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ORIGINAL ARTICLE

Magnetic resonance imaging of the breast: potential for lesion characterization

N. Rotaru[1], A. Luciani[2]

[1]Department of Radiology, "N. Testemitanu" University of Medicine and Pharmacy, Chisinau, Moldova; [2]Department of Medical Imaging, Henri Mondor University Hospital, Creteil, France

Summary

Purpose: *To study the diagnostic performance of conventional mammography and dynamic contrast-enhanced magnetic resonance mammography (MRM) with regard to the detection of breast malignancy and recognition of a multifocal cancer, in particular in a dense breast.*

Materials and methods: *Patients with abnormal breast findings (n=93; 30 malignant and 63 benign) were examined by mammography, sonography and MRM. In all patients, high-quality two-view mammography and 7.5 MHz sonography of both breasts were performed before MRM. Images were acquired on 1.5T scanner system. All lesions had been histologically confirmed.*

Results: *The highest detection rate for multifocal invasive disease was seen with MRM, which identified 21 (72.5%) out of 29 histologically confirmed multifocal invasive cancers, whereas mammography identified 6 (20.5%) out of 24 (p=0.003). Lymph node metastases were present in 11 (37%) of 30 patients with malignant invasive carcinoma. MRM showed a sensitivity of 94.6%, specificity 78.5%, and accuracy 79.5%.*

Conclusion: *Compared with triple assessment for clinically overt and occult breast disease, MRM offers higher sensitivity for the detection of multifocal cancer, which is important in selecting patients appropriate for breast-conserving surgery. In conclusion, the multiplanar capability of MRM enables it to provide more definite information than mammography and ultrasonography. MRM is presently able to better stage breast cancer locally and to measure more accurately breast cancer size, and determine multicentricity.*

Key words: breast cancer, breast lesions, diagnostic methods, magnetic resonance mammography, mammography, ultrasonography

Introduction

The use of magnetic resonance imaging (MRI) in the evaluation of breast disease has continued to gain recognition over the last 15 years.

Early detection and treatment of breast tumours are critical for a favorable outcome.

MRM relies on the presence of well-established morphological features that help distinguish malignant from benign lesions. In addition, angiogenesis induced by cancer is demonstrated by dynamic contrast-enhanced MRI. Areas of increased microvessel density are delineated following intravenous gadolinium (Gd).

Contrast-enhanced MRM has been shown to serve as a clinically useful additional diagnostic tool for selected diagnostic problems [1].

Compared with conventional mammography and breast ultrasonography for clinically overt and occult breast disease, MRM offers higher sensitivity for the detection of multifocal cancer, which is important in selecting patients appropriate for breast-conserving surgery.

These include preoperative staging before a planned breast-conserving surgery in patients with dense parenchyma to exclude multicentricity, additional evaluation of dense breast tissue and scarring

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Author and address for correspondence:

Natalia Rotaru, MD
Department of Radiology
"N. Testemitanu" University of Medicine and Pharmacy
165 Blv Stefan cel Mare
MD 2004
Chisinau
Moldova
E-mail: nataliarotaru@yahoo.com

after breast-conserving therapy, evaluation of breast implants, and detection of the primary carcinoma in patients with axillary lymph node metastases [2].

Unilateral multifocal cancer has a frequency of a least 30% and is seldom detected by clinical examination [3-5]. Definition of multifocal disease by way of histology represents a diagnostic difficulty in some cases, as these multifocal lesions may display different histological subtypes. It seems, however, that the presence of multifocal lesions implies a high probability of malignancy and poor prognosis.

The aim of this study was to assess the diagnostic performance of conventional mammography, breast ultrasonography, and dynamic contrast-enhanced MRM with regard to the detection of breast malignancy, and recognition of a multifocal cancer, in particular in a dense breast.

Materials and methods

One hundred equivocal mammographic abnormalities from 93 consecutive patients evaluated at the Henri Mondor Hospital (France) from October 2002 to May 2003 were included in the study. Patients had been selected and referred because of the presence of breast lesions detected by palpation and/or mammography and/or sonography.

Images were acquired on 1,5T scanner system. The MRM protocol consisted of the following sequences: T1-weighted coronal TSE, a dynamic EG T1 (TR =14 ms/TE=5.6 ms/flip angle=25^0, slice thickness 2.6 mm, FOV 320 mm, Tps Acq=52 sec, matrix 256×96), and finally a T2-weighted SE-image.

During dynamic sequence, one native and 7 sets of images were recorded each minute after intravenous injection of 0.1 mmol/kg Gd, followed by an injection of saline. Original images and subtraction images from the dynamic series were the basis for evaluation.

The most successful protocol in MRM that permits differentiation of malignant from benign lesions combines two techniques: 1) surface coils for adequate spatial resolution, and 2) dynamic contrast enhancement studies (2D high temporal resolution with low spatial resolution, or 3D low temporal with high spatial resolution).

