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# **Breast Tumors: Comparative Accuracy** of MR Imaging Relative to Mammography and US for Demonstrating Extent<sup>1</sup>

*PURPOSE*: To evaluate the comparative accuracy of magnetic resonance (MR) imaging relative to mammography and ultrasonography (US) for assessing the extent of breast tumors.

A present, the most effective imag-**1** ing technique for the detection of breast cancer is mammography. Its sensitivity was close to 90% in a screening population (1). However, the extent of the tumor is often underestimated with this technique (2). Ultrasonography (US) appears to be more accurate than mammography for determining actual tumor size, but results with respect to tumor detection remain disappointing (3). In recent years, contrast material– enhanced magnetic resonance (MR) imaging has been added to the list of imaging techniques for breast lesions. Differentiation between benign and malignant lesions is still problematic in some cases; however, application of the dynamic turbo, fast low-angle shot (TurboFLASH; Siemens, Erlangen, Germany) technique in the breast, which has recently been reported, appears to be promising (4–6). With regard to the performance of MR imaging in size determination, few data are available (7,8). Accurate determination of the extent of a given tumor and possible multifocality is essential when a breast-conserving surgical approach is considered. In the present study, a series of 60 patients with malignant breast lesions were examined with mammography, US, and MR imaging. The findings from these three imaging methods were subsequently compared with histologic examinations. Special emphasis was placed on determination of the size and multifocality of the tumors.

US. Various factors influence the decision to perform a mastectomy. Among these are the size of the tumor in relation to the size of the breast, a mammogram suggesting multifocality or an extensive intraductal component, and the preference of the patient. The mean age of the patients was 53 (range, 32–72) years. Three women who had undergone a previous breastconserving treatment were treated for recurrent cancer. One patient underwent bilateral mastectomy. A total of 61 mastectomy specimens were studied histologically. For the mammographic examination a CGR 600T unit (GE Medical Medical Systems, Milwaukee, Wis) was used. In addition to the standard oblique and craniocaudal projections, magnification views in both projections were obtained in most cases. Whole-breast US was performed with an SSD 650 unit (Aloka, Tokyo, Japan) with a 10-MHz transducer, which allowed sufficient penetration of the breast in all patients. The results of physical examination and mammography were generally known to the investigator. The US examination preceded MR imaging. MR imaging was performed with a Magnetom 63/84SP4000 imager (Siemens, Erlangen, Germany) at 1.5 T. Patients were studied in the prone position with a double breast coil. Gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) at a dose of 0.2 mmol per kilogram of body weight was applied. After sagittal localizer images were obtained, a three-dimensional (3D) magnetization-prepared rapid gradient echo (MP-RAGE) sequence without use of contrast medium was performed (repetition time msec/echo time msec/inversion time  $msec = 10/4/300, 8^{\circ}$  flip angle, 128 sections, effective section thickness of 1.4 mm,  $192 \times 256$  matrix, 300-mm field of view [FOV], transverse orientation, and an acquisition time of 5 minutes). With multiplanar reconstruction, the optimal axial

MATERIALS AND METHODS: Histologic results and preoperative imaging findings (mammography, US, MR imaging) were analyzed regarding tumor size and multifocality of 61 tumors in 60 women undergoing mastectomy for carcinoma.

*RESULTS:* In 10% of cases, the index tumor was not seen at mammography. With US, 15% of the index tumors were not recognized, while MR imaging missed 2% of the index tumors. On mammographic and US images, tumor size was underestimated significantly (P < .005), by 14% and 18%, respectively, while MR imaging showed no significant difference in size compared with that found in a pathologic evaluation. Mammography showed 31% of the additional invasive lesions, while US showed 38% and MR imaging showed 100%.

CONCLUSION: MR imaging was the most accurate of the three preoperative imaging modalities in assessing the size and number of malignant lesions in the breast.

