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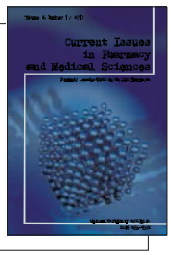

Contemporary diagnostic methods for breast cancer

BARBARA MADEJ-CZERWONKA

Department of Breast Surgery; Cardinal Rev. Wyszynski'sVoivodship Specialist Hospital in Lublin,
Department of Human Anatomy, Medical University of Lublin, Poland

ABSTRACT

Breast cancer is the most common malignant neoplasm diagnosed in Polish women. The results of treatment for breast cancer in Poland are worse than those received in highly developed European countries. The factor that is decisive in reducing mortality due to breast cancer is an early diagnosis. Conversely, the diagnosis, which is established too late contributes to poor prognosis and prevents obtaining satisfactory results in treatment even with expensive anti-cancer drugs. An early diagnosis of breast cancer is more and more difficult to reach; it requires experienced specialists and high quality equipment. This article presents contemporary diagnostic methods for breast cancer and analysis of diagnostic standards for every single procedure.

Keywords: breast cancer, diagnostics, standards for radiological examinations

INTRODUCTION

Breast cancer is the most common malignant neoplasm diagnosed in Polish women. Annually there are approximately 14,500 new patients diagnosed with breast cancer. Recent years have brought a significant breakthrough in the field of breast cancer diagnostics and therapy, yet the results of treatment for breast cancer in Poland are not equally as good as those from other countries of Western Europe or the USA. What still contributes to unsatisfactory results of treatment for breast cancer is the diagnosis, which is established too late.

Infiltrating ductal carcinoma is the most common type of breast cancer and it affects approximately 70-80% of women. Lobular carcinoma is diagnosed in approximately 10-15% of patients, whereas other rare types of breast cancer as: mucogenic, medullary, papillary, tubular and adenoid cystic carcinoma are present in 5-10% of cases. Due to the improvement in early diagnostics there has been an increase in the number of patients diagnosed with ductal carcinoma *in situ* (DCIS) and lobular carcinoma *in situ* (LCIS), the treatment of which sparks a lot of controversies now. The most common location for breast cancer is in 50% of cases an upper-outer quadrant. The upper-inner quadrant is affected in 15% of cases, lower-outer quadrant – in 10% of cases, lower-inner quadrant in 5% of cases. The location of tumour in an outer papillary layer – the most difficult to diagnose - concerns approximately 17-20% of patients [8, 11]. The presence of multifocal lesions is observed in approximately 10-12% of patients [12]. Another diagnostic problem is posed by so called latent forms of breast cancer, i.e. such cases in which metastases into axillary lymph nodes are observed, yet the primary focus in the gland cannot be detected.

An early diagnosis of breast cancer is still the most important factor, which increases the patients' chances for survival [12]. Available methods for early diagnosis of breast cancer include: a breast self-exam, clinical palpation of the breast, mammography (MMG), ultrasonography (USG), magnetic resonance imaging (MRI) and a positron emission *tomography* (PET). Among invasive methods, which play the most important role in diagnosis are: fine-needle aspiration biopsy (FNAB), coarse-needle biopsy, surgical biopsy and mammotomic biopsy. The following modern methods assessing the stage of advancement of the disease are being applied more and more frequently: sentinel lymph node biopsy (SLNB), imaging of non-palpation primary focus with the use of *radioisotope* occult lesion localization (ROLL) and a combination of those two methods, so called SNOLL [14, 15].

Corresponding author
Department of Breast Surgery; Cardinal Rev. Wyszynski'sVoivodship Specialist Hospital in Lublin, Department of Human Anatomy, Medical University of Lublin, Poland
e-mail: basia.madej@interia.pl

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CLINICAL EXAMINATION OF BREAST

The role of a breast self-exam is controversial. None of the studies conducted so far has detected a decrease in mortality among women who were performing a breast self-exam in comparison to control group. However, still about 40% of tumours are diagnosed by patients themselves [16].

