Early diagnosis of breast cancer – in respect to expectations of participants in screening programs and to contemporary research in imaging methods

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Abstract

On the background of new research results in screening of breast cancer, together with the expectation of the participants in a screening for breast cancer, the conventional mammography requires supplementation by means of tomosynthesis or additive ultrasound. Alternatively, ultrasound now seems to be an independent method of early detection of breast cancer because of its superior sensitivity, especially in the case of aggressive mammary carcinoma types. The MRI remains at present still a preferred method in high-risk cases and as an additive examination in case of insufficient presentation of the glandular tissue by conventional methods. MRI is also preoperatively valuable for more accurately measuring the extent of multifocal carcinomas.

Key words

brest cancer screening, mammography, breast ultrasound, breast MRI

Aim

This paper focuses on contemporary results of research with regard to the three main modalities in breast imaging: mammography, breast ultrasound and MRI. Recommendations for diagnostic procedures are orientated on expectations of the participant in screening in relation to contemporary research.

Introduction

Although many women affected by life can be saved by diagnostics and therapy of breast cancer, one woman dies on this tumor every 30 minutes due to the frequency of the disease in Germany (statistically) [1].
This relationship leads to the need for further progress in diagnostics and therapy. We are looking at the progress made in early diagnosis for breast cancer by established imaging methods.

Women's expectations in early diagnosis of breast cancer

The expectations of the woman participating in a screening examination on breast cancer may be as follows:

1. The tumor is to be discovered with high certainty in an early stage with good healing prospects.

2. Many "false alarms" (false positive findings) should not occur.

3. The method of examination should not be very unpleasant or painful.

4. The method of examination should not be inherently risk-prone.

These expectations cannot all be satisfied at the same time; it must be about getting as close as possible to it. Because, however, there is a gap between expectations and reality in the detection of breast cancer, therefore good information before the examination is important for the participating woman.

The main feature of the early detection method from the participant's point of view is its sensitivity, i.e. how accurate is it in its ability to detect tumors early not overlooking small carcinomas. Special attention is also given to sensitivity since laboratory diagnostics are at risk of taking early diagnosis in their competence.

 Sensitivity is weighted against specificity, i.e. the property that negative classified findings are actually negative. In general, an inverse ratio of these parameters is to be expected in medical diagnostics: If the sensitivity is increased, the specificity decreases and vice versa.

Before introducing a diagnostic method, an acceptable ratio of sensitivity and specificity – expressed by the positive predictive value (PPV) - is mandatory.

From an epidemiological and economic perspective, a good PPV is the most important parameter for health policymakers and health care providers prior to the introduction of a diagnostic test into general health care.

For the individual patient, who takes part of a screening examination, the sensitivity of the method - an actual disease is not overlooked - might be in the forefront. Secondly, she does not want to be unnecessarily worried

Advances in imaging methods

According to the X-ray regulation – in Germany -, screening mammography is strictly permitted only at an age of 50 and can only be carried out in the recognized screening centers. Issuing curative referrals or conducting the examination as individual health care circumvents these legal requirements. If one looks at the performance of

mammography, its sensitivity in women with breast density 1 (A) and 2 (B) (fat-rich mammals) is good to very good; its specificity is also satisfying.

However, the sensitivity of mammography is steeply lower the more densely the individual breast is built up and decreases in women with high density to 50% or less [2, 3]. Since a high proportion of women, 50% and more have a breast density above 2 (B) [4, 5]; therefore mammography is not general, but only sufficient for women with density 1 (A) and 2 (B).

Especially voluminous breasts with a small gland part benefit from mammography because of its good overview. Painful sensations caused by the pressing and the properties of the ionizing radiation are from the point of view of the women disadvantages of the method.

