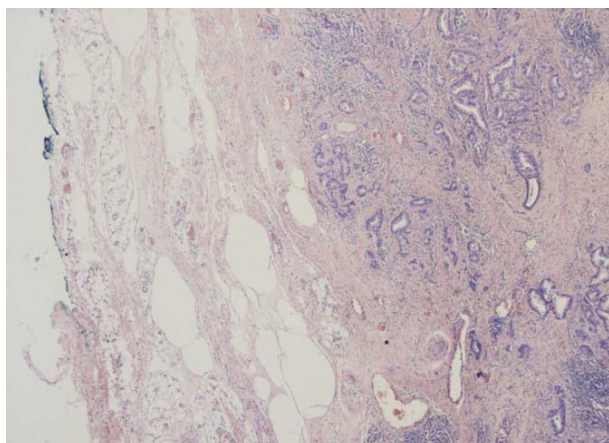


Figure 3. Photograph of the histopathological sample

- absence of margin,
- margin of 1-3 mm,
- margin of 4-6 mm,
- more than 6 mm.

Depending on the histopathological diagnosis, the treatment procedures for patients with cancer confirmed by microscopic examination are:

- removal of tumour,
- removal of the breast tumour and axillary lymph nodes, supported by radiotherapy,
- simple mastectomy,
- radical mastectomy *modo* Patey.

The number of excised lymph nodes and the possible locations of recurring cancer were also considered.

Having examined the tissue specimens, univariate analysis was applied. The correlation between the margins discerned in the mammographic and histopathologic examination has been described using linear regression. The level of statistical significance was set at $\alpha=0.05$.

Results

Pre-invasive breast cancer was reported in 14 women (20%) – in all cases it turned out to be *carcinoma intra-ductale*. Invasive carcinoma was reported in 56 women, in most cases as a form of intraductal carcinoma. Invasive ductal carcinoma was found in 38 patients:

- well differentiated histologic features (Bloom I) in 20 women (28.57%),
- less differentiated histologic features (Bloom II) in 15 women (21%),
- the least differentiated histologic features (Bloom III) in 3 women (4.29%).

The remaining cancer types were:

- lobular carcinoma in 5 women (7.14%),
- tubular carcinoma in 3 women (4.29%),
- papillary carcinoma in 2 women (2.85%),
- predominantly intraductal carcinoma in 8 women (11.43%).

No metastases to the axillary lymph nodes were reported. Lymphatic embolism was reported in 4 patients, the presence of necrosis was observed in one case.

In all 70 cases the surgical margin was duly determined mammographically and histopathologically. The absence of the mammographic margin was reported in 13 women, which was later confirmed by histopathologic examination (Figures 4 a, b). In the remaining 57 women the mammographic margin ranged from 1 to 30 mm. The

Table I. Results of histopathological examination in women who had undergone breast surgery

Lesion type	Histologic features	No. of patients	(%)
Non-invasive carcinoma	Intraductal carcinoma	14	5
Invasive carcinomas	Lobular carcinoma	5	7.14
	Papillary carcinoma	2	2.85
	Tubular carcinoma	3	4.29
	Intraductal carcinoma with focal lesions	8	11.43
	Invasive ductal carcinoma		
	Bloom- grade I	20	28.57
	Bloom- grade II	16	21.43
	Bloom – grade III	3	4.29
Total		70	100

