MRI of the Breast: Current Indications and Outlook to the Future

Karen Kinkel

Clinique des Grangettes, Chêne-Bougeries, Geneva, Switzerland

Introduction

Magnetic resonance imaging (MRI) of the breast has gained widespread clinical acceptance due to a large effort in standardization of image acquisition and interpretation partly due to the extensive use of the Breast Imaging Reporting and Data System (BI-RADS) lexicon. The role of MRI of the breast has evolved from the traditional question about local recurrence of breast cancer to a variety of indications such as high-risk screening, evaluating response to neoadjuvant chemotherapy, staging and screening for contralateral cancer, occult primary breast cancer, and implant evaluation [1, 2]. This jump from a third-line breast-imaging technique to a primary imaging technique is also due to the increased availability of MRI-guided biopsy systems and an increasing awareness for standardized follow-up protocols and quality assurance for MRI-only lesions [3]. This trend has encouraged newer indications, such as discordant radiopathologic findings, nipple discharge, or high-risk lesions after breast biopsy, for MRI of the breast to help solve complex clinical situations.

Screening the High-Risk Patient

Since the early 2000s, multiple prospective studies in patients at high risk for breast cancer have shown higher sensitivity of MRI compared with mammography and US in early detection of breast cancer (Table 1). Patients are considered at high risk if the cumulative lifetime risk of breast cancer exceeds 20% or if they were treated for Hodgkin's disease between the age of 8 and 30 years with mantle radiation therapy. Patients are sent to an oncologic genetic counselling consultation if the family history strongly indicates a suspicion of genetic mutation for breast cancer. This is the case for three instances of first- or second-degree relatives of patients with breast/ovarian cancer from the same parental side or two cases of first-degree relatives with breast cancer that occurred before the age of 40, or if the cancer was bilateral. A family history of two first-degree relatives of ovarian cancer, of one male breast cancer or one breast and ovarian cancer also suggests a possible genetic mutation. *BRCA* mutations affect a tumor suppressor gene, with dominant autosomic transmission by either the father or the mother, with a 50% chance of transmission. Breast cancer risk starts at the age of 25 (mean 45-48) years and 55 years for ovarian cancer. Male breast cancer is only seen in patients with the *BRCA2* mutation.

The lifetime risk for breast cancer in patients with *BRCA1* or *BRCA2* mutation is 60-85% but for ovarian cancer is 40-60% in *BRCA1* patients versus 10-30% in *BRCA2* patients. The risk of contralateral breast cancer is 30% within 5 years of the first breast cancer. Risk-reduction options include either bilateral mastectomy with (95% reduction) or without (90% reduction) oophorectomy, oophorectomy alone before the age of 50 years, or tamoxifen chemo-

Table 1. Sensitivity of screening magnetic resonance imaging (MRI)

Study	Year	No. patients	Cancer	N+	Mammography	MRI
Warner	2004	236 *BRCA*	22	9%	36%	77%
Kriege	2004	1,909	51	14%	40%	71%
Kuhl	2005	613	12	8%	42%	83%
Maribs	2005	349	35	14%	40%	77%
Lehman	2005	367 contralateral	4		25%	100%
Hagen	2007	491 *BRCA*	25	26%	50%	86%
Riedl	2007	327	28		50%	86%
Kuhl	2009	687	27	11%	33%	93%
Sardanelli	2011	501	52	22%	50%	91%

Diseases of the Abdomen and Pelvis 2014-2017,
DOI: 10.1007/978-88-470-5659-6_41

prevention (38% risk reduction). Other options include more intense and earlier screening starting at the age of 30 years with annual MRI of the breast. The role of mammography in *BRCA1* mutation carriers is controversial due to an increased risk of radiation-induced breast cancer in vitro. Compared with MRI as a screening method alone, the majority of comparative imaging screening trials shows a small number of additional cancers with mammography but no or very little value of US after annual MRI and mammography [4, 5]. Imaging features of breast cancer in high-risk women are often more benign appearing, particularly in *BRCA1* mutation carriers, in whom 23% of invasive ductal cancer demonstrates a fibroadenoma-like appearance with an oval or round shape and smooth margins but no dark septations [6]. Moreover, no mammographic calcifications are seen in invasive cancer. A posterior prepectoral location of breast cancer is seen in 67% of *BRCA1* mutation carriers [6]. Second-look US is crucial to identify suspicious lesions on MRI to allow subsequent US-guided biopsy. If US remains negative, spot-compression mammography or tomosynthesis may help identify MRI lesions. If no traditional imaging method identifies the suspicious MRI-only lesion, then MRI-guided biopsy with clip positioning and postbiopsy mammography allows adequate patient management. A 6-months' follow-up, MRI remains important to demonstrate no increase in size after a negative MRI-guided biopsy. The benefit of high-risk screening was shown in a study comparing breast cancer in *BRCA1* and *BRCA2* patients diagnosed with and without MRI. The group with MRI had significantly smaller tumors and less chemotherapy; however, the slightly higher 3-year and disease-free and overall survival was not significant [7].