Index terms: Breast neoplasms, MR, 00.121416, 00.12143 • Breast neoplasms, radiography, 00.32, 00.11 • Gadolinium • Magnetic resonance (MR), comparative studies • Magnetic resonance (MR), contrast enhancement • Ultrasound (US), comparative studies, 00.1298

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MATERIALS AND METHODS

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Histologic results and preoperative imaging findings (mammography, US, and MR imaging) in 60 consecutive women undergoing mastectomy for carcinoma were analyzed. These women were suspected of having breast cancer on the basis of clinical findings or conventional imaging studies—that is, mammography and

**Abbreviations:** DCIS = ductal carcinoma in situ, FLASH = fast low-angle shot, FOV = field of view, IDC = invasive duct carcinoma, ILC =invasive lobular carcinoma, MP-RAGE = magnetization-prepared rapid gradient echo, 3D =three-dimensional.

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section plane was then selected through the center of the index tumor. This plane always included a cross section of the descending aorta. In the same plane, 60 sequential breast images were obtained with a temporal resolution of 2.3 seconds during 2 minutes, by using the dynamic TurboFLASH sequence (9/4/15, 8° flip angle, 10-mm section thickness,  $128 \times 256$  matrix, 350-mm FOV, and two acquisitions). After the first four images were acquired, the contrast medium was administered intravenously within 10 seconds, followed by a bolus of 20 mL of normal saline solution. We recently reported a more detailed description of the dynamic TurboFLASH technique (6).

After the TurboFLASH sequence, the 3D MP-RAGE sequence was repeated with tuning parameters adjusted off line to match the precontrast parameter settings. The whole examination, including the precontrast MP-RAGE, the postcontrast dynamic TurboFLASH, and the postcontrast MP-RAGE sequences, lasted about 20 minutes. The data acquired with the TurboFLASH sequence were then transferred to a separate console for subtraction of postcontrast from precontrast images. The subtracted TurboFLASH images were used to determine the start and speed of enhancement, which were subsequently analyzed according to the following criterion: The image on which the descending aorta started to enhance was considered the reference image at time zero. Lesions that started to enhance within 11.5 seconds after a ortic enhancement were considered suspect for malignancy (6). From the subtracted MP-RAGE images, a 3D multiplanar reconstruction of the entire breast was generated to evaluate the index lesion in more detail and to identify other possible foci of enhancement. The images were then evaluated according to the pattern and shape of enhancement. Focal enhancement, especially with irregular borders, was considered suspicious for malignancy (9). Diffuse field enhancement, either homogeneous or inhomogeneous, was considered equivocal, since this pattern of enhancement may be seen in both benign and malignant lesions. MR imaging is always performed before needle biopsy, so surgical changes pose no diagnostic problems. All mastectomy specimens were examlated radiographic-histologic method (10). In this technique the surgical biopsy specimen and the whole-breast specimen are sectioned at 5-mm intervals in the transverse direction and each section is radiographed. Tissue blocks for histologic examination are taken from the radiologically suspicious lesions (ie, those with microcalcifications or architectural distortions) and from areas showing grossly suspicious changes. In any breast specimen, an average of 25 tissue blocks are taken from the quadrant containing the index lesion, in addition nipple, and the central area beneath the nipple-areolar complex. Both the pre-

ined with Egan's serial subgross and correto random samples from other quadrants, the Table 1 Index Tumors Not Recognized with the Different Imaging Modalities, by Histologic Subtype



Note.—CA = carcinoma, DCIS = ductal carcinoma in situ, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma. \* One IDC and one DCIS.

cise site of the tissue blocks taken and the microscopically verified extension of each lesion are indicated on the specimen radiograph (11). This method permits meticulous histopathologic assessment of the extent and possible multifocality of the tumorous process. Enhancing lesions on MR images were identified and located on the specimen radiographs and then in the tissue sections, and the corresponding tissue blocks were studied histologically. The size of the tumor was assessed with all three imaging techniques by determining the longest axis of the tumor. The tumor margins were defined by the area of microcalcification distribution, the extent of the soft-tissue component, and the area of architectural distortion of breast tissue. At MR imaging the longest axis was assessed by measuring the lesion on the subtracted and reconstructed 3D MP-RAGE images. The size differences between imaging-based measurements and specimenbased pathologic measurements were expressed in relative terms. P values for comparative performance in size determination were calculated.

