Abstract. Aim: This prospective double-blind study was designed to assess (i) if primary breast screening by ultrasonography is capable of detecting breast cancer independent of tissue density and (ii) if the rate of unnecessary biopsies remains acceptable when diagnostics are based on ultrasonography. Patients and Methods: Bilateral breast ultrasonography was performed in 448 asymptomatic women as the initial diagnostic method. Sonograms were interpreted using a set of standardized diagnostic criteria. Subsequently, mammograms were obtained. The radiologists reading the mammograms were blinded to the sonographic results. Results: Overall, 3 non-palpable breast cancers were detected by ultrasound and mammography. All 3 ultrasonographically detected breast cancers were smaller than 1 cm (0.7, 0.7, 0.6 cm). All 3 carcinomas were correctly detected by both methods. For ultrasonography, the false positive rate was 1.1% (n=5) and for mammography 0.6% (n=3). When both methods were combined, the rate of unnecessary open biopsies was 1.6% (n=7). The ratio of benign to malignant lesions was 3.7/1. Conclusion: Without prior mammography, primary high-resolution breast ultrasonography is capable of detecting non-palpable breast carcinomas in asymptomatic women at an early stage. The rate of unnecessary open biopsies is low and the ratio of benign to malignant biopsies acceptable.

So far, early detection by periodic mammographic screening represents the only method proven to lower mortality figures (1-4). Mammography (M) is associated with a false negative rate (FN) of 10 to 15% (5-7). Several authors agree that technical issues, such as outdated equipment incomplete visualization of the breast, insufficient compression, inadequate exposure, film or foil defects, superimposition and processes mimicking calcifications, and reading errors are two factors contributing to FN mammographic readings (8-11). Stringent quality standards and inspections can eliminate most such issues. Strict certification rules should help lower the risk of mammograms being interpreted by inexperienced staff. Rigorous regular recertification helps to minimize the human factor, but other issues may only be somewhat, or not at all, controllable. In addition to ethnic factors primarily patient age and breast tissue density are directly interrelated. In cases of dense breast tissue (ACR 3 and 4), one needs to expect up to a 40% rate of FN mammograms (5-7). A number of studies showed that, in patients with dense breast tissue, complementary ultrasonography (US) is capable of raising the sensitivity for the detection of breast cancer (12-23). The size of ultrasonographically detected non-palpable breast tumors was not different from the size of lesions detected by mammographic screening. The common feature of all these reports is that sonography was performed after mammography, and that the examiners were aware of the mammographic results. In our prospective double-blind study, breast ultrasonography was the initial diagnostic

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Key Words: Breast cancer, mammography, breast ultrasound, non-palpable lesions, screening.
method, followed by mammography as the second imaging modality. Radiographers were blinded to the sonographic results. Using a non-selected patient population, this study aims were: (i) to evaluate if primary sonographic imaging is capable of detecting non-palpable breast cancers at an early stage, independent of breast tissue density (ACR 1 to 4); and (ii) to assess if the rate of unnecessary biopsies is acceptable, i.e., comparable, to the approximately 10% false positive (FP) ratio reported for mammographic screening programs (24).

Patients and Methods

From November 30, 1994 to January 1, 2003, a total of 448 asymptomatic women underwent primary bilateral breast ultrasonography at Stralsund Women’s Hospital and at the Greifswald University Department of Gynecology and Obstetrics. All patients had been referred to one of these departments for outpatient or inpatient treatment of gynecologic conditions. For enrollment in this prospective double-blind study, patients had to consent to primary diagnostic breast ultrasonography without prior mammography and to subsequent mammography. Mammograms were interpreted by radiographers, who were unaware of the respective sonographic results, and who were not permitted to use supplementary sonographic imaging. Patients referred for treatment of breast conditions were excluded, except patients scheduled to undergo plastic or esthetic surgical procedures such as reduction or augmentation mammoplasty. Patients with a known history of breast cancer and those with a palpable lesion were also excluded. For sonographic evaluation, a standardized sequence was followed: patients were asked to lie on the examination table in the supine position with their arms crossed behind their head; both sagittal and transverse, as well as radial (ductal), planes were scanned in a meandering pattern; bilateral axillary sonography was compulsory.