Subtraction images were obtained with the use of a software subtraction function.

Breast density was estimated visually with quantitative measures, that is, the percentage of the area of the breast encompassed by fibroglandular tissue dense enough to obscure a cancer was estimated.

In all patients, high-quality two-view mammography and 7.5 MHz sonography of both breasts were performed before MRM. Therefore, for each lesion, a full set of examination data including histopathological diagnosis were available.

MRM was performed in women with suspicious or equivocal results in conventional mammography and ultrasonography because of either dense parenchyma or heterogeneous echogenicity with dorsal shadowing with a purpose to exclude multifocal disease or contralateral breast cancer.

Definition of multifocal carcinoma required a distance <3 cm and for multicentric carcinoma a distance >3 cm between various lesions.

Interpretation of the various diagnostic procedures was compared with the histological examination with regard to sensitivity, specificity, accuracy, positive (PPV) and negative predictive value (NPV). Sensitivity, specificity, positive and negative predictive 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.

PPV = Patients with histologically confirmed breast cancer/ patients with suspected breast cancer.

NPV = 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.

Statistical analysis was performed for all variables using Fisher's exact test and Pearson's χ^2 test. A p value less than 0.05 was considered statistically significant.

Results

All lesions were analyzed regarding their qualitative characteristics. Lesions were divided into two groups: small (≤ 10 mm) and large (> 10 mm). Estimation of breast cancer size by clinical examination, mammography and MRM are summarized in Table 1. Clinically, the mean estimated size of the lesion was 8.5 cm (range 4-13 cm), by mammography 8.5 cm (range 4-13 cm) and by MRM 7 cm (range 3.5-12 cm). Statistical analysis of the size is summarized in Table 2.

Table 1. Clinical, mammographic and MRM estimation of breast cancer size (cm)

Patient no	*Clinical*	*Mammographic*	*MRM*
1	9	5.5	5
2	13	12	11
3	diffuse	7	4
4	8	6.5	7
5	5	4.5	3
6	diffuse	10	6
7	6	6	5.5
8	12	13.5	9
9	55	12	6
10	7	7.5	7
11	7	diffuse	6.5
12	12	14.5	8
13	9	12.5	6
14	10	9	6
15	13	diffuse	10
16	11	8.5	11
17	9	9	7
18	9	5	6
19	6	3	3
20	8	diffuse	7
21	5	3	2.5
22	7	3	3
23	15	13	11
24	diffuse	13	12
25	5	10	10
26	8	11	8
27	8	7	6
28	4	4	4
29	diffuse	14	diffuse
30	10	11	8.5
Mean size (range)	8.5 (4-13)	8.5 (3-14)	7 (3.5-12)

Table 2. Statistical analysis of the lesions' size

	*Deviation, mean**	*DDL*†	*t*§	*p*	*95% C.I.*
Clinical/MRM	1.7	24	4.14	0.0004	0.85 - 2.55
Clinical/ Mammoghraphy	0.25	21	0.42	0.68	–0.99 - 1.5
MRM/ Mammography	–1.4	26	–3.5	0.0017	–2.24 - –0.58

*theoretical deviation=0, †difference of the maximal diameter of a lesion, §correlation factor

Additionally, the following lesions' characteristics were investigated separately on the first and last contrast-enhanced series: lesions' shape, characterized as regular (oval, round, or polygonal), or as irregular (linear, branching, or stellate); margin type (ill-defined or well-defined), and homogeneity of contrast medium enhancement (homogeneous or inhomogeneous; Table 3).

Uni-or multifocality is presented in Table 4. The highest detection rate for multifocal invasive disease was seen with MRM, which identified 21 (72.5%) out of 29 histologically confirmed multifocal invasive cancers, whereas mammography identified 6 out of 29 (20.7%; p=0.003).

Lymph node metastases were present in 11 (37%) of 30 patients with malignant invasive carcinoma.

The sensitivity of MRM was significantly higher compared to mammography and sonography ($p < 0.005$ and $p < 0.05$, respectively; Table 5). The specificity of sonography was significantly higher than those of mammography and MRM ($p < 0.05$ and $p < 0.005$, respectively; Table 5 and 6). The PPV of MRM was much higher than mammography and sonography ($p < 0.005$; Table 5). The NPV for sonography and MRM were significantly higher than that of mammography ($p < 0.05$ and $p < 0.005$, respectively; Table 5). With regard to accuracy, no significant differences between the 3 imaging methods were found (Table 5). Combination of all 3 diagnostic methods (MRM, mammography and sonography) yielded the best result for cancer detection (PPV=95.3%, $p < 0.005$).

