Breast MRI as a Screening Tool: The Appropriate Role

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Key Words

Breast cancer, magnetic resonance imaging, screening, high risk

Abstract

Magnetic resonance imaging (MRI) can detect breast cancer that is occult on mammography or ultrasound. However, although the high sensitivity of this imaging modality is desirable, its lower specificity, higher cost, variable technique and interpretation among institutions, exclusion criteria, and unproven effect on survival rate make it a less desirable screening test for the general population. Several studies have shown that using more than one imaging tool, such as MRI and mammography, increases cancer yield in high-risk patients, such as those with inherited *BRCA1* and *BRCA2* mutations. Recent studies show improved specificity of MRI, likely related to advances in technique and the development of interpretive guidelines. (*JNCCN* 2006;4:523–526)

In the United States, the average lifetime risk for women developing breast cancer by the age of 85 years is 1 in 7. The age-adjusted incidence is 134.4 per 100,000 women per year, based on statistics from 1998 to 2002.¹ For women in the general population, the incidence of developing invasive breast cancer increased approximately 4% between 1980 and 1987 and 0.3% between 1987 and 2002. The incidence of developing in situ breast cancer increased more than sevenfold between 1980 and 2001, partially because of increased diagnosis by mammography.²

The lifetime risk for developing breast cancer is increased in some women. These factors include 1) a history of biopsy-proven high-risk lesions (i.e., atypical ductal

hyperplasia or lobular carcinoma in situ), 2) previous radiation therapy to the chest area, 3) a strong family history of premenopausal breast or ovarian cancer, 4) genetic mutation, 5) early age of menarche, 6) late age at the birth of a first child, or 7) nulliparity. Women with *BRCA1* and *BRCA2* mutations have up to a tenfold increased risk for developing breast cancer. However, *BRCA* mutations account for only approximately 50% of the breast cancer cases that are actually caused by a gene mutation. Factors indicating increased likelihood of *BRCA* mutations include 1) a family history of multiple cases of early-onset breast cancer, 2) a family history of ovarian or breast cancer at any age, 3) breast and ovarian cancer in the same woman, 4) bilateral breast cancer, 5) Ashkenazi Jewish heritage, and 6) family history of male breast cancer. Women with *BRCA* mutations and breast cancer have a greater risk for developing a second breast cancer.^{3,4} The risk for a contralateral breast cancer increases up to 64% by age 70.⁵

Radiology Results to Date

In the general population, screening mammography has been shown to reduce mortality associated with breast cancer by at least 24%.⁶ Annual mammography should begin at age 40 for women at average risk. Experts have suggested aggressive surveillance and screening begin at a younger age for high-risk women than for the general population because of early onset of familial breast cancer. Current surveillance protocols for screening *BRCA1* or *BRCA2* mutation carriers include clinical breast examination (CBE) every 6 months and annual mammogram beginning at 30 years of age. Although the increased breast density in the younger age group makes mammographic screening difficult, high breast density in mutation carriers is associated with an increased risk of breast cancer compared with the general population.⁷ Using

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other imaging modalities in addition to mammography may increase detection.

Multiple studies have shown that magnetic resonance imaging (MRI) increases cancer detection.^{8–10} Data from 13 institutions studying mammography versus MRI for screening asymptomatic genetically high-risk women showed that MRI alone yielded 0.8% additional cancers when compared with mammography, which was not statistically different. A higher false-positive rate was seen with MRI than with mammography. The added cancer yield was seen in women with scattered fibroglandular densities to heterogeneously dense breasts. Of the 367 subjects enrolled in the study, the biopsy recommendation rate was 8.5% for MRI alone compared with 2.2% for mammography.⁸ Data from the International Breast Magnetic Resonance Consortium Trial showed MRI had an added cancer yield of 4% in the contralateral breast of women with recent unilateral breast cancer, whereas mammogram detected none of these lesions.¹⁰ Morris et al.⁹ had similar results, showing a 4% cancer yield in women undergoing initial MRI screening.