3D MP-RAGE images. For the 40 cases of IDC, the mean time to the start of enhancement on the TurboFLASH images was 6.2 seconds (range, 2.3– 11.5 seconds); for the eight cases of ILC, the mean time was 7.9 seconds (range, 4.6–11.5 seconds); and for the six cases of pure DCIS the mean time was 7.6 seconds (range, 6.9–9.2 seconds).

#### Size Determination of the Index Tumor

The pathologically determined tumor size, based on the largest diameter, varied from 1 to 15 cm. Deviations in the size of the lesions determined with mammography, US, and MR imaging, respectively, compared with those determined histologically, are shown in Figures 1–3. When sizes are expressed in relative terms, mammography and US underestimate the actual tumor size by statistically significant (P < .005) size differences of 14% and 18%, respectively, in contrast to a not significant size difference of only 1% for MR imaging (Table 2, Fig 4). The discrepancies in size for mammography, US, and MR imaging for the various tumor types (IDC, ILC, and DCIS) are listed in Table 3.

# RESULTS

# **Detection of the Index Tumor**

A total of 61 tumors were evaluated. The imaging findings and definite histologic results are summarized in Table 1. In six cases (10%) the index tumor was not visible on the mammograms. With US, nine of 59 (15%) tumors were not recognized. In one case of DCIS and one case of IDC, US was not performed.

All tumors but one were demonstrated with the combined Turbo-FLASH and 3D MP-RAGE MR imaging technique. The single MR imagingnegative tumor was a DCIS with a diameter of 9 cm. Three lesions were not apparent in the chosen Turbo-FLASH section, because the region of interest could not be properly identified on the precontrast 3D MP-RAGE images. However, all three were recognized on the postcontrast

# **Detection of Invasive Tumor** Multifocality

Of the 61 mastectomy specimens, 12 contained a multifocal invasive tumor at histologic examination, with, respectively, one (seven cases), two (two cases), and multiple (three cases) small tumor foci in addition to the index tumor. One specimen contained multicentric lesions at the site of the second invasive tumor, a distance of 4.5 cm from the index tumor (Fig 5). These findings are summarized in Table 4. MR imaging was

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# Table 2

Deviation in Tumor Size with Mammography, US, and MR Imaging Relative to Histologic Tumor Size

Deviation	Mammography $(n = 55)$	US ( <i>n</i> = 50)	MR Imaging $(n = 60)$
Grictonadio	T A 0% *	100/ *	10/ †

benign and malignant solid masses, especially because of the overlap between the features of certain types of fibroadenomas and carcinomas (14). In the present study, in nine of 59 patients no abnormalities were seen with US in the mammographically suspicious area, resulting in a sensitivity of 85%. However, five of the nine US-occult tumors were DCIS. This result is in agreement with the experience of Kopans et al (15), indicating that pure DCIS is often not seen on US scans, and thus US is not suitable for screening purposes. The sensitivity of MR imaging in various studies for detecting carcinoma of the breast is high. Harms et al (16) reported a sensitivity of 100%, while Heywang-Kobrunner et al (17) claimed a sensitivity of 99.5%. In a previous study in which the combined 3D MP-RAGE-Turbo-FLASH technique was used in 83 patients, we achieved a sensitivity of 95% and a specificity of 86% (6). The 3D MP-RAGE sequence has a high sensitivity for detecting lesions, while the TurboFLASH sequence is able to help differentiate between benign and malignant lesions. All but one of the index tumors in the present study were recognized at MR imaging and classified as malignant. The single tumor occult to MR imaging was a well-differentiated (non-comedo) DCIS detected by means of mammographic microcalcifications. On the whole, the most rapid start of enhancement was shown by the



100% accurate in identifying tumor multifocality, whereas mammography had an accuracy of 31% and US had an accuracy of 38%.

