Primary research

Comparison of written reports of mammography, sonography and magnetic resonance mammography for preoperative evaluation of breast lesions, with special emphasis on magnetic resonance mammography

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Abstract

Patients with abnormal breast findings ($n = 413$) were examined by mammography, sonography and magnetic resonance (MR) mammography; 185 invasive cancers, 38 carcinoma *in situ* and 254 benign tumours were confirmed histologically. Sensitivity for mammography was 83.7%, for sonography it was 89.1% and for MR mammography it was 94.6% for invasive cancers. In 42 patients with multifocal invasive cancers, multifocality had been detected by mammography and sonography in 26.2%, and by MR mammography in 66.7%. In nine patients with multicentric cancers, detection rates were 55.5, 55.5 and 88.8%, respectively. Carcinoma *in situ* was diagnosed by mammography in 78.9% and by MR mammography in 68.4% of patients. Combination of all three diagnostic methods lead to the best results for detection of invasive cancer and multifocal disease. However, sensitivity of mammography and sonography combined was identical to that of MR mammography (ie 94.6%).

Keywords: breast lesions, diagnostic methods

Introduction

Mammography and sonography are the standard imaging techniques for detection and evaluation of breast disease [1]. Mammography is the most established screening modality [2]. Especially in young women and women with dense breasts, sonography appears superior to mammography, and differentiation between solid tumours and cysts is easier. Sensitivity and specificity of sonography or mammography are higher if sonography and mammography are combined [3].

It is generally accepted that MR mammography is the most sensitive technique for diagnosis of breast cancer, whereas the reported specificity of MR mammography varies [4–12]. In those studies, MR mammography was performed and evaluated by highly specialized radiologists in a research setting. It was therefore the purpose of the present prospective study to compare the validity of MR mammography with mammography and sonography in clinical routine practice. Findings for the three diagnostic methods documented on routine reports that

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FFE = fast-field-echo; MR = magnetic resonance.

were available to the surgeon preoperatively formed the basis of this comparison. Special emphasis was placed on the identification of multifocal and multicentric invasive disease.

Patients and methods
Patients
Between September 1995 and September 1998, 413 patients with abnormal breast findings were referred for histological evaluation to the Department of Gynecology of the Friedrich-Schiller University, Jena, Germany. Patients had been selected and referred because of the presence of breast lesions detected by palpation and/or mammography and/or sonography. In addition, MR mammography was performed in all patients. We excluded five patients with invasive cancer who had a history of coreneedle or fine-needle biopsy cancer within 2 weeks before referral, because the presence of haematoma may mimic false-positive findings on MR mammography. In addition, five patients who did not keep still during MR mammography were excluded.

Imaging
Analysis of the sonograms taken in patients with histologically confirmed carcinoma *in situ* were excluded from analysis because the value of sonography for detection of premalignant disease is limited. Mammography was not performed in 32 patients who were younger than 30 years or who had had a mastectomy with suspected local recurrence. For all patients, written reports of mammographic, sonographic and dynamic MR mammographic findings were available preoperatively.

The majority of mammograms (68%) were performed at the Institute for Diagnostic and Interventional Radiology, Friedrich-Schiller-University, using a senograph DMR (GE Medical Systems, Milwaukee, Wisconsin, USA) with standard craniocaudal and mediolateral oblique projections. Mammograms obtained at other institutions that were considered to match the quality standards of our institution were also accepted for evaluation.

All sonography and MR examinations were carried out at the Department of Gynecology and the Institute for Diagnostic Interventional Radiology, Friedrich-Schiller-University, respectively. Sonography was done using a 7.5-MHz linear array probe with a Sonoline Versa Pro (Siemens, Erlangen, Germany). MR mammography was performed exclusively at the Institute for Diagnostic Interventional Radiology, using a Gyroscan ACS II (Philips, Nijmegen, The Netherlands) with a field strength of 1.5 T using a double-breast coil. Dynamic T1-weighted images were aquired using a multislice two-dimensional fast-field-echo (FFE) sequence. We used the following parameters: TR 97, TE 5.0, flip angle 80°, slice thickness 4.0 mm, gap 0.4 mm, field of view 350 mm and transverse orientation. In addition T2-weighted images

(4000/300/90°/4.0 mm/0.4/350 mm) were obtained. As contrast medium, 0.1 mmol gadolinium-DTPA/kg body weight (Magnevist; Schering, Berlin, Germany) was used and injected as a bolus. One unenhanced and seven enhanced studies were acquired with an acquisition time of 1 min. Criteria for malignancy were signal enhancement of 90% or more within the first 2 min after bolus injection and signal plateau or washout phenomena afterward. Additional criteria were irregular borders of the lesion and low signal intensity in the T2-weighted images.

