Magnetic Resonance Mammography: Actual Trends and Perspectives

Nechifor-Boila IA[1], Buruian M[1], Borda Angela[2]

[1] Department of Radiology and Medical Imaging, County Emergency Clinical Hospital, Tîrgu Mureș, Romania
[2] Department of Histology, University of Medicine and Pharmacy, Tîrgu Mureș, Romania

Introduction: Magnetic Resonance Mammography (MRM) is a new radiologic examination with wide perspectives in breast cancer diagnosis. We performed a systematic review of the literature, in order to obtain a clear view on the actual role of MRM, together with an accurate evaluation of its performance in clinical settings.
Material and methods: We conducted a thorough PubMed search, both directly and through MeSH (Medical Subject Headings), using specific keywords. We then applied the following filters: articles published only between 1999 and 2011 and written in English or French. Priority was given to reviews and clinic trials according to previously set criteria.
Results: We evaluated the clinical efficiency of MRM using sensitivity, specificity and predictive values (positive and negative). Sensitivity varied between 81 and 98%, while specificity had a much wider dispersion (65–93%), thus supporting the statement that MRM is a sensitive but not a specific examination. Diffusion MRM was comparable to standard MRM, while spectroscopy showed a low sensitivity and a high specificity.
Conclusions: MRM is a complex investigation, with well documented recommendations and good sensitivity. Diagnostic specificity remains an important issue, but with improvement perspectives from new techniques like diffusion and spectroscopy.

Keywords: MRI, mammography, breast cancer

Received: 15 April 2011 / Accepted: 12 July 2012

Introduction

Breast cancer is considered the most frequent cancer in women, with an estimate of 1.38 million new cases diagnosed in 2008, representing almost one quarter (23%) of all female cancers and the second most frequent (10.9%) cancer of all [1,2].

Incidence rates vary according to different regions. Low rates are recorded mainly in Eastern Africa (19.3 per 100,000), while much high rates are found Western Europe (89.7 per 100,000). However, mortality rates are significantly lower in developed regions (6–19 per 100,000), mainly due to better survival prognostics.

The diagnosis of breast cancer relies today on three essential elements (triple assessment): clinical examination, radiologic investigations and pathologic examination of biopsy specimens [3].

The most recommended radiologic examinations are mammography and echography, followed by magnetic resonance mammography (MRM), the latter gaining more and more ground in diagnostic importance, as new developments in radiologic technique are achieved.

The aim of our study is to perform a systematic review of the literature, in order to obtain a clear view on the actual role of MRM in the diagnosis of breast cancer, together with an accurate evaluation of its performance in clinical settings.

Material and methods

We performed a thorough PubMed search, directly and using MeSH (Medical Subject Headings) based on the following keywords:

- In MeSH: "Breast Neoplasms/diagnosis" OR "Breast Neoplasms/radiography" AND "Magnetic Resonance Imaging";
- Directly in PubMed: "breast MRI", "magnetic resonance mammography".

As the initial search retrieved a large number of articles, we had to refine our research, using filters for publication date (articles published between 1999 and 2011), language (articles written in English and French) and article type (reviews and clinical trials).

In the selection phase, priority was given to articles respecting key criteria. For reviews, methodology was the central factor – a systematic, thorough, bibliographic research, based on recent articles (1999–2011). For clinical trial articles, the minimum number of included patients was set at 80, together with an appropriate gold standard (pathology on surgical/biopsy sample) and an adequate interpretation (a minimum of 2 specialists). Additional attention was given to the target population, MRI protocol, interpretation criteria (BIRADS scale or another) and histopathologic type of breast cancer.