In order to compensate for the low sensitivity of mammography in the dense mammary, a new technique has been developed with 3D mammography - tomosynthesis. With tomosynthesis, the mammary is scanned radiographically in individual thin layers (under 1 mm) from different angles, so that the problem of superimposition of the structures in conventional mammography is solved (Fig. 1,2).
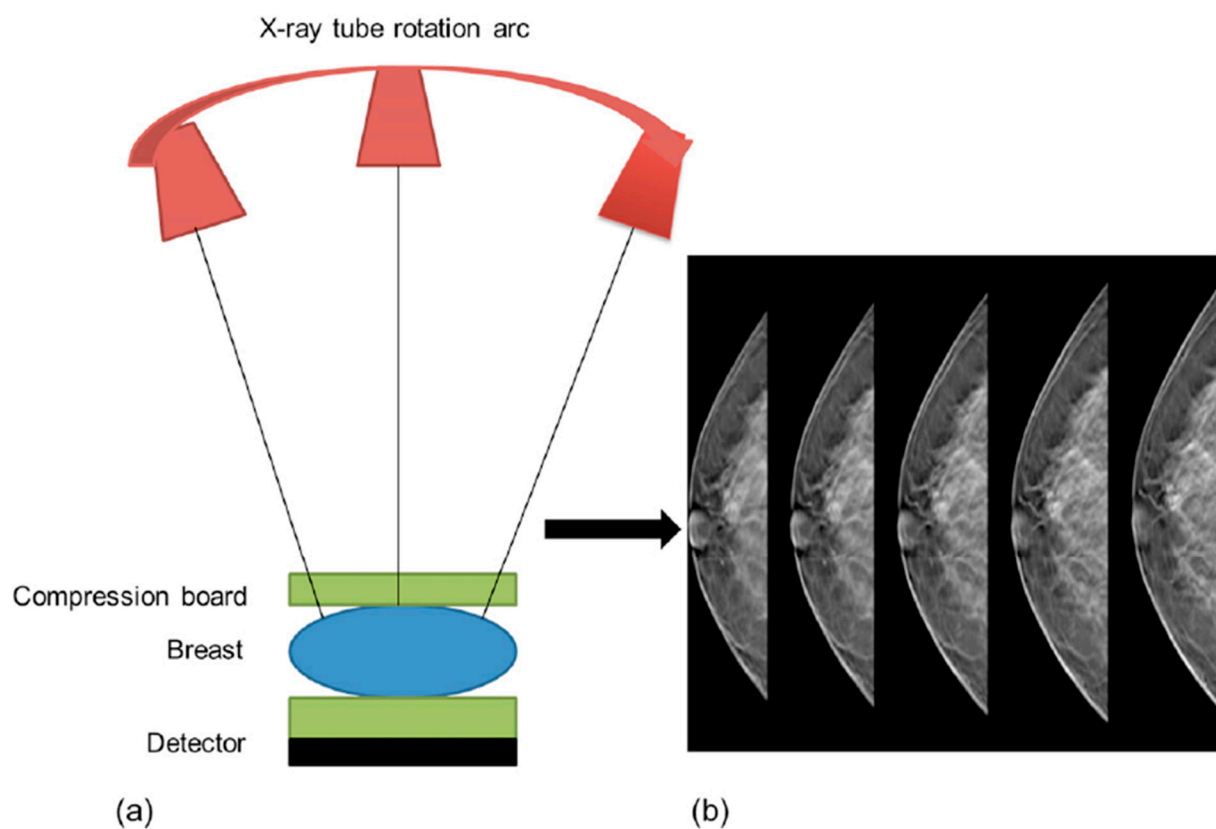