Clinical breast palpation plays a huge role in diagnosis of breast cancer especially in young women, those with dense breast tissue and patients suffering from lobular carcinoma, because the effectiveness of mammography in the last group is low. According to a *National Breast and Cervical Cancer Screening Program* conducted in the USA, the detectability of breast cancer among those who showed abnormalities on palpation and at the same time with normal mammographic image accounted for 5.1% [3]. It is estimated that the sensitivity of palpation examination among women before the age of 50 is 56%, and specificity 70%, whereas among patients over 50 the sensitivity and specificity are: 86% and 90% respectively. The results of palpation examination confirmed by cytological techniques and histopathological methods are still one of the elements of preliminary assessment of the advancement stage in case of locoregional cancer and frequently the reason for qualifying the patients for a given treatment scheme [12].

Ultrasonography

Ultrasonography is a widely available and frequently used type of breast examination. The ultrasound image shows an infiltrating cancer usually as a spicular structure,*hyperechogenic,* not clearly separated with decreased echogenicity in the posterior wall (so called tumour shadow).In some cases, microcalcifications can be observed. However, ultrasound images of breast cancer can vary from the typical ones. Hyperechogenicity is typical for approximately 75% of tumours [8].These are usually tumours similar in structure to ductal carcinoma. Medullary and lobular carcinomas are able to show normal echogenicity. Tumour shadow can be observed in approximately 35%of types of cancer. Tumours with small diameter can have regular tumour boundaries, typical for benign tumours (25–30% of cases) (Figure 1). Lesions characterised by rapid growth show necrosis of foci located within tumour. Ultrasound image shows them as hypoechogenic areas within tumour mass.

There are many indications for performing ultrasonography of breast and according to *American College of Radiology* (ACR) they include: assessment of lesions detected on palpation or in any other imaging technologies such as MMG or MRI. Ultrasound examination is recommended in women younger than 30, pregnant women, during lactation in case of lesions detected on palpation, in patients with breast implants, in case of microcalcifications, breast architecture abnormalities showing malignancy or indicating cancerous process, in case of biopsy or other invasive procedures, when planning breast irradiation. Randomized clinical examinations work on the analysis of usefulness of ultrasonography when assessing axillary lymph nodes being affected by breast cancer as well as the diagnosis of women at risk of developing breast cancer and showing dense, glandular structure of breasts.

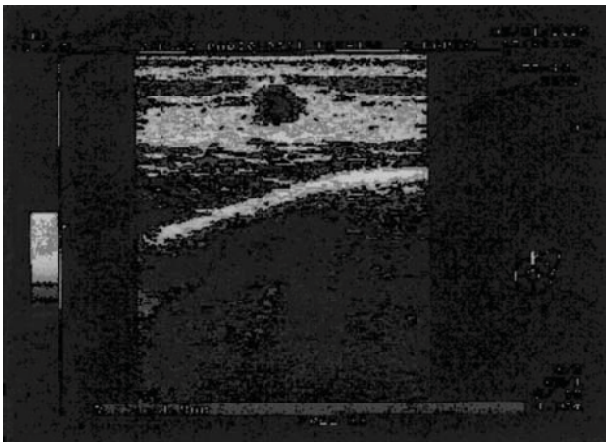

Fig. 1. An image of breast cancer in ultrasonography

In recommendations issued by ACR, it is underlined that it is necessary to make a protocol of ultrasound examination properly. Preferred description of ultrasound image should include i.e. the following information concerning described lesions: reference to clinical and/or mammographic symptoms described by either a doctor or patient as well as the result of previously performed ultrasound examination [6]. It should provide information about the size of the lesion measured in 2 different projections and include a printout with the image of the lesion without markers indicated. It should also describe the location of the tumour, i.e. the breast should be marked, location in a given breast in the clockwise direction and the distance measured from mammilla. The distance should be measured from mammilla and not from areola of the mamma because areola of the mamma can have various breadth. The lesions which are detected on ultrasonography examination should be described according to ACR's system operative now – BI-RADS® (*Breast Imaging Reporting and Data System*®) [1]. This system covers assessment of such parameters as tumour's size, its shape, location, tumour delimitation, echogenicity, tumour margins, tumour shadow or its consecutive intensification, the image of surrounding tissues. It is recommended that the ultrasonography examination should be performed within the first phase of menstrual cycle due to pain on pressure preceding menstruation, which makes examination difficult.