Results and Discussion

Recommendations for MRM

MRM passed through different time periods and achieved more and more important roles as techniques progressed [4,5]. At the beginning, MRM was recommended only in the case of difficult-to-interpret mammographies due to different reasons (most frequently an elevated breast density). MRM served then for a "second opinion" before deciding for a certain intervention. This approach has changed

Correspondence to Alin Nechifor
Email: nechiforalin@yahoo.com

Table I. Recommendations for breast MRI according to the 2008 ACR guidelines

Indication	Description
Screening	1. For high-risk patients (for patients having a risk higher than 20% for developing breast cancer during their lifetimes: – Patients with a genetic mutation : BRCA mutations; – Patients having a history of potentially carcinogenic treatments: radiation therapy for other cancers. 2. Investigation of the contra-lateral breast in the case of a certified breast cancer; 3. Follow-up of patients that benefited from interventions for breast augmentation/reconstruction (implants that make mammography difficult to perform;
Extension of the disease	1. Invasive or ductal in situ carcinoma – to evaluate the possibility of multifocality or multicentricity; 2. Evaluating a potential fascial or muscular invasion; 3. Evaluating the extension in the case of an excision with positive resection margins; 4. Evaluation before deployment of an neoadjuvant chemotherapy;
Supplementary evaluation	1. Detecting an eventual recurrence after medical and/or surgical therapy; 2. Identifying the primitive tumor in breast cancer cases that present themselves in a metastatic stage from the beginning; 3. Characterizing of lesions that are non-concordant with the other methods: echography and/or mammography; 4. Evaluation before breast reconstruction following a radically intended surgical procedure; 5. MRI-guided breast biopsy.

with the development of various possibilities for obtaining percutaneous biopsies and, subsequently, a wider access to a histopathologic diagnosis. In the case of lesions visible on mammography or echography, guided biopsies can be performed, and no further investigations are necessary. However, in the case of difficult to see lesions, MRI "second opinion" remains essential [4,5].

Another essential indication was to settle conflictual situations between mammography and echography, mainly due to its high negative predictive value [6–8]. This is strongly influenced by the radiologist's experience and the composition of patient groups. MRM is generally not re-commended as a stand-alone examination and authors propose a complementary approach as an integrated mammography-echography-MRM protocol. These protocols must consider the strengths and weaknesses of each procedure, and deploy them only when they can guarantee efficiency. For example, in the case of a conservatory excision, MR is the only one capable of differencing a scar from a tumor recurrence [4,5].

In 2008, the American College of Radiology (ACR) published the "ACR practice guideline for the performance of contrast-enhanced magnetic resonance imaging (MRI) of the breast", giving a synthesis of the main indications for MRM according to each situation with the corresponding description [9]. To the best of our knowledge, the ACR 2008 guideline is the most recently published one. Table I shows a synthesis of this guideline.

MRI technique and protocols

The MRI techniques, as reported by different authors, respect generic MRM principles, like main sequence types, scan planes and contrast administration, but also show a large variability concerning manufacturer-specific parameters. Different manufacturers mean different sequence names and definition parameters like echo and repetition times, flip angles, pulse types, 2D or 3D, deployment on different filters and use of parallel imaging [4].

The sequence types can be divided in two categories: a standard MRM protocol (morphology sequences together with a dynamic T1 Gadolinium-injected one) and novel sequences (diffusion and spectroscopy). The scan plane generally used is axial (transverse) [10,11,8,7,6] but there are authors preferring other planes, such as coronal [12].

The standard MRM protocol comprises a T2 with or without fat saturation, a native T1 before injection and dynamic Gadolinium-injected T1 scans (an average of 4) for the dynamic exam. Sometimes, additional T1 scans are performed in the sagital or coronal planes after the Gadolinium injection [10,11,8,7,6].

The breast has a high quantity of fat tissue, which can be a problem both for T2 and T1 sequences, as it generates high signal intensity. This can mask or "create" apparent breast lesions, resulting in both false negative and false positive results [4]. In order to eliminate this, the sequences are generally fat-saturated, by removing its signal with the use of a fat saturating pulse during examination [4]. When performing a dynamic examination, lesions usually enhance faster than the rest of the breast tissue, and to highlight it, signal from the rest of the enhancing breast tissue must be suppressed. This can be done by digital subtrac-

Table II. Representative studies aimed at evaluating clinical efficiency of MRM both in screening and non-screening study models