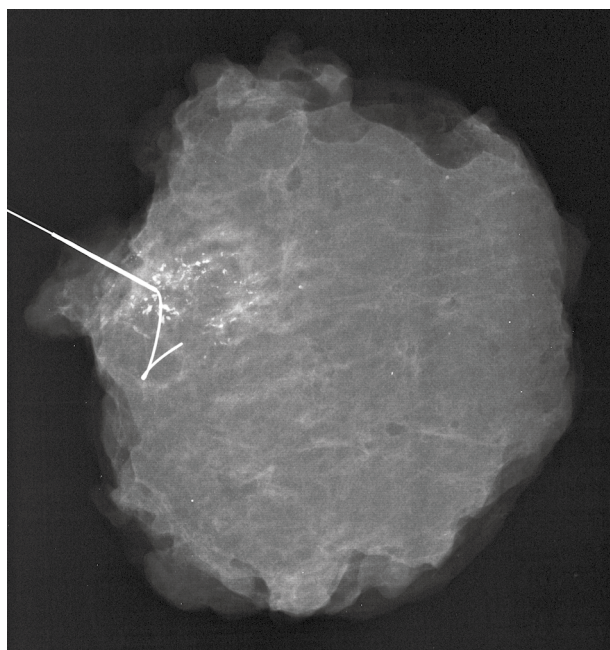


Figure 4a

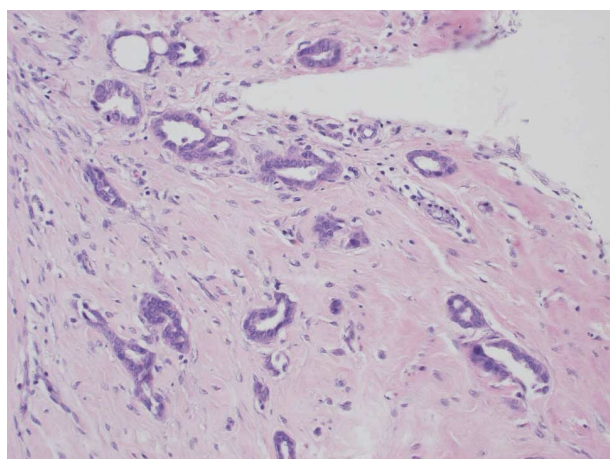


Figure 4b

Figure 4.
a. Lack of margin in mammography
b. Lack of margin in histopathology

histopathologic examination revealed the absence of the margin in 6 women from that group. In the remaining cases the margin varied from 1 to 15 mm.

In the next stage the mammographic and the histopathological margins were compared (Table II). The

absence of margins in both the mammographic and histopathological examination was reported in 13 patients (100%). A mammographic margin of 1-5 mm was reported in 17 patients. In 3 of these patients (18%) no margin was found on histopathological examination, a margin of 1-3 mm was reported in 8 patients (47%), 4-6 mm in 5 patients (29%) and in one case (6%) the margin exceeded 6 mm (Figures 5 a, b).

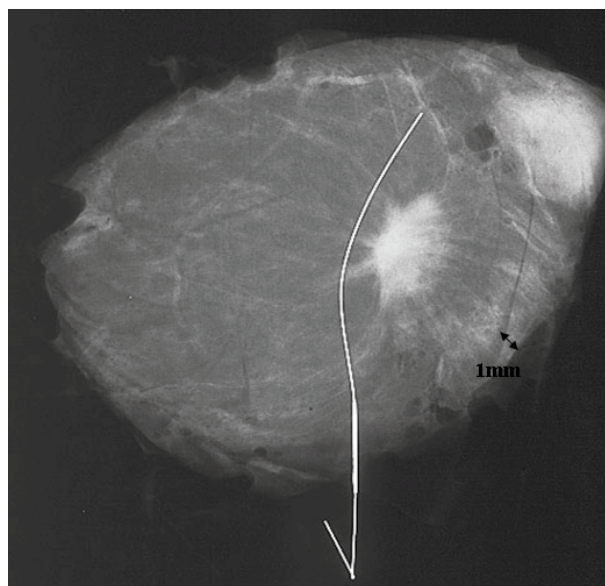


Figure 5a

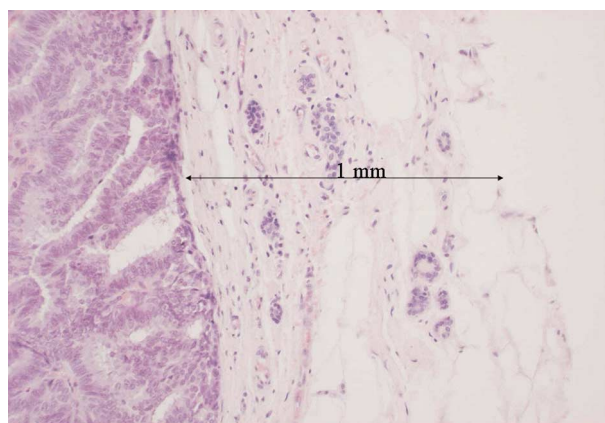


Figure 5b

Figure 5
a. Mammographic margin of 1-5 mm
b. Histopathological margin of 1-3 mm

Table II. Comparison of surgical margins and the margins discerned in mammographic and histopathological examination