Discussion

If MRM detects multicentric or multifocal breast cancer, which is a major correlate of local disease recurrence, then both the patient and her physician could reach a more correct treatment choice about the type of mastectomy, axillary clearance and adjuvant chemohormonotherapy and/or radiotherapy. If the patient accepts the increased risk associated with the presence of multicentric disease and chooses a minor surgical treatment, she can then be more closely monitored through MRM during follow-up after radiation therapy ± chemohormonotherapy.

Multicentric breast cancer is quite common. Holland et al. [5] demonstrated additional cancer foci separated from the primary cancer in 63% of cases of mastectomy specimens of 282 invasive T1 (< 2 cm) and T2 (2-5 cm) cancers. Forty-three percent

Table 3. MRM findings in 93 pathologically characterized breast lesions

Lesion characteristics	*Carcinoma (n=30)*	*Fibroadenoma (n=36)*	*Other benign conditions (n=27)*
Morphology			
Shape			
regular (round, oval, or polygonal)	2	24	19
irregular (linear, branching, or stellate)	28	12	8
Margin type			
well-defined	27	7	6
ill- defined	3	29	21
Enhancement pattern			
homogeneous	5	20	20
heterogeneous	6	16	7
peripheral	5	–	–
plateau unique	2	32	26
multifocal	20	4	1
Dynamics			
Initial enhancement (%)			
< 50	1	34	25
50-100	26	2	2
> 100	3	2	–
Signal intensity curve			
continuous enhancement	1	30	26
plateau	2	6	1
washout	27	0	0

Table 4. Histologically confirmed breast cancer extent as detected by mammography and MRM

	Mammography, n (%)	*MRM, n (%)*	*p-value*
Unifocal	16 (55)	7 (24)	0.005
Bifocal	4 (14)	1 (3.5)	0.005
Multifocal	6 (20.5)	21 (72.5)	0.003
Diffuse	3 (10.5)	–	–

(27% *in situ* and 16% invasive) were more than 2 cm away from the primary tumor.

To determine enhanced MRI sensitivity for multicentric breast cancer, Harms et al. [6], Orel et al. [7] and Boetes et al. [8] studied women with MRM who had breast cancers with good pathologic analysis for multicentricity. A total of 153 breast cancers were analyzed in the 3 studies. Forty (26%) of these women were pathologically proven to have additional macroscopic cancer foci separate from the primary tumor. Ninety-eight percent of these additional cancer foci were detected by MRM, and over 70% were missed by mammography. Esserman et al. [9] detected multifocality by MRM in 100% of their cases *versus* 44% by mammography.

Accumulated data on sensitivity and specificity of MRM are given in Table 6.

We found a detection rate of multifocality of 72.5% by MRM, as compared with 20.5% by mammography and sonography.

Table 5. Comparison of mammography, sonography and MRM for preoperative prediction of invasive cancer (n=30) or benign disease (n=63)

Diagnostic method	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*[1]	*NPV (%)*[2]	*Accuracy*
Mammography	83.7	68.5	67.8	84.1	77.1
Sonography	89.1	79.1	65.7	90.9	73.4
MRM	94.6	78.5	78.6	94.6	79.5

[1]positive predictive value; [2]negative predictive value

Table 6. Sensitivity and specificity of MRM in the detection of breast cancer according to several authors

Authors	*No of studies*	*Sensitivity %*	*Specificity %*
Heywang-Kobrumer 1993 [1]	525	99	65
Kaiser 1994 [2]	991	97	97
Harms 1993 [6]	67	100	29
Orel 1994 [11]	44	94	71
Boetes 1994 [12]	87	95	86
Gilles 1994 [13]	143	95	53
Fobben 1995 [14]	91	83	83
Stomper 1995 [15]	51	92	62
Bone 1996 [16]	250	93	73
Kramer 1998 [17]	33	100	93
Malich 2001 [18]	100	98	81
Belli 2002 [21]	22	100	88.8

However, in 24% of the patients diagnosed with multifocal invasive disease by MRM, mammography showed unifocal tumor.

Kramer et al. [4] reported that MRM yielded the highest sensitivity for detection of multicentricity as compared with mammography and sonography (89.66 and 79%, respectively, in 38 patients).

The present TNM staging system takes into consideration tumor size, nodal involvement, and metastases. MRM is able to improve the determination of breast tumor size and extent over presently used techniques. It is now more critical to know the size and tumor extent within the breast, whether it invades adjacent tissues, and if multicentric disease is present.

Tumor size and extent primarily influences the choice of local treatment. In a study palpation was incorrect in 25% and mammography was incorrect in 10% [10].

MRM is more accurate for measuring breast cancer size. Since MRM can acquire data in a volumetric method, it should be able to obtain even more accurate tumor volume measurements based on 3-dimensional depiction of the frequently irregular tumors [3].

In conclusion, the multi-planar capability of MRM enables to provide more definite information than mammography and ultrasonography. MRM is presently able to better stage breast cancer locally and to measure more accurately breast cancer size, and determine multicentricity.

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