Examinations were performed by nine ultrasonographers: 44.6% (n=200) of all examinations were completed by ultrasonographer #1, 31% (n=139) by ultrasonographer #4. When the study was started, none of the ultrasonographers had more than one year of experience with breast ultrasonography.

Image interpretation was based on a set of standardized ultrasonographic criteria for distinguishing benign from malignant lesions (25, 26); final reports were made in accordance with the Breast Imaging Reporting and Data System (BI-RADS) classification 1 to 5 adapted for sonography (27).

Sonographic interpretability was classified as good, limited, or poor. The parenchymal pattern was reported as "extremely dense" (ACR 4 equivalent), "heterogeneously dense" (ACR 3 equivalent), "scattered fibroglandular densities" (ACR 2 equivalent) and "almost entirely fat" (ACR 1 equivalent). Mammography was performed after completing the ultrasonographic examination.

The following units were used to perform mammography: Mammomat 33 Stereo (Philips, The Netherlands) with Agfa HDR PQ (Germany), Mammo Diagnost U6 (Philips, The Netherlands) with Fuji AD Mammofine (Japan), Mammomat C3 and Mammo Diagnost C3 (Siemens, Germany) with Agfa MR Detail S (Germany) or Kodak Min R 2000 (USA), Mammo Diagnost UC (Philips, The Netherlands) with Agfa MR Detail S (Germany). In total, 448 mammograms were performed by 11 radiographers: Radiographer #1 completed 77.5% (n=347) and radiographer #7 10.5% (n=47) of the studies. All radiographers had extensive experience with mammography, having practised mammography for 5 to 22 years. Mammograms were evaluated in accordance with the ACR/BIRADS classifications (27).

After histological results from open or core needle biopsies were available, sensitivity, specificity, positive and negative predictive value, and efficiency of sonography and mammography and the combination of these two imaging modalities were calculated as follows:

\[
\text{Sensitivity:} \quad \frac{\text{True Positive (TP)}}{\text{TP} + \text{FN}} \times 100
\]

\[
\text{Specificity:} \quad \frac{\text{True Negative (TN)}}{\text{TN} + \text{FP}} \times 100
\]

\[
\text{Positive predictive value:} \quad \frac{\text{TP}}{\text{TP} + \text{FP}} \times 100
\]

\[
\text{Negative predictive value:} \quad \frac{\text{TN}}{\text{TN} + \text{FN}} \times 100
\]

\[
\text{Efficiency:} \quad \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FN} + \text{FP} + \text{TN}} \times 100
\]
The combination of ultrasonography and mammography was considered TP when one of the methods showed a suspicious lesion (US-BI-RADS 4 or 5 equivalent, or M-BI-RADS 4 or 5) and a carcinoma was found histologically. Results of the combination of both imaging techniques were considered FP when one or both studies were interpreted as suspicious for a carcinoma.

Based on the histopathological results, a 2-by-2 contingency with absolute numbers (frequencies) was constructed (Table I). Findings reported as "negative" (BI-RADS 1 equivalent), "benign" (BI-RADS 2 equivalent), and "undetermined, probably benign" (BI-RADS 3 equivalent) were eventually assessed as "probably benign", whereas lesions reported as "undetermined, more likely malignant" (BI-RADS 4 equivalent) or "malignant" (BI-RADS 5 equivalent) were assigned to the "probably malignant" group.

**Results**

Mean patient age was 49.12 years (minimum: 21 years, maximum: 89 years). Patients with newly detected breast cancer had a mean age of 71 years (minimum: 51 years, maximum: 84 years). The majority of women were between 40 and 49 years of age (n=146, 32.6%), 23.4% (n=105) were between 30 and 39 years old, 18.8% (n=84) between 50 and 59 years, and 14.3% (n=64) between 60 and 69 years. A total of 261 women were younger than 50 years of age (58.3%). (Figure 1). Three newly-detected breast cancers occurred in post-menopausal women.

Ultrasonographic interpretability was good in 66.2% (n=259), limited in 31.2% (n=122) and poor in 2.6% (n=10) of cases (Figure 2). The breast tissue was reported as extremely dense (ACR 4) in 6.5% (n=26) and as heterogeneously dense (ACR 3) in 7.8% (n=31) of cases. Scattered fibroglandular densities (ACR 2) were seen in 67.7% (n=270) and in 18.0% (n=72) of cases the breast was almost entirely fat (ACR 1) (Figure 3).