# DISCUSSION

Accurate definition of the extent and possible multifocality of tumors is essential for making the choice between the therapeutic options of breast-conserving treatment and mastectomy.

In the present study the results of

# **Detection of the Index Tumor**

The reported sensitivity of mammography for the detection of breast cancer varies between 69% and 90%. Peeters et al (12) reported a sensitivity of 93% and a specificity of 99% for mammography in a breast screening study. Baker (1) reported a multicenter study in which 90% of all malignant lesions were detected in a screening population. In a symptomatic patient population the sensitivity of mammography for malignancy varied from 81% to 96% (13). The sensitivity of 90% in the present study of 60 symptomatic patients is within this range. The most important role of US is the differentiation between cystic and solid masses. While US is 96%–100% accurate in identifying a cyst, it is less reliable in differentiating between

mammography, US, and MR imaging were compared with the final histologic results in 61 mastectomy specimens for determining the actual size of the reference tumor as measured at histologic examination. Also, the accuracy in recognizing additional tumor foci—that is, tumor multifocality was evaluated.

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**Figure 4.** Images of a 65-year-old woman with suspicious microcalcifications in the left breast detected at routine screening. (a) Cephalocaudal and (b) oblique-lateral projection mammograms show microcalcifications in a 3.5-cm-diameter region (arrows). No abnormality was seen in the right breast. (c) Subtracted reconstructed 3D MP-RAGE image shows enhancement in a 7-cm-diameter area. Histologic examination revealed an IDC with a 7-cm diameter.

IDCs. The six cases of pure DCIS began enhancing an average of 1.4 seconds later, while the eight cases of ILC began enhancing at a mean of 7.9 seconds, or 1.7 seconds later than the IDCs.

# Size Determination of the Index Tumor

Fornage et al (3) compared the clinically, mammographically, and sonographically determined sizes of cancers in a series of 31 patients and concluded that mammography is less accurate than sonography in assessing tumor size. Harms et al (5) reported that tumor size can be better assessed with MR imaging than with mammography and that MR imaging often provides better delineation of a lesion than does mammography. In a series of 47 malignant lesions, tumor size measured with MR imaging correlated more closely with histologic measurements than did mammographic measurements in 33 cases (7). Gribbestad et al (18) also demonstrated that MR imaging showed better accuracy in tumor size determination than did mammography. In the present study, MR imaging proved to be the most accurate method for assessment of tumor size (Figs 1–3, Table 2). Nevertheless, an extreme discrepancy was noted in the case of an ILC in which the pathologic tumor diameter was 15 cm, but only part of it—namely, 4 cm—enhanced. Also, a well-differentiated (non-comedo) type of DCIS with a diameter of 9 cm showed no enhancement at all. In a subset of eight patients, we also studied the capability of MR imaging

## Table 3

Deviation in Tumor Size with Mammography, US, and MR Imaging Relative to Histologic Tumor Size, by Tumor Type

Tumor Type	Mammography	US	MR Imaging
IDC	-5%* (37)	-9%* (37)	-3%* (41)
ILC	-37% <sup>†</sup> (7)	-43% <sup>†</sup> (8)	-16%* (9)
DCIS	-29% <sup>†</sup> (8)	(2) <sup>‡</sup>	-8%* (7)

- Note.—Numbers in parentheses are number of tumors.
  - \* Not significant.
- $^{\dagger} P < .05.$
- <sup>‡</sup>Not performed.

to show an extensive intraductal comporient in association with the invasive tumor (19). While the size of the invasive part was correctly estimated, the DCIS component, with an average extension of 3.5 cm (range, 1–7 cm), was underestimated by more than 1 cm in all patients. In six of these eight patients the DCIS was histologically of the well-differentiated (non-comedo) type. This finding is in accordance with the results of Greenstein Orel et al (20), who describe how some cases of DCIS may be impossible to identify with MR imaging. In contrast, Heywang-Kobrunner (21) describes a series of 19 DCIS tumors that apparently all enhanced.