Mammograms were read by three different radiologists, sonography was done by three different gynaecologists and MR mammography was interpreted by a total of six different radiologists.

Definition for multifocal carcinoma was a distance of less than 3 cm and for multicentric carcinoma a distance over 3 cm between various lesions.

Statistical analysis
Interpretation of the various diagnostic procedures was compared with the histological examination with regard to sensitivity, specificity, accuracy, and positive and negative predictive value. Criteria for suspected malignancy in the written reports were the terms 'cancer', 'malignant lesion or tumor', or 'suspicious for cancer'. Sensitivity, specificity, negative and positive predicitive value, and accuracy were evaluated as follows:

Sensitivity = patients with suspected breast cancer/ patients with histologically confirmed breast cancer

Specificity = patients with suspected benign disease/ patients with histologically confirmed benign disease

Positive predictive value = patients with histologically confirmed breast cancer/patients with suspected breast cancer

Negative predictive value = patients with histologically confirmed benign disease/patients with suspected benign disease

Accuracy = patients with true-positive and true-negative detected disease/patients with histologically confirmed breast cancer

A result was classified as false-negative when a diagnostic method classified a histologically confirmed cancer as benign. A result was classified as false-positive when a diagnostic method classified a histologically confirmed benign lesion as cancer. We compared the preformance of all diagnostic methods individually and in combination using the results from all patients. Statistical analysis was performed for all variables with Fisher's exact test and Pearson's χ^2 test.

Results

All patients underwent breast surgery and all abnormal lesions identified by mammography, sonography or MR mammography were surgically removed. A total of 477 breast lesions were examined histologically, revealing the presence of 185 invasive cancers, 38 carcinomata *in situ* and 254 benign lesions (fibroadenoma, papilloma, intraductal or adenoid ductal hyperplasia, cystic mastopathia). There were four patients with malignant lesions in both breasts. In 42 patients multifocal tumours and in nine patients multicentric tumors were found on histological examination. Among the 185 invasive lesions, 178 were primary cancers, five were recurrences, one was metastatic and one was an angiosarcoma. The majority of invasive breast cancers were staged as pT1c (44%). Six per cent of tumors were detected in stage pT1a, 18% in stage pT1b, 25% in stage pT2, 3% in stage pT3 and 4% in stage pT4. The distribution of histopathological tumour types is shown in Table 1. The mean age of patients was 58 years (range 19–85 years).

The sensitivity of MR mammography was significantly higher than those of mammography and sonography ($P < 0.005$ and $P < 0.05$; Table 2). The specificity of sonography was significantly higher than those of mammography and MR mammography ($P < 0.05$ and $P < 0.005$; Table 2). The negative predictive values for sonography and MR mammography were significantly higher than that of mammography ($P < 0.05$ and $P < 0.005$; Table 2). With regard to accuracy, no significant difference between the three modalities was found (Table 2). Combining of all three diagnostic methods yielded the best results for detection of cancer ($P < 0.005$; Table 3). The sensitivity and negative predictive value for the combination of mammography and MR mammography, and the combination of sonography and MR mammography were significantly higher than those for the combination of mammograpy and sonography ($P < 0.05$; Table 3). The highest result for accuracy was seen for a combination of all three methods ($P < 0.05$; Table 3).

Mammography was false-negative in 30 out of 184 invasive cancers, sonography was false-negative in 20 out of 185 cancers, and 10 out of 185 invasive cancers were missed by MR mammography. The majority of false-negative findings was found in stage 1 disease, ductal carcinoma and grade 3 tumors (Table 4). Of 10 invasive cancers missed by MR mammography, eight were found by mammography and sonography. By all three techniques, one invasive ductal carcinoma (pT1b) was misinterpreted as fibroadenoma. In another patient, a microinvasive lobular carcinoma of 5 mm diameter was not detected with mammography and MR mammography, whereas sonography detected a solid, benign tumour. MR mammography identified 10 invasive cancers (5.2%) that were missed by mammography and sonography, whereas one invasive cancer was found by mammography alone. By sonography alone, not a single case of invasive disease was detected when MR mammography or mammography were nonsuspected.