Figure 1: Tomosynthesis scans the breast from different angels creating thin layers without superimposition (Figure Hologic Inc.; with permission)
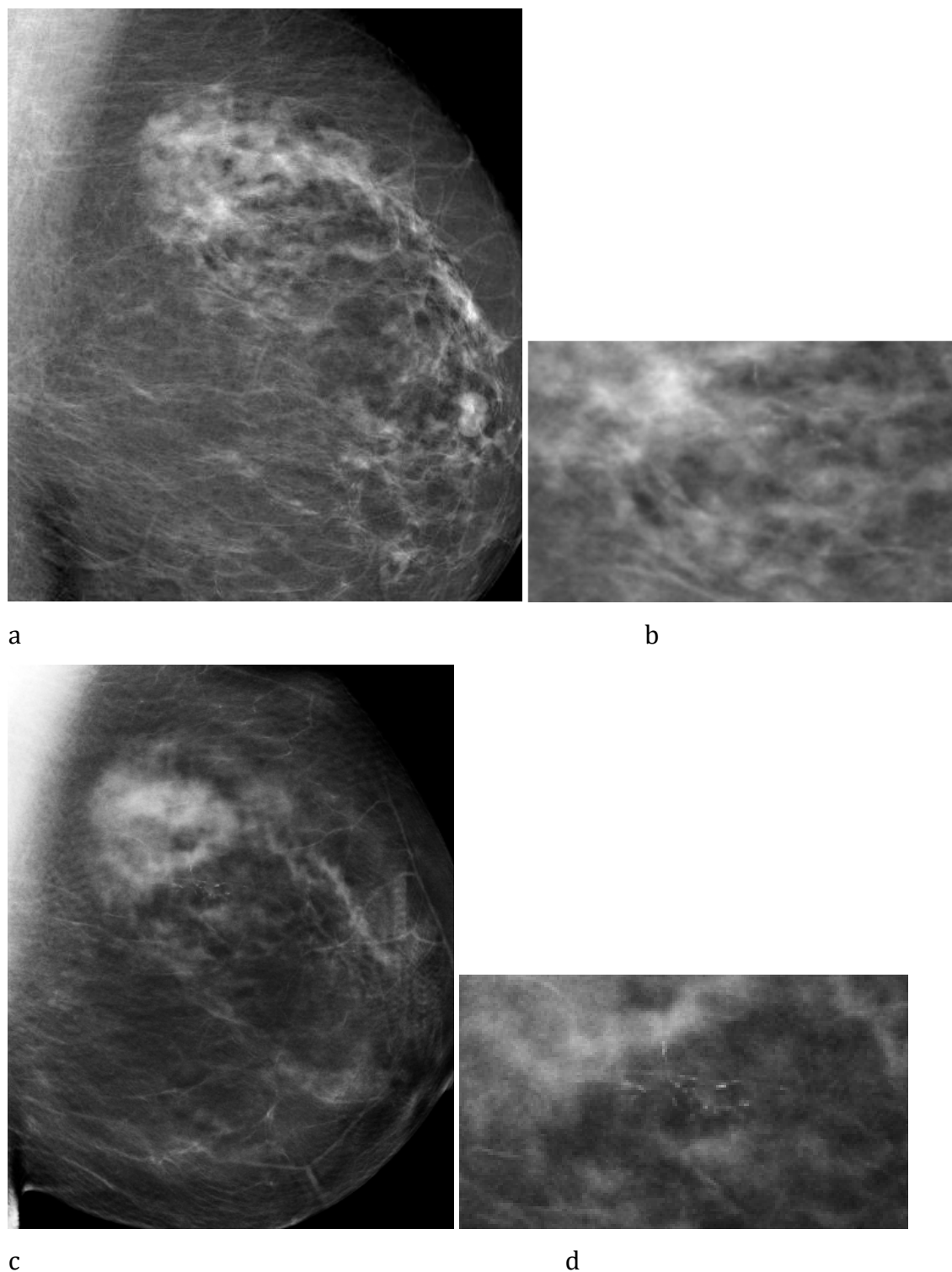
Figure 2, a-d

a: 2D mammography , b: lupe zoom (small picture), microcalcifications not visible; c: tomosynthesis layer ,same patient, d: clearly microcalcifications (lupe zoom). (Figures Dr. Rückner, Mammadiagnostik, Hamburg, with permission)

Whether tomosynthesis should be carried out without the conventional mammography or only in adjunct in the case of dense breasts is still a subject of discussion in radiology [6]. The radiation dose is different for the devices used - in some cases equal to a 2-plain mammogram, in others higher - any additional use of tomosynthesis must also take an additional radiation exposure into account.

Tomosynthesis can increase the sensitivity of 2-plain- mammography by up to 40% in dense breasts [7,8]. A particular positive feature appears to be its accompanying increase in specificity, so that the use of tomosynthesis may generate less unnecessary clarification cases. The main gain in diagnostic capacity is in the collective of women with breast density 3 (C), whereas the sensitivity at very high density also decreases in the case of tomosynthesis [9-11].

Ultrasound has the advantage that it is not dependent on the density of the breast in its performance and there are no restrictions on the age of the patient. Furthermore, it can be carried out in a decentralized and cost-effective manner and also in gynecological practices. It is becoming increasingly apparent that its sensitivity is superior in the normal collective, but especially in the clientele with dense breasts. The sensitivity of ultrasound in recent comparative publications is about 20% higher than that of mammography, can be up to 40% in defined collectives [12-19].

Disadvantage is its subjectivity (observer dependency) and its lower specificity (higher number of false positive findings).

The use of automated volume scanners (ABUS) could now be used to reduce subjectivity.

In respect to inferior specificity, it must be taken into account that BIRADS 3 (very probably benign) findings (mainly fibroadenomas) are usually counted to be false positive, which is questionable. If BIRADS 3 findings are counted as correct negative, there must be no significant difference in the specificity of ultrasound compared to mammography [17, 20].

Magnetic resonance imaging (MRI) is the most accurate method in its sensitivity and is superior to the other methods, particularly in women with very complex architecture of the breasts as well as in high-risk collectives.