Implant Evaluation

MRI of the breast for implant evaluation has a sensitivity of 89% and a specificity of 97% in the diagnosis of implant rupture [8]. The incidence of rupture increases with implant age, with most ruptures occurring between 10 and 15 years after implantation. The imaging protocol includes four T2-weighted sequences: native, fat-suppressed, water-suppressed, and dedicated to silicone only (fat and water suppression). The silicone-only sequence should be performed in two different slice orientations to differentiate a rupture from implant folds.

Intracapsular implant rupture is defined as rupture of the implant shell, with silicone leakage that does not extend beyond the fibrous capsule. The most reliable MRI criterion for intracapsular rupture is the presence of multiple curvilinear low-signal-intensity lines within the high-signal-intensity silicone gel, the so-called linguine sign. These curvilinear lines represent the collapsed implant shell floating within the silicone gel [9]. The linguine sign is missing in an uncollapsed rupture, and instead, MRI shows free silicone outside the implant shell but still contained by the fibrous capsule. Focal silicone invagination between the inner shell and fibrous capsule are common, resulting in the teardrop sign and the key-hole sign. Extracapsular silicone implant rupture is defined as rupture of both the implant shell and the fibrous capsule, with macroscopic silicone leakage that extends beyond the fibrous capsule into surrounding tissues. Focal areas of high signal intensity in the silicone-only sequence represent free silicone. Capsular contracture can be confirmed at MRI in the event of a round breast implant with increased capsular thickness. Implant infection is more common in oncoplastic procedures and demonstrates rim enhancement around the implant. Contrast-enhanced MRI is indicated in addition to the four T2 sequences whenever there is an oncoplastic question about the glandular breast tissue, a mass in the breast, or an associated high-risk situation.

Breast Cancer Staging

MRI of the breast has several roles in this situation:

- To measure the extent (size and location) of the known breast cancer
- To identify additional foci of cancer elsewhere in the breast (multifocality)
- To define adequate resection margins of the cancer
- To screen the contralateral breast for breast cancer.

A large number of papers confirm the superiority of MRI compared with US and mammography to fulfil these tasks, particularly in patients with invasive lobular cancer [10], cancer in high-risk patients, patients with a size discrepancy >1 cm between mammography and US, and patients eligible for partial breast irradiation. However, there are no randomized trials that demonstrate evidence for reduced recurrence rate or mortality from breast cancer. Moreover, the Comparative Effectiveness of MRI in Breast Cancer (COMICE) trial, a multicenter trial from the UK, demonstrated no difference in re-operation rate between breast cancer patients with and without breast MRI [11]. The study was limited by poor design and absent MRI quality assurance, as most centers started the use of breast MRI and had no MRI-guided biopsy. Therefore, the study represents poor use of MRI technology and should not be considered. Identifying occult foci of breast cancer in the ipsilateral or contralateral breast does not necessarily increase the percent of patients undergoing mastectomy.

Indeed, multiple lumpectomies for several small breast cancers within a large breast volume may represent a valid surgical alternative to mastectomy. Moreover according to the initial tumor size before vacuum-assisted biopsy, watchful waiting for very small lesions treated by radiation therapy and adjuvant therapy may be another alternative.

Neoadjuvant Chemotherapy

Patients with locally advanced tumors undergo neoadjuvant chemotherapy to increase the rate of breast-conserving

surgery. Surgical success depends on breast volume and residual disease after the end of neoadjuvant chemotherapy. Assessing the type of shrinkage pattern is important because it impacts the type of surgery: if the shrinkage pattern is concentric, lumpectomy can be performed; if the shrinkage pattern consists of tumor fragmentation, there is no change in the widest tumor margins and mastectomy is required. Comparison between pre- and postchemotherapy MRI is crucial for adequate residual tumor assessment. Moreover, the decreased enhancement rate of residual tumor after chemotherapy should lower the threshold for residual tumor diagnosis to avoid underestimation of tumor volume. This situation is increased in patients with estrogen-receptor-positive and human epidermal growth factor receptor (HER2)-negative tumors. The inclusion of diffusion-weighted imaging has shown promising results for assessing residual disease after chemotherapy [12]. Another potential indication of MRI is the early prediction of response to avoid delay in surgical treatment if the chemotherapy regimen is not efficient. However, this indication requires larger studies to establish the value of MRI in distinguishing responders from nonresponders [13].

Occult Primary Cancer

Histopathology of metastases helps determine the mammary origin of the primary cancer. However, clinical examination, mammography, and US are not able to identify the cancer. MRI sensitivity for detecting unknown breast cancer ranges from 25% to 86% [14]. When MRI is positive, adequate surgical treatment consists of lumpectomy or mastecomy according to lesion size and location. When MRI is negative, breast surgery is not performed and axillary dissection and breast radiation therapy are performed instead.

Outlook to the Future

New emergent indication of breast MRI include nipple discharge and high-risk lesions at breast biopsy (stage B3). Cancer is present in 10% of patients with spontaneous, unilateral, discharge from one nipple orifice that is of various colors but not white.