Author	No. of subjects	Gold standard	Cancer type	Interpretation scale	Sensitivity	Specificity
Trop et al, 2010	184	Pathology result on biopsy sample	All (Screening on BRCA1/2 carriers)	BI-RADS MRI	83	93.6
Kuhl et al, 2007	167	Pathology result on biopsy/surgery sample	Pure DCIS	BI-RADS MRI	92	N/A
Tozaki et al, 2006	155	Pathology result on biopsy/surgery sample	All	BI-RADS MRI	99	89
Bluemke et al, 2004	821	Pathology result on biopsy/surgery sample	All	BI-RADS MRI	88.1	67.7
Sardanelli et al, 2004	90	Pathology result on total mastectomy sample	All (Multifocal/multicentric cancers)	Other	81	N/A No benign lesions included
Fischer et al, 1999	463	Pathology result on biopsy/surgery sample	All	Other	93	65

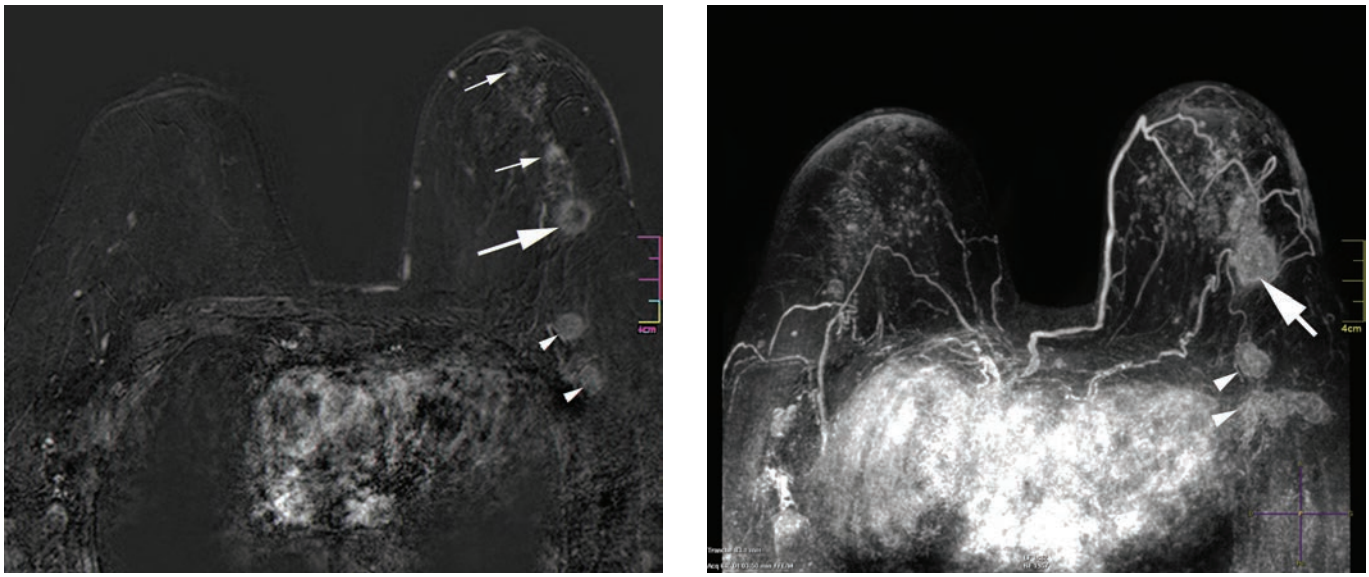

Fig. 1. A 63-year-old patient presented with a mass in her left breast together with enlarged lymph nodes. Digital substraction imaging (1A) shows a central excavated mass (large arrow), together with satellite enhancement foci (small arrows) and pathologically enhancing lymph nodes (arrow heads). Maximum Intensity Projection (MIP) reconstruction (1B) shows abnormal vessels surrounding the tumor as well as abnormal skin enhancement. The pathology exam confirmed the presence of an invasive ductal carcinoma together with carcinomatous lymphangitis.

tion, consisting in the removal of the non-enhanced image (mask) from the Gadolinium-injected images, leaving only the enhanced lesion in the final section. It is very commonly used, both alone and in combination to fat suppression [4].