Only 6 (1.3%) mammograms and 27 (6%) ultrasonograms were classified as BI-RADS 4 or 5 (Table II). In 14 cases, the diagnosis was verified histologically, i.e., in 3.1% of the 448 breast ultrasonograms and mammograms. The remaining women with sonographic BI-RADS 4 or 5 results, but lower mammographic classification, did not consent to histological confirmation. Among the 14 histological results, three are based on core needle biopsies and 11 on open biopsies. Therefore, the actual rate of open biopsies was 2.4% of 448 sonographic studies and mammograms. Among 448 primary sonographic studies, three
led to the detection of breast cancer in asymptomatic women (0.7%). In these three cases, radiographers, blinded to the sonographic results, interpreted the respective mammograms as malignant. All three of these non-palpable breast cancers were invasive. Histological evaluation revealed two invasive ductal carcinomas and one invasive lobular carcinoma. All three cancers were less than 1 cm in size (0.6, 0.7 and 0.7 cm), therefore pT1b lesions. All malignant findings were visualized sonographically, as well as mammographically. Using both imaging methods combined, all three findings were correctly interpreted as malignant (Table III) (Figure 4-6).

Sonographic imaging by itself was calculated to have 100% sensitivity, 54.5% specificity, a positive predictive value of 37.5%, a negative predictive value of 100% and a 64.3% efficiency (TP: 3, FN: 0, FP: 5, TN: 6, Table IV).

Mammography alone was associated with 100% sensitivity, 72.7% specificity, a positive predictive value of 50%, a negative predictive value of 100% and a 78.5% efficiency (TP: 3, FN: 0, FP: 3, TN: 8, Table V).

The combination of both methods had 100% sensitivity, 36.4% specificity, a positive predictive value of 26.2%, a negative predictive value of 100% and a 50% efficiency. (TP: 3, FN: 0, FP: 7, TN: 4, Table VI).

Table II. Patients broken down by BI-RADS classes 1-5 and ultrasonography and mammography.

<table>
<thead>
<tr>
<th>BI-RADS (Ultrasonography)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>250</td>
<td>149</td>
<td>22</td>
<td>18</td>
<td>9</td>
<td>448</td>
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<td>Percentage</td>
<td>55.8</td>
<td>33.3</td>
<td>4.9</td>
<td>4.0</td>
<td>2.0</td>
<td>100</td>
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<table>
<thead>
<tr>
<th>BI-RADS (Mammography)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
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<tr>
<td>Number of patients</td>
<td>142</td>
<td>268</td>
<td>32</td>
<td>2</td>
<td>4</td>
<td>448</td>
</tr>
<tr>
<td>Percentage</td>
<td>31.70</td>
<td>59.82</td>
<td>7.14</td>
<td>0.45</td>
<td>0.89</td>
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Table III. Study participants with newly detected breast cancer (n=3).

<table>
<thead>
<tr>
<th>Number</th>
<th>ID</th>
<th>Age</th>
<th>US-BI-RADS</th>
<th>M-BI-RADS</th>
<th>Histology</th>
<th>pT in cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E. M.</td>
<td>84</td>
<td>4</td>
<td>4</td>
<td>ILC</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(J-No.: 05490/95)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>G. L.</td>
<td>78</td>
<td>4</td>
<td>5</td>
<td>IDC</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(J-No.: 605/03)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>I. G.</td>
<td>51</td>
<td>4</td>
<td>5</td>
<td>IDC</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
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Discussion

When used as the primary imaging modality, independent of and without knowledge of the respective mammographic results, breast ultrasonography allows the detection of non-palpable breast carcinomas in asymptomatic women, as demonstrated in this study. This confirms the report by
Madjar et al. (28) of a prospective single-blind study. In their study on 1,000 women undergoing breast sonography, 4 breast cancers were detected by ultrasonography, equivalent to a detection rate of 0.4% (28). In our double-blind study, which included both sonography and mammography in 448 patients, 3 malignant lesions were
detected (0.7%). All detected carcinomas were non-palpable. These results demonstrate that high-resolution breast ultrasonography is capable of delineating non-palpable breast cancers, a fact in agreement with many publications (12, 14, 21, 23, 26, 29-35).