Cytology, mammography, and US demonstrate false-negative results in 30-50% of cases. Performing a ductography helps demonstrate the extent of an abnormal milk channel but does not exclude cancer. MRI of the breast has therefore been suggested in demonstrating both suspicious lesions and the abnormal duct in performing an indirect ductography through heavily T2-weighted sequences [15]. This technique has high sensitivity and negative predictive value for cancer in patients with otherwise negative conventional imaging findings.

There is a large group of heterogeneous benign breast lesions (stage B3) diagnosed with percutaneous biopsy and at variable risk of being upgraded to malignancy at surgical excision. They include lobular neoplasia, atypical ductal hyperplasia, radial sclerosing lesions, and papillary lesions. Several studies show the high negative predictive value of MRI in excluding cancer, particularly in patients with radial scars and papillomas. These patients can safely undergo follow-up examination rather than surgical excision [16].

Higher field strengths (3T) offer greater signal-to-noise ratio (SNR), enabling fast acquisition strategies and the opportunity of introducing new imaging techniques, which can help differentiate and characterize breast lesions, e.g., diffusion-weighted imaging (DWI) and magnetic resonance spectroscopy (MRS). The combination of DWI, proton MRS, and contrast-enhanced MRI show increased sensitivity and specificity in detecting and differentiating breast cancer from benign disease [17, 18]. These promising technical advances require further technical standardization and teaching to become part of routine clinical practice in MRI.

References

1. Mann RM, Kuhl CK, Kinkel K, Boetes C (2008) Breast MRI: guidelines from the European Society of Breast Imaging. Eur Radiol 18:1307-1318.
2. Sardanelli F, Boetes C, Borisch B et al (2010) Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group. Eur J Cancer 46:1296-1316.
3. Heywang-Köbrunner SH, Sinnatamby R, Lebeau A et al; Consensus Group (2009) Interdisciplinary consensus on the uses and technique of MR-guided vacuum-assisted breast biopsy (VAB): results of a European consensus meeting. Eur J Radiol 72:289-294.
4. Kuhl C, Weigel S, Schrading S et al (2010) Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. J Clin Oncol 28:1450-1457.
5. Sardanelli F, Podo F, Santoro F et al; High Breast Cancer Risk Italian 1 (HIBCRIT-1) Study (2011) Multicenter surveillance of women at high genetic breast cancer risk using mammography, ultrasonography, and contrast-enhanced magnetic resonance imaging (the high breast cancer risk Italian 1 study): final results. Invest Radiol 46:94-105.
6. Schrading S, Kuhl CK (2008) Mammographic, US, and MR imaging phenotypes of familial breast cancer. Radiology 246:58-70.
7. Chéreau E, Uzan C, Balleyguier C et al (2010) Characteristics, treatment, and outcome of breast cancers diagnosed in BRCA1 and BRCA2 gene mutation carriers in intensive screening programs including magnetic resonance imaging. Clin Breast Cancer 10:113-118.
8. Hölmich LR, Vejborg I, Conrad C et al (2005) The diagnosis of breast implant rupture: MRI findings compared with findings at explantation. Eur J Radiol 53:213-225.
9. Juanpere S, Perez E, Huc O et al (2011) Imaging of breast implants: a pictorial review. Insights Imaging 2:653-670.
10. Bedrosian I, Mick R, Orel SG et al (2003) Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer 98:468-473.
11. Turnbull L, Brown S, Harvey I et al (2010) Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. Lancet 375:563-571.

12. Woodhams R, Kakita S, Hata H et al (2010) Identification of residual breast carcinoma following neoadjuvant chemotherapy: diffusion-weighted imaging—comparison with contrast-enhanced MR imaging and pathologic findings. Radiology 254:357-366.
13. Prevos R, Smidt ML, Tjan-Heijnen VC et al (2012) Pre-treatment differences and early response monitoring of neoadjuvant chemotherapy in breast cancer patients using magnetic resonance imaging: a systematic review. Eur Radiol 22:2607-2616.
14. de Bresser J, de Vos B, van der Ent F, Hulsewé K (2010) Breast MRI in clinically and mammographically occult breast cancer presenting with an axillary metastasis: a systematic review. Eur J Surg Oncol 36:114-119.
15. Hirose M, Otsuki N, Hayano D et al (2006) Multi-volume fusion imaging of MR ductography and MR mammography for patients with nipple discharge. Magn Reson Med Sci 5:105-112.
16. Linda A, Zuiani C, Furlan A et al (2012) Nonsurgical management of high-risk lesions diagnosed at core needle biopsy: can malignancy be ruled out safely with breast MRI? AJR Am J Roentgenol 198:272-280.
17. Bogner W, Gruber S, Pinker K et al (2009) Diffusion-weighted MR for differentiation of breast lesions at 3.0 T: how does selection of diffusion protocols affect diagnosis? Radiology 253:341-351.
18. Gruber S, Debski BK, Pinker K et al (2011) Three-dimensional proton MR spectroscopic imaging at 3 T for the differentiation of benign and malignant breast lesions. Radiology 261:752-761.