REVIEW ARTICLE
UDC: 618.19-006:616.072

Magnetic resonance mammography in diagnostics of breast tumour

Dragana Bogdanović

ABSTRACT

Breast cancer is the most common malignant neoplasm in female population. The complexity of early breast carcinoma diagnostics is conditioned by the variability of the breast structure during life, as well as cyclic, hormone conditioned changes. Today, the most important and the most widely applied radiological modality is mammography, which value has been proved by many studies. Up-to-date diagnostic algorithm also includes the breast evaluation by ultrasound with the probes of 7.5 and 10 MHz that provide for high tissue resolution. Magnetic resonance currently presents the most up-to-date visualization modality. Its basic technical possibilities: multiplanarity, high area, and tissue resolution combined with biological noninvasiveness, unambiguously make MR the most sensitive and the most specific radiological method for evaluation of the majority of organism regions.

KEY WORDS: *Mammography; Magnetic Resonance Imaging; Breast Neoplasms; Diagnosis; Sensitivity and Specificity*

Institute of Oncology Sremska Kamenica, Serbia & Montenegro, Address correspondence to: Dr. Dragana Bogdanović, Institute of Oncology Sremska Kamenica, Institutski put 4, 21204 Sremska Kamenica, Serbia & Montenegro; The manuscript was received: 02.03.2004, Provisionally accepted: 04.04.2004, Accepted for publication: 04.04.2005

INTRODUCTION

Breast cancer is the most common malignant neoplasm in female population. It is estimated that each ninth women is affected during the lifetime. The incidence of the breast cancer has slightly increased during the last 50 years, in contrast to the majority of other malignancies in women, which show continuing decrease. Yearly, about 800-900 new cases of breast cancer are discovered in Vojvodina.

The complexity of early breast carcinoma diagnostics is conditioned by the variability of the breast structure during life, as well as cyclic, hormone conditioned changes.

Today, the most important and the most widely applied radiological modality is mammography, which value has been proved by many studies. Nevertheless, the method also has its limits, the knowledge of which contributes to avoid falsely adverse results. The basic lack of the mammography is the impossibility of lesion demarcation in dense breast with well-preserved fibrograndular tissue, as well as with diffuse fibrocystic changes. Further on, the sensitivity and specificity of the mammography is limited by the fact that early malignancy often shows non-characteristic image. The evaluation of post-therapeutic breast also falls into the group of the changes where the mammography does not demonstrate satisfactory results.

Up-to-date diagnostic algorithm also includes the breast evaluation by ultrasound (US) with the probes of 7.5 and 10 MHz that provide for high tissue resolution. The main role of ultrasound application is the differentiation of palpable changes, as well as the differentiation solid vs. cystic lesions, where the specificity is 98%. The evaluation of secretory breast, the suspected rupture of silicon implant, as well as the detection of the tumour within radiographically dense breast with positive familiar history, fall into the group of relative indications. Except for the visualisation capabilities, the application of US is exceptionally significant in interventional procedures. Today this diagnostic modality is widely accepted in aspiration of cysts, in core biopsy, and ductography.

Color Doppler ultrasonography is applied in benign/malignant differentiation detecting increased capillary flow in the areas of newly founded vascular bed (1).

Magnetic resonance (MR) currently presents the most up-to-date visualization modality. Its basic technical possibilities: multiplanarity, high area, and tissue resolution combined with biological noninvasiveness, unambiguously make MR the most sensitive and the most specific radiological method for evaluation of the majority of organism regions.

IMAGING PROTOCOL

The protocol of breast screening includes the use of special surface coil, where the patient is in prone position. Examination technique is different from the examination methodology of other body regions. Namely, contrast application is necessary and the dynamic study is mandatory, i.e. the monitoring of contrast dynamics within the respectively repeated time intervals.

Paramagnetic contrast agent (Gd-DTPA) is applied through extended system during the period of the first series of the dynamic study and approximately ten seconds before its end. The contrast is applied in bolus and immediately after the contrast dose 20ml of 0.9% NaCl is injected in the system. The whole process must not last longer than 30 seconds in order for the examination to be valid (2) (the protocol in the Centre for imaging diagnostics means the injection of the contrast and physiological solution in the duration of maximum 15 seconds). Prolonged initiation of contrast medium (CM) consecutively decreases its presence in potential lesion and deforms $\Delta S/\Delta t$ curve and thus devalues correct image analysis.