Sonographically, tumors measured between 6 and 7 mm with an average size of 6.3 mm. All 3 sonographically-detected carcinomas were smaller than 1 cm. These figures confirm the results of Buchberger et al. (12), Leconte et al. (21), Crystal et al. (14) and Kolb et al. (19), who were also able to show that it is feasible to use ultrasonography for the detection of early breast cancer <1 cm which were in fact mammographically occult in those studies. A multitude of reports have shown conclusively that lesions that are mammographically occult or FN can be detected ultrasonographically, i.e., become TP (28, 30, 31, 36-59) and (5, 13, 14, 16-21, 23, 26, 34, 35, 42, 54, 60-82).

Countless clinical trials indicate that breast ultrasonography is associated with higher sensitivities than mammography; this relates primarily to palpable lesions (29, 38, 44, 50, 54, 66, 69-73, 76, 83-101). Sonography is also the most accurate predictor of the status for axillary lymphnodes (102). Furthermore Color-Doppler ultrasound is the first step in assessing the efficacy of neocochemotherapeutic treatment in patients affected by locally advanced breast carcinoma (103). The fact that breast ultrasonography is more specific than mammography has also been pointed out in numerous studies (44, 54, 66, 71, 73, 76, 86-89, 94-97, 104-112). Many authors used breast ultrasonography as a screening tool (12-23, 31-33, 42, 45, 58, 113-119). The reports by Buchberger et al., Kolb et al., Kolb et al., Crystal et al., Leconte et al. and Zonderland et al. (13, 14, 18, 19, 21 and 23, respectively) in particular cover well-designed studies on large patient populations and show that in patients with mammographically dense breast tissue (ACR 3 to 4), a significant number of additional breast cancers can be detected by breast ultrasonography, thereby increasing diagnostic sensitivity when diagnostic modalities are combined.

Between 1996 and 1998, Buchberger et al. (12) performed high-frequency ultrasonographic examinations, in addition to mammography, in 6,113 asymptomatic women (mean age 48 years) whose breast tissue was classified as ACR 2 to 4. In 21 patients, 23 malignant lesions which had been mammographically occult were detected by ultrasonography. The average tumor diameter of sonographically-detected invasive carcinomas did not differ significantly from the diameters of mammographically-detected tumors. In addition, ultrasonography was used as a supplementary method in 687 women with palpable or mammographically suspicious lesions. In 6,800 women, a total of 103 carcinomas were detected in 96 patients. The average diameter of the 55 invasive and 20 non-invasive carcinomas was 11.7 mm. Among these 75 carcinomas detected by mammography, 66 were also sonographically apparent. Sonographically, 9 carcinomas were not visible, while 8 of these were shown to be ductal carcinomas in situ (DCIS). Microcalcifications were the sole diagnostic clues.
in these cases. A total of 28 carcinomas in 26 women were mammographically occult. The rate of lesions only detectable by ultrasonography was, therefore, 27.1%.

In their prospective study, Kolb et al. (18) showed results comparable to those of Buchberger et al. (12) In a study on mammographic screening (11,220 women), 3,626 women with mammographically-dense breast tissue underwent supplementary ultrasonography (18). In addition to the 61 non-palpable carcinomas detected by mammography, 11 were only sonographically evident. Tumor sizes were not significantly different from the size of mammographically detected carcinomas: 9 out of 11 were <1 cm.

Supplementary ultrasonographic screening increased the detection rate for carcinomas by 17% (18).

Between 1994 and 1996, Zonderland et al. (120) conducted a prospective trial, including 4,811 mammograms. Supplementary ultrasonography (n=1,103) was performed for distinct lesions, mammographically-apparent palpable lesions, palpable lesions without a mammographic correlate and mammographically-apparent non-palpable lesions. A total of 338 carcinomas (312 invasive, 40 in situ) were detected. With supplementary ultrasonography, sensitivity increased significantly from approximately 83% to 91%. In 96 mammographically unremarkable cases, supplementary ultrasonography was used in 27. Among these, 12 were FN, but 25 were TP, including 19 palpable and 5 non-palpable tumors; in one case, the nipple was clinically suspicious. Of the 25 FN mammograms that were TP by ultrasonography, 12 were mammographically occult (8 after an additional review of the mammograms) and 13 were falsely classified as benign.