According to the latest findings, it may also be appropriate in the normal collective to provide better early detection than all other methods together, and possibly even at greater intervals (3 years) [21]. MRI becomes increasingly important preoperative to

determine the exact extent, especially of multifocal carcinomas. Both mammography and ultrasound often underestimate intraductal spread, not only in lobular carcinomas. MRI, however, is only available to a limited extent in a high degree of expertise, is significantly more expensive and requires a (invasive) contrast injection. Concerns about adverse effects of the contrast medium for the brain and kidneys are not eliminated [22].

Approximately equivalent results to MRT can be achieved with contrast-enhanced mammography (CESM) [23], but until now, this method is only available in a few places.

The sensitivity of the method in general is not the only important aspect, but also - with a view to reducing the risk of breast cancer mortality - its competence to diagnose the aggressive types of breast cancer is at the forefront. The large older screening trials had not yet been able to make any distinctions. The Luminal A, Luminal B, Her 2 neu positive, Triple negative, more precise: basal cell type- we now have criteria to distinguish tumor types from their malignant potential. If the diagnostic competence is correlated with these types of tumors, we have further criteria that assign methods to their relevance to mortality reduction. According to the present studies, ultrasound is superior in the diagnosis of basal cell carcinomas due to the more frequent absence of typical mammographic signs of malignancy [24-47].

Current recommendations on the background of new developments

If mammography is performed as a screening examination, tomosynthesis should be available for women with a higher density of the breast or an ultrasound examination (possibly with automatic whole breast volume scanning - ABUS) should be connected in adjunct.

If the woman participates in organized mammographic screening with a two-year interval, she should take an ultrasound examination in the year between - for reasons of tumor growth: a two-year examination interval is too long for aggressive mammary carcinomas. If an individual gland density 4 (D) is present, an additional ultrasound examination should be performed annually.

Ultrasound additive to mammography detects more additional carcinomas than additive tomosynthesis. Ultrasound achieves better results in cases with extreme density and with carcinomas with conventional as benign recognized features [9-11].

Nowadays, as an early detection method for all age groups, irrespective of the density of the gland, qualified ultrasound as its own is an available and cost-effective method. Whether this is carried out in the form of the classical handheld ultrasound (HHUS) or in the form the automatic volume scanner (ABUS) is probably not essential [48,49]. Both methods have advantages and disadvantages. Additional modules such as color Doppler and elastography, as well as the special dynamics of the HHUS, especially in the examination of lesion findings are advantages of the HHUS. ABUS is less dependent on the examiner and the ability to scan through the entire breast in the supine plane (C-plane) may reduce the risk of false negatives.

The quality and experience of the investigator determines the percentage in which a complementary method is recommended. For BIRADS 0 cases, e.g. in the case of very inhomogeneous and/or sound-absorbing parenchyma, the recommendation for MRI would be given. In the case of a localized structural abnormality with irregular mammary gland architecture or a total inhomogeneous sonographic view, mammography should be used to exclude a DCIS.

Ultrasound has a weakness with respect to some forms of DCIS, as it does not recognize finely distributed microcalcifications without hypoechoic environmental structures. On the other hand, ultrasound detects mass-like DCIS (with and without microcalcifications) better than mammography and can also recognize forms with gross calcifications [50, 51, 52]. It is advisable to draw the patient's attention to this possible gap in ultrasound diagnostics and to suggest mammography in addition if early diagnosis of DCIS is the target.

Of course one will get the best results if all methods are used in a complementary way. But neither from the diagnostic necessity, nor from an economic point of view, does this appear justified in general.

For extremely complex mammals or high-risk patients, an MRI should be carried out at regular intervals (1-2 years).

If ultrasound, as described above, is a screening method suitable for all women [13,17], why breast ultrasound is recommended mainly as a supplementary examination (complementary to mammography)?

The following three reasons are listed regularly:

1. Only mammography has demonstrated an effect on mortality in breast cancer in large randomized studies.

2. The use of ultrasound leads to a lower positive predictive value (PPV) due to an increase in false positive results with subsequent further investigation procedures, which also leads to cost increases.

3. A quality assurance of ultrasound application was not given.

To 1: The large randomized mammographic screening studies with a follow-up period of 10 or more years, which were carried out in the second half of the 20th century, are not likely to be reissued with other modern methods. The argument refers to a methodological standard over 30 years old and cemented it. But science has, by its very nature, a progressive-dynamic character. Today, the methods are to compare to how well they diagnose breast carcinomas in an early stage and which type of tumors they recognize well or less well.

To 2: As stated above, the specificity of ultrasound does not have to differ significantly in mammography if the probably benign findings (BIRADS 3) are counted as being negative.