Gd-DTPA dosing is the subject of many studies and primarily depends on the dynamic study that is undertaken, as well as on the intensity of MR scanner magnetic field. According to the recommendation of Sylvia Heywang et al., for 2D-FLASH dynamic study the dose is 0.1mmol/kg, and with such conditions the obtained $\Delta S/\Delta t$ curve has a logarithm form, while using 3D-FLASH technique, the CM dose is 0.166 mmol/kg, presented $\Delta S/\Delta t$ curve has linear trend. Comparative studies with different contrast doses and the same puls sequence showed higher sensitivity to the detection of small lesions with the use of the dose of 0.16 mmol/kg. Such a dosing means the application of the contrast in the dose of 1/3 in relation to the body mass expressed in millilitres; it does not mean that the patient with the weight of 60 kg should get the contrast dose of 20 ml (3).

The necessity of such a technique is based on the fact that both benign and malignant lesions result in postcontrast amplification of signal intensity, but in contrast to benign ones, malignant ones have the characteristic curve of the rapid signal intensity increase. Biologically, time monitoring of the contrast in internal tumour milieu defines the phases that are consecutively visualized by postcontrast increase of the signal intensity, and after that they are numerically processed and graphically presented.

The first one is early dynamic phase that starts from the moment of the contrast medium emergence in the region of interest from the artery blood vessel. From the pharmacokinetic point of view, in this phase, due to maximum difference in the concentration of contrast medium intravascularly and extracapillarly, the transition is devised with maximum speed, which results in the rapid increase of curve inflection in malignant tissue and consequently increased permeability of newly-founded tumour capillary network.

After the contrast comes to the tumour tissue and the signal intensity achieves maximum value, there is a short contrast preservation, which results in plateau phase, and pharmacokinetically the balance is achieved in transcapillary transfer in both directions. From this moment, the behaviour of paramagnetic contrast has a threefold character and, indeed, in the further dynamic development of the $\Delta S/\Delta t$ curve the differentiation between the benign and malignant lesion is shown (Figure 1,2).

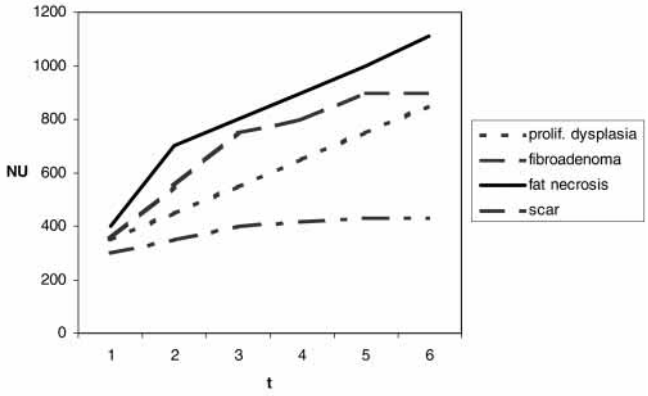

Figure 1. Benign $\Delta S/\Delta t$ curve

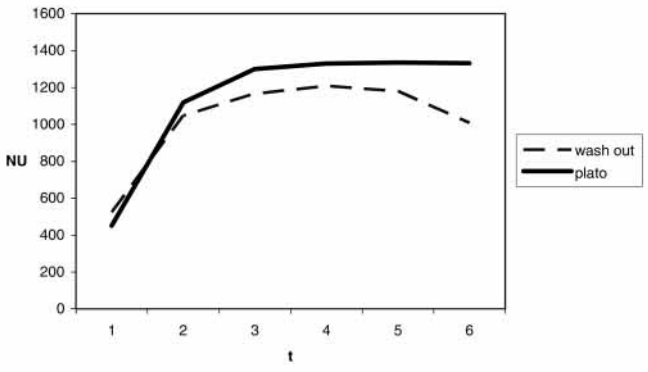

Figure 2. Malignant $\Delta S/\Delta t$ curve

The characteristic of the malignant lesion is its tumour angiogenesis, which leads to wash out, i.e. the exiting of the contrast medium which, on one hand, results in the decrease of the signal intensity in the region of interest, or continuing preservation of the contrast in the tissue in longer time period, consequently related to pathological, fragile neovascularity. In contrast to the malignant one, the benign lesion demonstrates further slight trend of the signal intensity increase in its internal milieu (4).

The function of the paramagnetic contrast is to: Mark the lesion which is not visualised before contrast administration; Mark the lesion from the healthy parenchyma; Place emphasis on the type of signal intensity increase after contrast administration; Create dynamic and functional study in the region of interest. The biological basis of the contrast presentation in the malignant lesions is the consequence of the presence of neoangiogenesis, the phenomenon that is typical form invasive tumours; the presence of newly-created pathological capillary network is correlated with increased pathological vascularity, vascular permeability, as well as with the increase of interstitium in the malignant tumour (in comparison with the benign one) and the consecutive increase of the paramagnetic increase in the region of interest.