In 2002, Kolb et al. (19) published the results of another screening study which included 11,130 asymptomatic women who underwent 27,825 screening mammograms. Supplementary breast ultrasonography was completed in 5,418 women (13,547 examinations). The indication was mammographically-dense breast tissue (ACR 2 to 4). In 221 women, 246 carcinomas were detected. Screening breast ultrasonography could increase the number of detected non-palpable invasive carcinomas from 30 to 71; 37 carcinomas (invasive: 36; non-invasive: 1) were only ultrasonographically apparent. In women with dense breast tissue, 25.5% (n=37) of all carcinomas, 29% (n=36) of all invasive and 37% (n=37) of all non-invasive carcinomas were only seen by ultrasonographic imaging. The average diameter of carcinomas solely detectable by ultrasonography was 9.9 mm, including 26 of 37 lesions <1 cm.(19)

Since ultrasonographic screening was capable of detecting tumors as small as those found by mammography at an early stage, and since it also revealed occult carcinomas, Kolb et al. (121) concluded that ultrasonographic screening would add survival benefits.

Between 2000 and 2002, Crystal et al. (14) used breast ultrasonography as ”second line“ screening method in 1,517 asymptomatic women with dense breast tissue (ACR 2-4) and unremarkable mammograms (ACR 2-4). Average patient age was 52.1±8.1 years. Ultrasonography revealed 7 additional carcinomas (0.46%), including 4 in patients with familial predisposition. The rate of ultrasonographic detection of cancer was lower than in some screening mammography studies (122, 123) equivalent to others (124, 125) but higher than in ultrasonographic screening studies.
(12, 20). Upon staging, all 7 carcinomas were pT1 lesions (4-12 mm) with an average tumor diameter of 9.6 mm.

For a screening method to be associated with reduced mortality, 50% of all detected invasive carcinomas should <1.5 cm, as pointed out by Tabar et al. (126). In the study reported by Crystal et al. (14), all invasive carcinomas were <15 mm (67%, <10 mm).

The frequency of minimal-invasive interventions was 2.5% (n=38, 17 fine-needle aspiration cytologies, 21 core needle biopsies).

Biopsy rates reported in the literature run between 5.2% (20) and 7.4% (12). For mammographic screening, a biopsy rate of 1-3% is considered acceptable. We believe that our rather low biopsy rate of 2.5% is due to our stringent criteria for image interpretation. During 8 to 30 months of follow-up, we did not detect any interval carcinomas in our population. This short follow-up period does not allow any conclusions regarding reduced mortality figures. Some authors hypothesize, however, that ultrasonography would detect interval cancer at an earlier stage and, therefore, result in lower mortalities (14). It is known that women with interval cancer have higher lethality (127). Several authors evaluated screening mammography in women with dense breast tissue and in high risk cases (14) and urged that multicenter trials should be conducted (128).

Between 2000 and 2001, Leconte et al. (21) assessed 4,236 women. Independent of breast tissue densities (ACR 1-4), bilateral ultrasonography was performed after initial mammography. For ACR 1-2 cases (88% vs. 80%; not significant), ACR 3-4 cases (88% vs. 56%; significant) and non-palpable carcinomas with breast tissue classified as ACR 1-4 (88% vs. 69%; significant), ultrasonography was more sensitive than mammography. Overall, 161 carcinomas (including 50 non-palpable tumors) were detected. Average patient age was 60.7 years. Of the total number of 50 non-palpable carcinomas, 16 (32%) were only seen on ultrasonography, 5 out of 25 in ACR 1-2 tissue, 11 out of 25 in ACR 3-4 tissue. The average diameter of tumors detected by either mammography or ultrasonography was 10.3 mm (2-30 mm), sonographically detected tumors measured 7 mm (4-17 mm). All lesions except one were <10 mm. The authors believe that these excellent results are due to: (i) the two ultrasonographers having many years of experience, and (ii) mammography and ultrasonography were conducted by the same staff. Stringent use of ultrasonography with Tissue Harmonic Imaging (THI) is another explanation (21). THI increases image contrast and resolution and simultaneously suppresses artifacts (129-131).