Mammography examination

Tumours stage T0 and T1 are most frequently clinically „mute". Their detection is possible only thanks to diagnostic imaging technologies, which nowadays play a major role in an early detection of breast cancer. A method of choice is mammography examination (Figure 2). MMG has a much-diversified sensitivity in different age groups. In young women with dense breast tissue the sensitivity of MMG is only 30%, whereas in a group of older women with prevalent adipose tissue of the breasts - 80% [17]. An unparalleled success was the fact that mammography examination was included in screening examination for women over 40, which enabled to detect preinvasive carcinomas and tumours up to 1cm in size, and therefore it contributed to the decrease of mortality rate by 30% [4, 10]. Due to the introduction of the system of images assessment by two independent radiologists (so called double reading) it was possible to improve perception of cases with very small foci of microcalcifications. This method increased detectability of breast cancer by 10%. The development of a computer-based method supporting the analysis of received mammograms (so called CADS – *computer-aided detection system*) was the next step forward. Computer-based system enabled an increase by 10.5-19.5% in the number of detected cases of breast cancer [19]. Currently, it is more and more popular to make use of digital mammography (DM). In clinical practice, especially in case of young women with dense breast tissue, MMG is complemented by ultrasonography. Such diagnostic procedure helps to increase the sensitivity of detecting an early breast cancer by approximately 10% [17]. In order to unify the system of MMG description a 7-pointBI-RADS® scale was introduced. Category 0 means that further diagnostic procedure of a lesion described in MMG is required, i.e. performing a complementary USG or comparing the result with the previous MMG image. Category 1 – no lesions, category 2 – benign lesion, category 3 – lesion probably benign, observation and/or biopsy recommended, category 4 – suspicious lesion, biopsy recommended, category 5 – lesion probably neoplastic, further immediate diagnostic procedures recommended, category 6 – neoplastic lesion verified under the microscope [18]. Mammography screening examinations are performed in women over 40, every 2 years. Diagnostic mammography can be performed at every age whenever an oncological worrying lesion is found. Characteristic features of cancer observed in MMG images include architectural distortion, focus of microcalcifications, shadowing with spiky outline. Scattered micro- calcifications are often observed in *in situ* carcinoma.