Literature data show the fact that majority of invasive carcinomas behave according to this type, providing fast and intensive postcontrast intensification, and on the basis of such approach, very high sensitivity and specificity are achieved, which ranges, according to different authors, from 86% to 100% and from 51% to 100%, respectively (4).

LESION ANALYSIS

Quality analysis

The quality analysis of images is based on the detection of the postcontrast focal/diffuse enhancement. The lack of the postcontrast enhancement with suspected clinical and/or radiological finding indicates further monitoring.

The analysis of lesion contours characteristics may only partially be applied in the evaluation of MR mammography, since it provides far more sophisticated discrimination criteria. It is necessary to mention that old inflammatory, dysplastic lesions, as well as the zones of fatty necrosis may be presented with exceptionally badly defined contours, and even with pseudospiculated extensions and with the disturbance of the architectonics. Such cases require careful analysis of postcontrast study and the evaluation of the postcontrast curve in the function of time. However, even besides the defined criteria benign/malignant, falsely positive results are evident in particular number of cases. Therefore, the analysis of the contours defining presents only one of the differentiation criteria, and not the decisive one (5,6). The analysis of the internal structure i.e., the detection of degenerative intralesional changes is reliable in tumours larger than 2cm, which significantly limits the setting of the diagnosis of smaller tumours on the basis of this criterion. However the smaller tumours are actually the subjects of clinical and radiological interest.

It has been noted that the intratumor heterogeneity is demonstrated in phyllodes tumour, which is in a way specific, however on the basis of this criterion it is impossible to perform the differentiation between the benign and malignant type of tumour (7).

In the evaluation of the distribution of postcontrast intralesional increase of SI in the function of time, the basic difference between benign and malignant lesions is centrifugal i.e. centripetal enhancement. This parameter differentiates the lesions with high reliability, especially well defined tumours with intensive, initial postcontrast enhancement (8).

Quantitative image analysis

Published analyses performed on large series imply that only 80% of DCIS show increased SI postcontrastly, and minimal postcontrast enhancement is often demonstrated by the scirrhoid forms of tumour (8). The majority of benign lesions also enhance postcontrastly, which additionally limits the differentiation.

However, very important characteristic of malignant tumours is their dynamics of postcontrast enhancement. The invasive malignant tumours that result from the neoangiogenesis, enables prompt injection of the contrast medium into hyper-permeable pathological blood vessels; the consecutive early postcontrast enhancement are clearly separated from benign lesions after the prompt and intensive injection of the contrast.

The second crucial parameter of the discrimination benign vs. malignant is the analysis of formed $\Delta S/\Delta t$ curve. Two types of the curve demonstrate all malignant changes: the plateau type and wash out type. Such formed curves are not found in the benign lesions. The study by Fischer et al. found this type of the curve in 30% to 40%. The published data by S. Heywang et al. suggest that the type of washout may be found with proliferative dysplasias in the patients with hormonal stimulation. Also, smaller fibroadenomas with predominant

adenomatous component, according to Powell and Steling, are presented by prompt intensive postcontrast enhancement SI and with the curve of the wash out type. Such a presentation, with the limited evaluation of the intralesion distribution of postcontrast enhancement, presents differential diagnostic problem, thus medullar, mutinous, papillary, and well-defined ductal carcinomas, but also phyllodes tumour, primary lymphoma and metastasis must be taken into account while being considered. According to literature data 5% to 10% of invasive carcinomas show late and delayed postcontrast enhancement (9).

Through the analysis of postcontrast intralesion signal distribution, it has been observed that the malignant tumours shows centripetal type enhancement in 33.33% of cases, which is histologically in correlation with the peripheral zone of the tumour activities (tumours demonstrate degenerative changes centrally, as a result of devaluated vascularity due to increased growth). The benign changes do not demonstrate centripetal distribution, which virtually means that such a type of the distribution excludes the benign behaviour of the lesion. Also, in the group of the benign lesions (25.9%), the centrifugal postcontrast enhancement is noted, which excludes the presence of malignancy. The diffusive postcontrast enhancement is noted in 66.66% of malignant lesions and in the same percentage of benign changes, thus the presentation of the diffusive intensification presents the non-specific sign, on the basis of which the individual lesion discrimination is impossible (10) (Figure 3).