In 2000, Buchberger et al. (13) published a study, reporting data on 8,970 women with breast tissue classified as ACR 2-4. Normal findings on physical examination and mammography were observed in 8,103 women. Using supplementary ultrasonography, 32 additional carcinomas were detected. The average size of carcinomas was 9.1 mm. The authors achieved an acceptable benign/malignant biopsy ratio of 6.3/1. Our 3.7/1 benign/malignant biopsy ratio study was even lower. The claim that screening ultrasonography raises the number of unnecessary surgical procedures cannot be substantiated.

Finding the greatest common denominator among the countless clinical and screening studies is difficult or impossible. Flobbe et al. (132) unsuccessfully attempted a meta-analysis; we were equally unsuccessful.

As a result of methodological differences (regarding patient populations, indications, population sizes (sometimes too small), examination methods, sonographic techniques, equipment, frequencies, lack of standardized diagnostic criteria, approaches for distinguishing benign from malignant lesions, dependence on the personnel performing the examinations, approaches to previous findings, i.e., mammographic results known or unknown to the radiographer performing breast ultrasonography, non-uniform statistical analysis, objectives, non-uniform assessment of comparative methods, nonuniform histological tumor classification), it is basically impossible to compare the multitude of published reports.

Several limiting factors of our study need to be pointed out, varying equipment, examinations performed with different frequencies, no standardized follow-up, and the varying background of radiographers and ultrasonographers. Despite these shortcomings with our and with many other studies, all studies do show the significant role breast ultrasonography has for early recognition of breast cancer. Neither our study nor any of the other studies were designed to demonstrate that relying on ultrasonography alone would make sense or that ultrasonography could replace mammography. Many studies, including this, aimed at closing the diagnostic gap inherent in mammography in cases of dense breast tissue, invasive lobular carcinomas (ILC) and high risk patients. Instead of replacing mammography by breast ultrasonography, a sensible supplement to mammography should be found, aiming at increased diagnostic safety for patients. Recent reports by Buchberger et al. (12, 13), Kolb et al. (18, 19), Crystal et al. (14) and Leconte et al. (21) are the best proof that this can be accomplished. Our results and those of the cited authors allow the conclusion that breast ultrasonography should become a mandatory part of mammographic screening protocols, initially in high risk patients with dense breast tissue. Data from such a protocol would be suitable for answering the question whether screening supplemented by breast ultrasonography would lead to decreased mortality figures. The success of a screening program is usually thought to be directly dependent on the resulting mortality reduction.

No study directed towards this goal has been published. In the US, such a study was expected to be published, but was only authorized for a high risk group (133, 134). Therefore,
the exciting question of potential mortality reduction in patients with dense breasts remains unanswered. A study in patients with ACR 1 and 2 breast composition appears to be worthwhile, at least in terms of the rate of detected carcinomas. Difficulties in breast ultrasonography as a screening method have several underlying factors; costs on top of those for mammography are one factor, the higher need for experienced staff is another, and this is aggravated by the additional time needed for ultrasonography. Before one considers these factors truly limiting, a study protocol should be designed to obtain hard figures. Conducting country-wide breast ultrasonography as a supplement to mammographic screening for breast cancer will only become feasible after uniform diagnostic criteria are implemented everywhere (23, 26, 79). The BI-RADS lexicon (ultrasonographic BI-RADS equivalent) represents an initial step (27). Standardizing ultrasonographic diagnostic criteria was proven to significantly lower inter- and intra-observer variability, which are markedly higher with ultrasonography than with mammography (20, 26, 79, 99, 104, 135-141).

There is some potential for automated systems contributing to reduced observer variability (105, 136, 142-152). In addition, one needs to ensure that sonographers are highly skilled and that the ultrasonographic equipment is of high quality. Quality assurance with respect to both staff and equipment (as implemented for mammography) is an indispensable prerequisite. In summary, if the aforementioned prerequisites are met in the future, it should be possible to successfully incorporate breast ultrasonography as a supplement to mammography in breast screening programs.

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