Pathology	Absence of margin		Margin 1-3 mm		Margin 4-6 mm		Margin > 6 mm		Total
Mammography	Number of patients	(%)	Number of patients	(%)	Number of patients	(%)	Number of patients	(%)	
Absence of margin	13	100	0	0.00	0	0.00	0	0.00	13
Margin 1-5 mm	3	18	8	47	5	29	1	6	17
Margin 6-10	1	4	8	35	6	26	8	35	23
Margin > 10 mm	2	12	3	18	0	0.00	12	71	17
Total	19		19		11		21		70

A mammographic margin of 6-10 mm was reported in 23 patients. In one of these patients (4%) no margin was found on histopathological examination, a margin of 1-3 mm was reported in 8 patients (35%), of 4-6 mm – in 6 patients (26%) and of 6 mm or more – in 8 patients (35%), (Figures 6 a, b).

A mammographic margin exceeding 10 mm was reported in 17 patients. In two of these patients (12%) no

margin was found on histopathological examination, a margin of 1-3 mm was reported in 3 patients (18%), no case of a 4-6 mm was reported and a margin of 6 mm or more was reported in 12 patients (71%), (Figures 7 a, b).

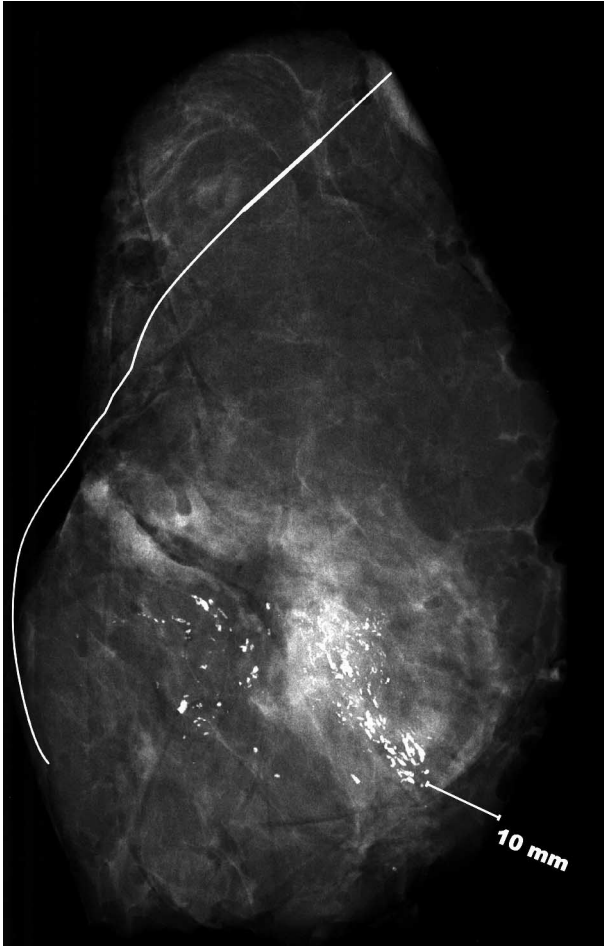


Figure 6a

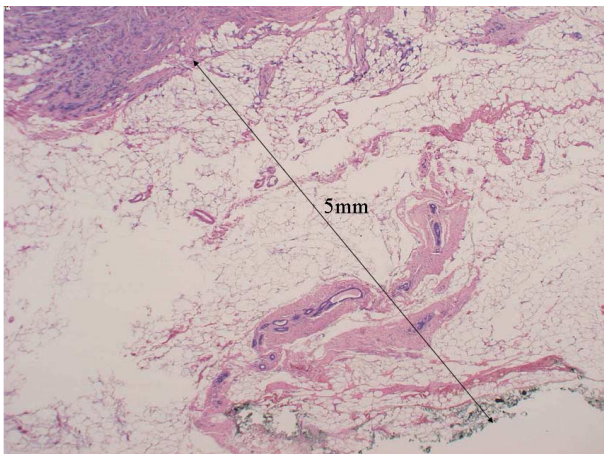


Figure 6b

Figure 6
a. Mammographic margin of 6-10 mm
b. Histopathological margin of 4-6 mm

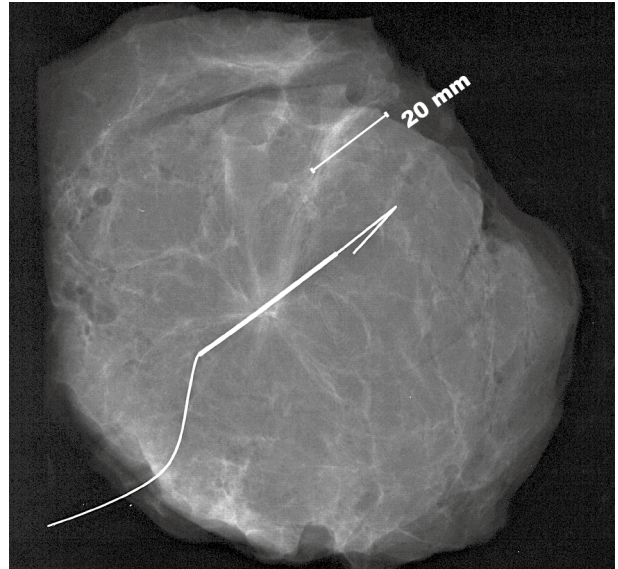


Figure 7a

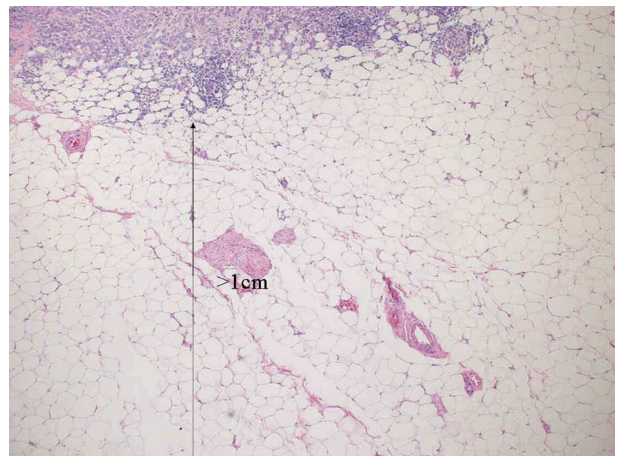


Figure 7b

Figure 7
a. Mammographic margin exceeding 10 mm
b. Histopathological margin exceeding 6 mm

It is apparent that the absence of margins in mammographic and histopathological examinations correlate as statistically significant features. The p-value in the Chi-square independence test is 0.0000 (Table III).

Table III. Correlation between the margins in the mammographic and histopathological examination

Margin	Histopathologic examination		
	Absent	Present	Total
Mammography	Absent	0	13
	Present	38	57
	Total	38	70

Accordingly, when the absence of margins on histopathological examination is inferred from the absence of the mammographic margin, this decision-making rule has a sensitivity of 41%, a positive prediction value 100% and a negative prediction value of 67%.

The correlation between the margins in the mammographic and histopathological examination is evaluated on the basis of the regression equation. The equation ought not to include any free terms ($p=0.9248$), which means that the absence of mammographic margins should imply the absence of the histopathological margins.

The equation of regression is rewritten as:

Histopathological margin = $0.5250 \times$ mammographic margin.

The mean model fitting error approaches 3.3, while the determination factor equals 0.774. The regression factor expresses the fact that the size of the histopathological margin is slightly more than half of the mammographic margin (Diagram I).