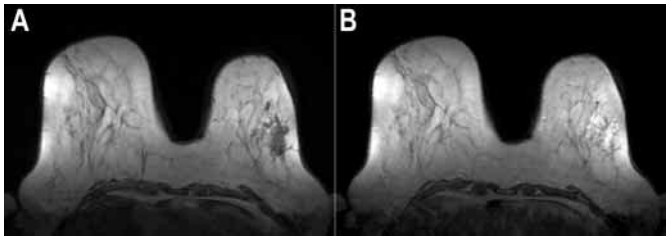

Figure 3. Typical MR appearance of ductal invasive carcinoma. A strongly and early enhancing corresponded with neoangiogenesis (A - precontrast, B - postcontrast)

INDICATIONS FOR MR MAMMOGRAPHY

MR mammography is a highly selective examination that is performed within very narrow spectrum of indications when other available methods do not provide enough information.

Absolute indications for MR mammography are:

(1) The evaluation of post-therapeutic breast with breast conserving surgical therapy (with or without radiotherapy) and evaluation of suspicious relapse in the zone of extensive scar. It is necessary to emphasise that such an examination may be validly performed only after 9-12 months after the surgery and 15-18 months after the radiotherapy (11). This prolonged time is necessary due to development of neovascularisation in young granulation tissue and consecutive postcontrast enhancement in relation to possible malignity. After the adequate time the scar fibroses does not enhance postcontrastly, thus the discrimination scar vs. relapse is reliable (12);

(2) The evaluation of silicon implant means the analysis of the implant integrity, as well as the potential detection of the malignity behind and around the implant. The tissue changed by the scar, masks mammographically detectable malignity, thus the use of MRM has full justification (13,14) (Figure 4);

(3) The monitoring of neoadjuvant chemotherapy - MRM provides information about the reaction to therapy and the estimation of tumour viability. Although it may not exclude the existence of possible cellular remainders, monitoring of the size, morphology, and postcontrast dynamics of the therapeutic results, might be validly estimated (15).

Relative indications for MR mammography are:

(1) Dense breast, i.e. the breast with mammographically dense fibrograndular tissue that masks the potential malignity, as well as with extensive fibrocystic changes. In young women with high risk factor, who have suspect clinical/US finding, MRM may clearly demonstrate some higher number of falsely positive results due to frequently present proliferate dysplasia (16);

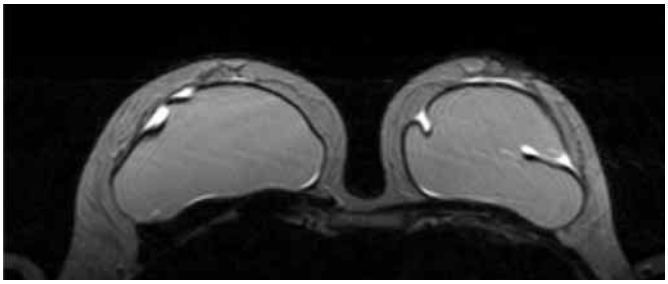

Figure 4. T2W transverse image of a patient with bilateral breast implants. Both implants show no signs of rupture. The configuration of implant on left side is more rounded, suggesting capsular contraction

(2) In pre-surgery preparation in order to exclude multicentricity and bilateralism, MRM, according to the majority of authors, is the most sensitive method (16) (Figure 5);

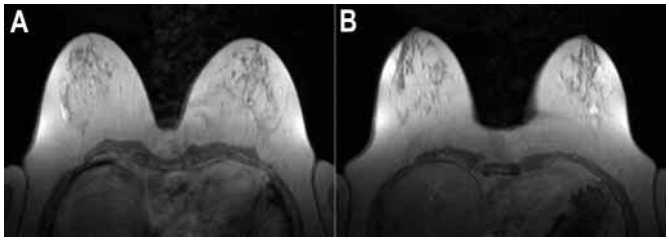

Figure 5. MR appearance of bilateral carcinomas mammography and US invisible, (A - precontrast, B - postcontrast)

(3) Complicated findings where there is a discrepancy between clinical and radiological finding;

(4) CUP (carcinoma unknown primary), i.e. with axillary metastatic illness potentially resulting from the breast and with non-defined clinical/radiological finding.

It is important to emphasise that in particular cases MR mammography provides no information:

(1) During pregnancy and lactation due to expressive hormonal stimulation and increased consecutive vascular permeability, the diffuse postcontrast enhancement of glandular parenchyma disables the valid discrimination of possible pathological changes;

(2) Hormone substitutive therapy has the same, above-mentioned effect (17);

(3) Inflammatory process of malignant or non-malignant etiology also enhances all involved structures in diffusive postcontrast manner and also masks potential malignant process;

(4) The verified conditions of proliferative dysplasia, with multiple focal or diffusive contrast alternation zones, may imitate malignancy;

(5) Detected microcalcifications are not the indication for MR mammography because they correlate with DCIS in high percentage, for which MRM shows relatively low sensitivity; in such cases there is the indication of biopsies, which is more specific and cheaper as well (18,19).