The highest detection rate for multifocal invasive disease was seen with MR mammography, which identified 28 out of 42 (66.7%) histologically confirmed multifocal invasive cancers, whereas mammography and sonography both identified 11 (26.2%) of these cancers ($P < 0.05$). The combination of all three diagnostic methods leads to the best result for detection of multifocality (76.2%; $P < 0.05$), whereas the detection rate with the combination of mammography and sonography was 35.7%, with the combination of sonography and MR mammography it was 69% ($P < 0.05$ versus mammography + sonography), and with the combination of mammography and MR mammography it was 73.8% ($P < 0.05$ versus mammography + sonography). Multifocal invasive disease was suspected in 12 patients by mammography, in 13 patients by sonography, and in 16 patients by MR mammography, but only unifocal disease was confirmed by histology. Out of nine patients with histologically confirmed multicentric invasive cancer, eight (88.8%) of these cancers were detected by MR mammography and five (55.5%) by mammography or sonography. One patient was diagnosed with multicentric invasive–lobular carcinoma stage pT2G2, which had been misinterpreted as benign tumour by sonography and mammography, and as haematoma by MR mammography.

Out of 38 patients with carcinoma *in situ*, mammography (suspicious microcalcifications, exclusively) identified 30 cases (78.9%) and MR mammography identified 26 cases (68.4%). When combining mammography and MR mammography, sensitivity for detection of carcinoma *in situ* increased to 87% (not significant).

Discussion

When the validity of individual diagnostic methods for detection of invasive breast cancer was analyzed, the

Table 1

Histopathology of 185 invasive cancers

Histopathologic diagnosis	Number of lesions
Ductal carcinoma	109
Lobular carcinoma	36
Mixed ductal/lobular carcinoma	16
Mucinous carcinoma	2
Medullary carcinoma	3
Tubular carcinoma	13
Others (metaplastic carcinoma, angiosarcoma, metastases)	6

Table 2

Comparison of mammography, sonography and MR mammography for preoperative prediction of histologically confirmed invasive cancer (*n*=185) or benign disease (*n*=254)

Diagnostic method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Mammography	83.7	68.5	67.8	84.1	77.1
Sonography	89.1	79.1*†	65.7	90.9‡	83.4†
MR mammography	94.6*‡	68.5	68.6	94.6†	79.5

*$P<0.005$, versus MR mammography; †$P<0.05$, versus mammography; ‡$P<0.05$, versus sonography. NPV, negative predictive value; PPV, positive predictive value.

Table 3

Comparison of various combinations of three diagnostic methods for preoperative prediction of histologically confirmed invasive cancer (*n*=185) or benign disease (*n*=254)

Diagnostic methods	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Mammography + MR mammography	98.9*	90.5	88.4	99.1*	94.1
Sonography + MR mammography	98.9*	93.3	91.5	99.2*	95.7
Mammography + sonography	94.6	92.1	89.7	95.9	93.2
All three methods combined	99.4†	95.3	93.9	99.6†	97.0†‡

*$P<0.05$, versus mammography and sonography; †$P<0.005$, versus mammography and sonography; ‡$P<0.05$, versus MR mammography and mammography. NPV, negative predictive value; PPV, positive predictive value.

Table 4

Analysis of false-negative diagnosis of mammography (*n*=30), sonography (*n*=20) and MR mammography (*n*=10) for 185 invasive cancers

Cancer characteristics	Mammography	Sonography	MR mammography
Tumour stage			
1a	1	4	3
1b	8	5	2
1c	11	6	3
2	6	2	2
3	1	1	0
4 (inflammatory)	3	2	0
Histological type			
Ductal	15	13	2
Lobular	11	3	4
Others	4	4	4
Grading			
1	2	3	1
2	10	6	5
3	18	11	4

sensitivity and specificity of mammography ranged from 79.9 to 89% and from 64 to 93.5%, respectively [6,7,13]; for sonography from 67.6 to 96% and from 93 to 97.7%, respectively [13,14]; and for MR mammography from 91 to 98.9 and from 20 to 97.4%, respectively [6–10, 15–17].

The performance of mammography, sonography and MR mammography was compared in three large series (Table 5). The present results are similar with regard to sensitivity and specificity for the detection of malignant breast lesions, with MR mammography reaching the highest sensitivity of all imaging procedures.