In MRM the length of the examination is essential, as a longer examination can result in a greater chance for movement artifacts. Quality results from use of a high resolution matrix (512×512) which, in turn means longer examination time. In order to perform the dynamic examination as well, authors recommend using a lower matrix (256×256) and parallel imaging, to gain time with a loss in image precision [4,13].

Some authors have separated the morphologic from the time dynamic parts of the MRM in two different examinations, in order to obtain both a high image-resolution and a good time-resolution examination. They propose performing a standard protocol with a single-phase T1 first instead of the dynamic multiphase T1, in this way allowing the use of a higher matrix value (512×512), consistent with higher quality images. If enhancing lesions are found, the examination would be repeated after a minimum of 17 hours with a simpler protocol: pre-contrast T1 and multiphase post-contrast T1, the latter using similar parameters as in the standard all-in-one protocol.

Contrast is administered either in a bolus or in a constant injection rate, but generally in the same quantity (0.1 or 0.2 mmol/kg), according to the product brand and concentration [14,15,12,10,7,8].

Warren et al. performed a review of MRM publications and found that there is a large inconsistency when analyzing MRM technique (scanner, sequences, sequence parameters), injection protocol (quantity, speed, type) and interpretation method [15]. On the other hand, Kuhl et al suggest that there might not be necessary for a high consistency in parameter values between centers for assuring reproducibility but a more general approach like in the case of brain or cardio-vascular examinations [4].

Interpretation and efficiency

MRI interpretation is based on the two imaging subsets of the MRM examination: the morphology and the dynamic parts, which are interpreted together or independently, depending on the authors [6,12,7]. Studies published before 2003 and some even after, generally use evaluation scores or classifications that emerge from previous studies [7,16].

In 2003 the American College of Radiology published the "ACR Breast Imaging-Reporting and Data System (BI-RADS) Atlas" with a MR imaging section that presented the first edition of the BI-RADS lexicon adapted for MRI [17], which was adopted by most authors afterwards [4,6,11,8].

Our study found a large array of studies concerning the accuracy and clinical efficiency of MRM, most of them using the same type of gold standard (pathology result). They are generally clinical trials, most being performed on patients with a documented suspicion of breast cancer. There are however studies performed as screening trials on patients that have genetic mutations (BRCA mutation carriers), with a high probability of developing breast cancer when compared to the regular population [18].

The clinical efficiency of MRM was generally evaluated using sensitivity, specificity and predictive values (positive and negative) [18,6,19,7] (Table II). In studies that did not include benign lesions, specificity could not be calculated and so, only sensitivity and positive predictive values were reported [8,12]. Sensitivity was reported being as low as

81% and as high as 98% while specificity had an even wider interval (65–93%), supporting the statement that MRM is a sensitive, but not specific examination [19,12,7,10].

As a consequence, there are several studies aimed at testing new methods for improving diagnostic accuracy for MRM like diffusion and spectroscopy.

Diffusion is a special MRI sequence that can appreciate and quantify the degree of water movement in tissues, being able to detect lesions with modified dynamics like tumors and inflammation [4,13]. The results of diffusion research in MRM are similar to standard MRM, with good sensitivity (80–98%) and wide specificity values (46–93%) with the recommendation of deployment within the standard protocol [20–23].

Spectroscopy is a novel technique, with wide use in neuroradiology, able to measure the level of cellular metabolism markers like cholin, with a possibility of orienting towards a benign or malignant nature [13]. A study by Tozaki et al. reported a low sensitivity (44%) but a high specificity (85%) in small lesions (less than 15 mm), with improved sensitivity for larger lesions [24].

Conclusions

MRM is a complex investigation, with well documented recommendations and good sensitivity. Diagnostic specificity remains an important issue, with wide value intervals, based upon the clinical setting and author experience, but with improvement perspectives from new techniques like diffusion and spectroscopy.

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