CONCLUSION

Taking into account all above mentioned advantages and limits, MR mammography has its realistic place in diagnostic algorithm with the correlation with clinical and other radiological modalities. It is important to point out that the narrow field of indication of MR mammography covers approximately 5% of cases. Current MR devices with the possibility of stereotaxy and software packages with various pulse sequences and the adequate post-processing extend MRM's indication field. However, future aspects of MR mammography

development are based on the design of highly specific gadolinium melanin polymers fussed with monoclonal antibodies specific for breast carcinoma.Through the design of new software packages, achieving ultra-fast sequences, the possibility to study good differentiation between benign and malignant is done within first ten seconds.

REFERENCES

1. Tabar L. Calcifications localized within lobules. In: Breast Imaging and Interventional Procedures, ESDIR, Braco (ed.); 1996. p. 27-9.
2. Heywang S. Technique. In: Heywang S, Beck R, editors. Contrast enhanced MRI of the breast. 2nd ed. Berlin: Springer; 1998.
3. Heywang S, Viehweg P. Sensitivity of contrast-enhanced MR imaging of the breast. In: Davis PL, editor. Magnetic resonance. Imaging Clin N Am Breast Imaging 1994;2(4):527-36.
4. Fischer U. Practical MR mammography. New York: Thieme; 2003.
5. Rosculet KA, Ikeda DM, Forrest ME, Oneal RM, Rubin JMJeffries DO, Helvie MA. Ruptured gel-filled silicone breast implants: sonographic findings in 19 cases. AJR 1992;159:711-6.
6. Fentiman IS. Detection and treatment of early breast cancer. London: Dunitz; 1990. p. 58.
7. Adams AH, Brookeman JR, Merickel MB. Breast lesion discrimination using statistical analysis and shape measures on magnetic resonance imagery. Comput Med Imaging 1991;15:339-49.
8. Barentsz JO. MR mammography: Diagnostic criteria. In: MRI of the breast, ERASMUS course. Göttingen; 1997.
9. Heywang S. Appearance of various tissues and leasions. In: Heywang S, Beck R, editors. Contrast enhanced MRI of the breast, 2nd ed. Berlin: Springer; 1995.
10. Bogdanović D. Prilog optimizaciji protokola za dinamičko magnetno rezonantnu mamografiju. (disertacija). Novi Sad: Univerzitet u Novom Sadu; 2001.
11. Morakkabati N, Leutner CC, Schmiedel AF, Schild HH, Kuhl CK. Breast MR imaging during or soon after radiation therapy. Radiology 2003;229:839-901.
12. Dao TH, Rahmouni A, Campana F, Laurent M, Asselain B, Fourquet A. Tumor recurence vs. fibrosis in irradiation breast: differentiation with dynamic gadolinium-enhanced MR imaging. Radiology 1994;187(3):751-5.
13. Heywang SH, Eiermann W, Bassermann R, Fenzl G. Carcinoma of the breast behind a prosthesis-commparasion of US, mammography ang MRI. Comput Radiol 1985;9:283-6.
14. Berg WA, Anderson ND, Zerhouni EA, Chang BW, Kuhlman JE. MR imaging of the breast in patients with silicone breast implants: normal postoperative variant and diagnostic pitfalls. AJR 1994;163:575-8.
15. Rieber A, Tomczak R, Rosenthal H et al. MR mamography after chemotherapy of the breast carcinoma. Radiologe 1995;35 suppl1:S82.
16. Oellinger H, Heins S, Sander B et al. Gd-DTPA enhanced MR breast imaging: the most sensitive method for multicentric carcinomas of the female breast. Eur Radiol 1993;3(3):223(abst.)
17. Sachse S, Wiegand C, Thomas M, Kaiser WA. Changes in MR mammography under hormone-replacement-therapy. Eur Radiol 2000;10:F1.
18. Liberman G, Dershaw DD, Rosen PP, Abramson AF, Deutch BM, Hann LE. Sterotaxic 14-gauge breast biopsy. How many core biopsy speciment are needed? Radiology 1994;192:793-5.
19. Viehweg P, Lampe D, Buchmann J, Heywang-Kobrunner SH. In situ and minimally invasive breast cancer: morphologic and kinetic features on contrast-enhanced MR imaging. MAGMA 2000;11:129-37.