When combinations of all three technique were analyzed, mammography and sonography (standard method) had a sensitivity of 83% and a specificity of 92% for detection of malignant disease [3]. A combination of mammography, sonography and MR mammography (combined method) showed a sensitivity of 95% and a specificity of 64% [3]. For nonpalpable lesions, sensitivity increased from 73% by the standard method to 82% for the combined method. Specificity for the standard method (89%) was higher than that for the combined method (71%). For palpable lesions a sensitivity of 85% for the standard and 98% for the combined method was achieved, whereas specificity for the standard method was 100% compared with 45% for the combined methods [3]. The positive predictive value was 94% for the standard and 80% for the combined methods, and the negative predictive values were 78 and 89%, respectively [3]. In the present study, we also found the highest sensitivity, specificity, and positive and negative predictive values for the combination of all three methods. Combination of mammography and sonography was as sensitive as MR mammography alone (94.6% versus 94.6%).

Table 5

Review of the literature: case series that compared mammography, sonography and MR mammography in patients with benign tumours and invasive cancer

Reference	n	Mammography		Sonography		MR mamography	
		Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)
[29]	60	82	96	79	50	95	64
[14]	150	88	88	96	93	98	99
[30]	98	91	–	83	–	98	–

–, not indicated; Sens, sensitivity; Spec, specificity.

The majority of false-positive results for invasive cancer by MR mammography (80 out of 439) were caused by papillomas, intraductal hyperplasia grade 2 or 3, or fibroadenomas in the present series. These lesions have a good blood supply and may mimic invasive cancer [16,18].

Ten out of 185 (5.4%) malignant lesions were classified as false-negative by MR mammography. On histology, the majority of false-negative invasive cancers were lobular cancers (four out of 10). Bone et al [18] reported false-negative results in 11 out of 155 readings, with the majority being lobular cancers on histology. Lack of tumour-induced neovascularity may explain such findings. In particular, invasive lobular cancers infiltrate the normal tissue with columns of single cells, and receive adequate oxygenation without the requirement for increased vascularization [19]. Buadu et al [11] found that lobular and mucinous carcinomas had a low microvessel density.

Multifocality of breast cancers can be recognized adequately by MR mammography [20,21]. Boetes et al [22] reported that all 61 multifocal cancers were detected by MR mammography, compared with 31% by mammography and 38% by sonography. Esserman et al [20] detected multifocality by MR mammography in 100% (10 out of 10) versus 44% (four out of nine) by mammography. Relevant changes in therapy due to additional multicentric and contralateral tumour findings by MR mammography occur in 18% of patients as compared with conventional imaging [23]. We found a detection rate of multifocality of 66.7% by MR mammography, as compared with 26.2% by mammography and sonography. However, in 16 patients multifocal invasive disease as diagnosed by MR mammography was shown to be unifocal by histology.

Kramer et al [24] reported that MR mammography yielded the highest sensitivity for detection of multicentricity as compared with mammography and sonography (89, 66 and 79%, respectively) in 38 patients. These findings are comparable with the present results, in which eight out of nine multicentric cancers were diagnosed correctly.

Carcinoma in situ is identified by mammography through the presence of suspicious microcalcifications. Suspicious microcalcifications are more frequent in intraductal than in infiltrating cancers [25], which was also observed in the present series. Mammography showed a detection rate for carcinoma in situ of 78.9%, as compared with 65.8% by MR mammography; the combination of mammography and MR mammography lead to a detection rate of 86.4%. Fischer et al [26] reported that carcinoma in situ was identified by MR mammography in 25 out of 35 patients (72%); three ductal carcinomata in situ were detected by MR mammography exclusively. Sittek et al [27] reported that 14 out of 20 carcinomata in situ (70%) were correctly diagnosed by MR mammography on the basis of focal increase of signal intensity. Those authors concluded that carcinoma in situ is not reliably detected by MR mammography because of lack of a uniform pattern of enhancement. Esserman et al [20] reported a detection rate of 43% for ductal carcinoma in situ by MR mammography. Among 36 woman with carcinoma in situ, Gilles et al [28] demonstrated two cases without early contrast enhancement.

The present study showed that, for detection of breast cancer, MR mammography is not superior to a combination of sonography and mammography. For identification of multifocal or multicentric disease, MR mammography proved to be the most accurate technique.

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