The ultrasound examination is offered much cheaper than mammography. An additional complementary examination is much less frequently required in primary ultrasound diagnostics with good quality than in primary mammography because of high density. In addition, the gain in life-years must be taken into account by the carcinomas diagnosed only by ultrasound (Fig. 3).
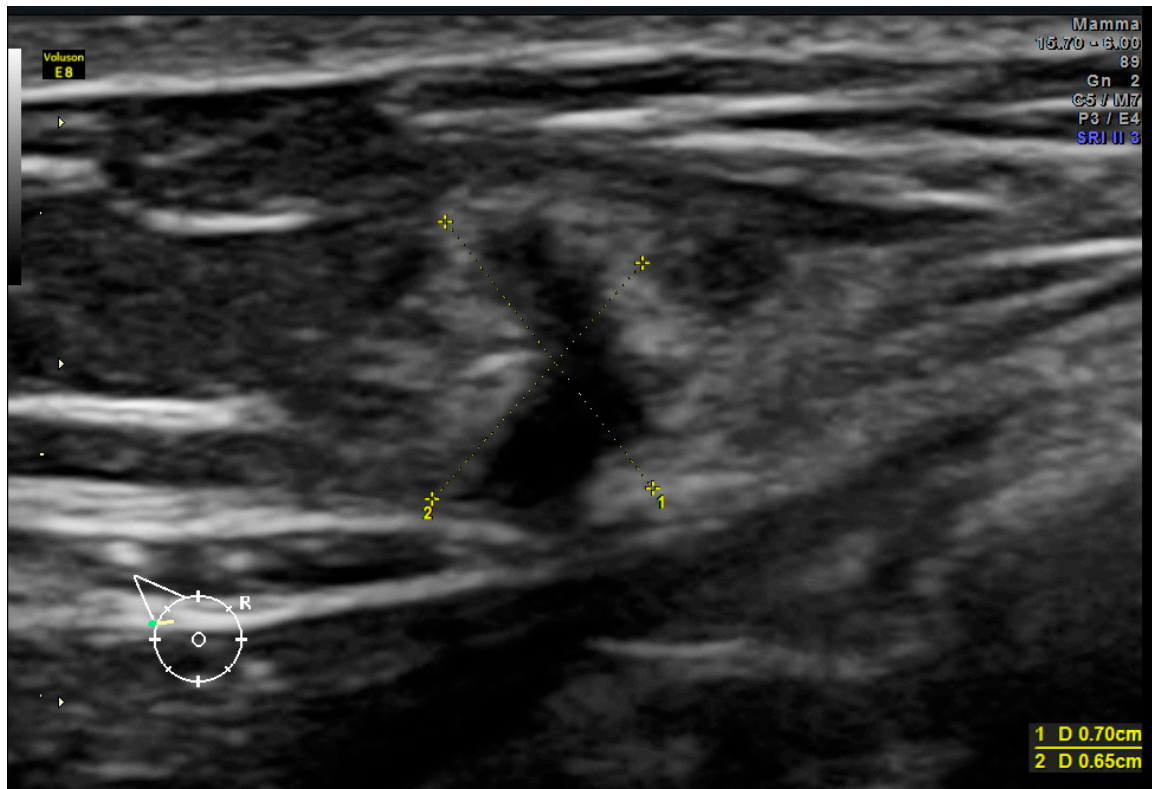
Figure 3:

50-year-old patient with an induration located upper outer site right breast. Clearly visible lesion by ultrasound, BIRADS V; Mammography: no suspicious findings, BIRADS II; MRI: small nodular contrast enhancements, not suspect. Ultrasound-guided core biopsy: invasive ductal carcinoma (NST)

It is certain that more biopsies are induced by sonography, since BIRADS 3 findings are often invasively clarified (at the request of the patient).

To 3: Expertise levels can also be established in breast ultrasound by means of performance assessment. In general, in the case of sophisticated methods - diagnostic or therapeutic - good results can only be achieved with good quality, in this respect ultrasound is not a special feature.

The fact that decentralized breast ultrasound in offices can be performed sufficiently is well documented [53, 54].

In summary: Mammographic screening needs a supplement or replacement by tomosynthesis or an ultrasonic examination in adjunct in the case of dense breast.

Alternatively, ultrasound nowadays seems to be an independent imaging method irrespective of age and density. To establish ultrasound as a method of early detection of breast carcinoma by its own, larger trials with ultrasound application with means of new technologies and mammography in adjunct should be initiated to find out to which extent ultrasonography alone may miss small carcinomas and if mammography remains necessary together with breast ultrasound. MRI is likely to play a greater role in early detection of breast cancer in the future.

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