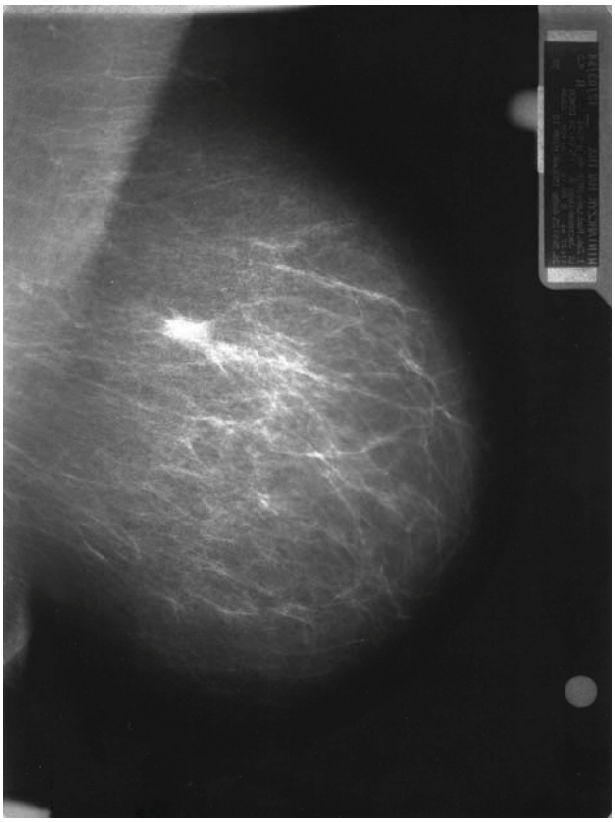

Fig. 2. An image of breast cancer in mammography

Magnetic resonance imaging

Technical progress in recent years has contributed to the wider use of magnetic resonance imaging (MRI) in breast cancer diagnostics. MRI is a dynamic examination in which neoplastic lesions are differentiated from other lesions on the basis of the analysis of the differences in strength of signal after administering contrast agent (Gd-DTPA). Malignant tumours are subject to rapid and clear strengthening only 1 min after having injected contrast agent. Then an extremely fast migration of contrast agent from neoplastic focus is observed. Such method is applied in case of neoplasms with the diameter over 0.3cm. Tumour of that size is characterised by better vascularisation in comparison to a benign lesion as well as intensified processes of neoangiogenesis ,which condition the accumulation of contrast agent. *In situ* neoplasm or invasive carcinomas of a very small diameter are not very well seen by imaging with that method. MRI is mostly applicable when assessing whether the primary neoplastic process is multi-central and multi-focal. It helps to highlight an infiltration into the wall of thoracic cavity when there is such or metastases into axillar and retrosternal lymph nodes. The above mentioned information is used i.e. when qualifying patients for breast sparing operations. Currently MRI is recommended as a screening examination in patients at risk for breast cancer, in patients with diagnosed breast cancer in order to assess non-affected breast as well as in patients after breast reconstruction. A significantly higher sensitivity of magnetic resonance imaging has been proven in a group of patients with non-palpable breast tumour as well as with a tumour not noticeable in

MMG [7]. The performance of that examination in patients with diagnosed breast cancer showed clinical benefit because the presence of breast cancer in the other breast was observed in as many as 3-5% of patients. MRI is done in order to assess the size of the tumour, its proportion in comparison to fascia and the wall of thoracic cavity, multifocality, foci of *in situ* carcinoma and neoplastic foci not noticeable in MMG. This examination is more sensitive than MMG when assessing breasts after breast conservation therapy (BCT) and after radiotherapy. It can also be useful when deciding about the degree of radicality of surgery and when diagnosing local recurrence after BCT and after reconstructive procedures. It is recommended that patients should be referred to MRI by a specialist having experience in breast diagnosis. An appropriate patients' qualification to MRI which should be based on the results of medical history of a patient, clinical investigation and the result of MMG is indispensable to establish correct MRI diagnosis and decrease the number of false-positive results.MRI is not recommended as a screening examination for patients without any clinical symptoms.

Positron emission tomography

A positron emission *tomography* (PET) similarly to MRI is a dynamic method which is based on the increased accumulation of 18f-fluoro-deoxy-glucose (FDG) in malignant neoplastic cells. This method helps to detect not only the primary focus of neoplasm but also metastases into lymph nodes and other organs. It is recommended when assessing the stage of advancement of the disease and when searching for unknown neoplastic foci. Due to its very high cost, the availability of that examination is limited.

Cytological and histopathological assessment

Tumours detected by imaging technologies are cytologically verified by means of fine-needle aspiration biopsy supervised by USG, MMG or MRI as well as histopathologically by means of oligobiopsy, mammotomic biopsy or surgical biopsy [13, 20]. Currently, there are attempts to receive the histopathological examination results prior to operation [5, 9].Full pathological diagnosis with marked receptor status helps to decide about optimum treatment scheme. In case of tumours of small diameter surgeons often resign from intra-operative examination and prefer a 2-stage procedure [2]. Now it has become a diagnostic standard to perform sentinel lymph node biopsy in order to assess the degree to which axillary lymph nodes have been affected. Modern techniques such as ROLL and SNOLL make the treatment of breast conservation therapy easier in case of non-palpable breast tumours and improve the quality of the treatment.

CONCLUSIONS

Recent years have brought a significant quality improvement of diagnostic equipment used in breast disease examination. Popularity of information programmes regarding breast cancer induced increase in social awareness on the subject of prevention and early diagnostic methods. It resulted in the increased number of patients taking part in screening survey. However, the key to effective breast cancer diagnostics is the choice of an appropriate method and good quality of performed examinations. It seems that breast units organisation that employ breast specialist, can bring the solution of this problem.

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