Detection of Invasive Tumor Multifocality mammography. These data indicate that while mammography is accurate in detecting the reference lesion, it is less accurate in identifying multifocality.

To our knowledge, no results on the ability of US in detecting breast tumor multifocality have been reported. Harms et al (7) reported that MR imaging depicted all additional mammographically occult cancers in 11 of 30 cases in which the wholebreast specimen was serially sectioned (7). Heywang-Kobrunner and Oellinger (22) reported that MR imaging was able to show 80% of all malignant foci, whereas mammography showed only 20%. In the present study, all histologically proved additional malignant invasive lesions were identified on MR images (Table 4). All these foci were characterized by irregular edges on the 3D MP-RAGE images. Two fibroadenomas were correctly identified on 3D MP-RAGE images; however, three additional lesions that fulfilled our MR imaging criteria for malignancy turned out to be fibroadenomas. The results of this study indicate that MR imaging can play a comple-

Holland et al (2), in a study of 282 invasive cancers, showed that in 43% of the tumors, additional tumor foci were present beyond 2 cm from the margin of the index tumor (2). The majority of these foci were occult at

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 Table 4

 Sensitivity of the Three Imaging Modalities for Detecting Invasive Tumor

 Multifocality and Unifocality

Туре	Mammography	US	MR Imaging
Multifocality $(n = 13)$ Unifocality $(n = 48)$	31% (4) 100% (48)	38% (5)	100% (13)
		10070 (40)	/ ( ( )

Note.—Numbers in parentheses are number of tumors.

vide a better assessment of the extent and multifocality of the malignant process. In this retrospective study, we analyzed 61 mastectomy specimens. Multifocality was noted histologically and with MR imaging in 13 patients, whereas it was seen with mammography in only four cases. Since the choice between breast-saving therapy and mastectomy is not only based on preoperative imaging findings but also on the judgment of the surgeon and the wish of the patient, it is difficult to isolate the effect of MR diagnosis alone on patient treatment. Because false-positive diagnoses are rare in our experience, it can be concluded that MR imaging was decisive in a maximum of nine patients. In conclusion, the histologic findings of 61 mastectomy specimens were correlated with preoperative mammography, US, and MR imaging results. MR imaging showed all histologically proved malignant lesions except one and allowed estimation of the size of the tumor more accurately than did mammography or US. The size of larger tumors was especially underestimated with mammography and US. Additional malignant lesions, in particular invasive foci of multifocal tumors, were best identified with MR imaging.

- 7. Harms SE, Flamig DP, Hesley KL, et al. MR imaging of the breast with rotating delivery of excitation off resonance: clinical experience with pathologic correlation. Radiology 1993; 187:493–501.
- Davis PL, Staiger MJ, Harris KB, Ganot MA. 8. Accuracy of breast cancer measurements with MR imaging, US, and mammography (abstr). Radiology 1994; 193(P):267. Heywang-Kobrunner SH. Contrast-en-9. hanced MR imaging of the breast. Basel, Switzerland: Karger, 1990; 47. Egan RL. Multicentric breast carcinomas: 10. clinical-radiographic-pathologic whole organ studies and 10-year survival. Cancer 1982; 49:1123–1130. Holland R, Hendriks JHCL, Verbeek ALM, 11. Mravunac M, Schuurman Stekhoven JH. Extent, distribution, and mammographic/ histological correlation of breast ductal carcinoma in situ. Lancet 1990; 335:519–522. Peeters PHM, Verbeek ALM, Hendriks 12. JHCL, van Bon MJH. Screening for breast cancer in Nijmegen: report of six screening rounds, 1975–1986. Int J Cancer 1989; 43: 226 - 230.Holland R, Hendriks JHCL, Mravunac M. 13. Mammographically occult breast cancer. Cancer 1983; 52:1810–1819. Jackson V. The role of US in breast imag-14. ing. Radiology 1990; 177:305-311. Kopans DB, Meyer JE, Lindfers KK. 15. Whole-breast US imaging: four-year fol-