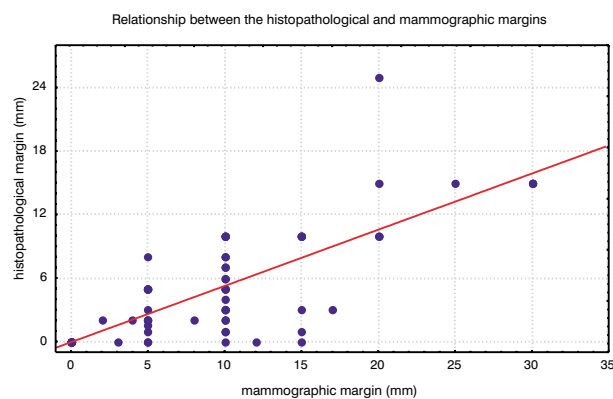


Diagram I

Discussion of results

The results were derived from the cohort study of 70 women patients who underwent surgical excision of a breast tumour evident in mammographic examination. Prior to surgery the suspicious lesions were localised with a needle. Breast cancer was diagnosed in all cases.

The surgical margin round the tumour was determined. The surgical “free-from-tumour” margin evident in the mammographic examination of the removed tissue specimen was compared with the histopathological margin.

Localisation of the suspicious lesion with a needle is necessary as the localisation of detected abnormalities allows the tumour to be removed with an appropriate tissue margin. Also the localisation procedure is necessary for the precise diagnosis of nonpalpable cases, radiologically suspicious abnormalities and indeterminate breast lumps [2, 5-9].

There exist reports that fine-needle biopsy does not allow the pathologist to distinguish precisely between invasive cancers and intraductal carcinoma (CDIS) [7, 10, 11, 16]. The diagnosis has to be verified by open surgical biopsy or core needle biopsy.

When the findings of the fine-needle biopsy or the core-needle biopsy are negative and yet the mammographic examination reveals a spiculated mass or suspicious microcalcifications, open surgical biopsy is necessary for the correct diagnosis.

A thorough study of literature on the subject and the Author’s findings show that the excision of the tumour following its localisation is the only reliable method which allows to distinguish between breast cancer and radial scar [2, 10, 11].

Most authors tend to emphasise the fact that open surgical biopsy is more costly than other procedures [9, 12]. Nevertheless, it is the only available method which allows for complete diagnosis of mammographically suspicious abnormalities and, in some cases, offers effective treatment of the patients [4, 13-16].

In this study the absence of margins in the mammographic examination was reported in 13 patients, which was later confirmed by histopathological examination. The author thus concludes that the correlation between the absence of mammographic and histopathological margins is statistically significant. The p-value in the Chi-square independence test is 0.0000.

Furthermore, the mammographic margin around the tumour is larger than the histopathological margin by 3.3 mm on average.

Accordingly, when the absence of margin on histopathological examination is inferred from the absence of the mammographic margin, this decision-making rule has a sensitivity of 41%, a positive prediction value of 100% and a negative prediction value of 67%.

The author’s data are fully consistent with those cited in literature. Graham et al. [5], Stomper et al [7] and Homer et al. [20] report that the margin in the mammographic examination is larger than the histopathological margin. According to those authors, the difference between the margins in the mammographic and the histopathological examination may be attributed to the fact that a radiological image shows the lesion in two projections only, whilst on histopathological examination the margin is viewed in four projections [5]. Also, on mammographic examination cancer may take the form of microcalcifications, however such microcalcifications occur not only in malignant tumours, but also within mastopathic lesions or they may not be revealed on images at all [7, 15, 16, 18, 19].

The author’s experience shows that the difference between the margins in mammographic and histopathological examination may be attributed to breast compression while the mammogram is performed. Compression is required to ensure the best possible visibility of the tissue specimen, hence the tumour itself, and the margins, are larger than the margins in histopathological examination. Without compression, however, neither the

focal change nor the surgical margin can be evaluated. No such reports are found in literature.

The thorough scrutiny of literature and of the author's material shows that mammography findings are the determining factor for deciding how radical the breast surgery ought to be in the case of non-palpable breast cancers [5, 15, 16, 20]. Basing on the mammographic image of the breast tissue, the radiologist decides to terminate surgery. Therefore, the effectiveness of the treatment depends upon the close cooperation of surgeons and radiologists [2].

Conclusions

1. A surgical biopsy of a lesion localised with a needle should always be accompanied by mammographic examination of the breast tissue.
2. Mammographic examination allows to determine the surgical margin.
3. Recent studies have shown that:
 - the absence of the mammographic margin always implies the absence of margin on histopathological examination,
 - the mammographic margin exceeds the histopathological margin by about 3.3 mm.

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