**Figure 5.** Images of a 44-year-old woman who had undergone breast-saving therapy 2 years previously for an IDC of the left breast and who now presented with a palpable lump in the lateral upper quadrant of the same breast. (a) Mammogram shows an irregular 1.5-cmdiameter lesion (arrow), along with a surgical clip from the previous operation. US findings confirmed the presence of the lesion. (b) Subtracted sagittally reconstructed MP-RAGE image shows two enhancing lesions (arrows),

#### References

- 1. Baker LH. Breast Cancer Detection Demonstration Project: five year summary report. CA 1982; 32:194–225.
- Holland R, Veling SHJ, Mravunac M, Hendriks JHCL. Histologic multifocality of tis, T1–2 breast carcinomas. Cancer 1985; 56: 979–990.
- 3. Fornage BD, Toubas O, Morel M. Clinical, mammographic and sonographic determination of preoperative breast cancer size. Cancer 1987; 60:765–771.
- 4. Flickinger FW, Allison JD, Sherry RM, Wright JC. Differentiation of benign from

low-up. Radiology 1985; 157:505–507.

- 16. Harms SE, Flamig DP, Hesley KL, et al. Fat-suppressed three-dimensional MR imaging of the breast. RadioGraphics 1993; 13:247–267.
- 17. Heywang-Kobrunner SH, Wolf A, Pruss E, Hilbertz T, Eiermann W, Permanetter W. MR imaging of the breast with Gd-DTPA: use and limitations. Radiology 1989; 171: 95–103.
- Gribbestad IS, Nilsen G, Fjøsne H, et al. Contrast-enhanced magnetic resonance imaging of the breast. Acta Oncol 1992; 31: 833–842.
- 19. Boyages J, Recht A, Connolly JL, et al. Early breast cancer: predictors of breast recurrence for patients treated with conservative surgery and radiation therapy. Radiother Oncol 1990; 19:29-41.
- 20. Greenstein Orel S, Schnall MD, LiVolsi VA, Troupin RH. Suspicious breast lesions: MR imaging with radiologic-pathologic correlation. Radiology 1994; 190:485–493.
- 21. Heywang-Kobrunner SH. Brustkrebsdiagnostik mit MR: überblick nach 1,250 patienten. Electromedica 1993; 61:43–52.

one corresponding to the index tumor and an additional 1-cm-diameter lesion just caudal to the mamilla. Histologic examination revealed that both lesions were IDCs.

mentary role to mammography and US in guiding the surgical treatment of breast cancer, by its ability to promalignant breast masses by time-intensity evaluation of contrast enhanced MR imaging. Magn Reson Imaging 1993; 11:617–620.
5. Harms SE, Flamig DP, Hesley KL, Evans WP. Magnetic resonance imaging of the breast. Magn Reson Q 1992; 8:139-155.
6. Boetes C, Barentsz JO, Mus RD, et al. MR characterization of suspicious breast lesions with a gadolinium-enhanced Turbo-FLASH subtraction technique. Radiology 1994; 193:777–781.  Henten, Electromedica 1993; 61:43–52.
 Heywang-Kobrunner SH, Oellinger H. Breast: Magnevist monograph. Oxford, England: Blackwell Scientific Publications, 1994; 79–84.

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