MRI is reported to have a higher sensitivity but lower specificity in detecting breast cancer when compared with mammography or ultrasound (Table 1). The reported sensitivities of MRI for detecting breast cancer in women with genetic mutations or strong family histories of breast cancer range from 77% to 100% for invasive carcinoma, compared with 25% to 42% for mammography.^{2,11,12} Kriege et al.¹³ reported a sensitivity of 80% for MRI, compared with 33% for mammography and 18% for CBE. In 1909 eligible women with at least a 15% lifetime risk for breast cancer, these investigators diagnosed 51 cancers, 44 of which were invasive carcinoma. Overall, MRI detected 32 of these lesions, whereas mammography detected only 18.¹³

In a retrospective study from the Netherlands involving women with a hereditary risk for breast cancer, Stoutjesdijk et al.¹² showed MRI to be more accurate than mammography. Of the women in the cohort, 40 underwent mammography alone, 49 underwent MRI alone, 15 underwent both mammography and MRI within at least a year of each other, and 75 underwent mammography and MRI within 4 months. Cancer was detected in 13 of 179 participants. For MRI, the sensitivity and specificity were 100% and 93%, respectively, compared with 42% and 96% for mammography. Some MRI examinations were per-

formed because of abnormal mammogram results. Of the 8 malignant lesions detected only through MRI, 2 of these lesions were seen in 1 woman who did not undergo mammography.¹²

Warner et al.¹⁴ compared the sensitivity and specificity of CBE, mammography, ultrasound, and MRI. The 3 imaging modalities were performed on the same day and repeated annually, whereas CBE was performed every 6 months. In the 236 *BRCA1* or *BRCA2* mutation carriers, 22 cancers were detected. MRI detected the most cancers compared with the other screening modalities. At 77%, the sensitivity of MRI was higher than the other modalities, compared with 9% for CBE, 36% for mammography, and 33% for ultrasound. The highest sensitivity (95%) occurred when all 4 screening modalities were combined. The combined sensitivity for CBE and mammogram was only 45%. CBE, mammography, and ultrasound combined had a sensitivity of 64%.

In a recent study, Kuhl et al.¹⁵ also compared mammography, ultrasound, and MRI. CBE and all 3 imaging modalities were performed within 8 weeks, with 43 cancers identified in 529 participants. Of these cancers, 34 were invasive carcinoma and 9 were DCIS. Imaging with both mammography and MRI had the highest sensitivity of 93%, and MRI alone had a higher sensitivity compared with the other modalities. Unlike in prior published data, MRI and mammography had equivalent specificity at 97%.

Liberman's¹⁶ meta-analysis of 7 published results showed that 33% of the cancer detected in high-risk women were DCIS. Although the sensitivity of MRI for detecting invasive cancer approaches 100%, its sensitivity for detecting DCIS is variable and reported to be between 40% and 100%. Because mammography allows good visualization of microcalcifications, it has been the primary imaging modality for evaluating the extent of DCIS. However, not all DCIS lesions calcify because the microcalcifications represent tumor necrosis. MRI has the potential to detect calcified and noncalcified DCIS. In retrospective studies reviewing pure DCIS cases, MRI showed a higher sensitivity for detection (80%–90%) compared with mammography.^{17,18} The higher number of DCIS cases reported in the study by Morris¹⁸ may have been caused by technical differences and interpretation criteria that emphasized lesion morphology. As experience with MRI increases, its role in evaluating the extent of DCIS will likely improve, especially in high-risk patients.

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Table 1 Sensitivity and Specificity of Screening Modalities

	<i>N</i>	CBE	Mam	US	MRI	Mam+US	Mam+MRI
Stoutjesdijk et al. ¹² 2001	179	q6m	q1y	–	q1y		
Sensitivity			42%	–	100%		
Specificity			96%	–	93%		
Kriege et al. ¹³ 2004	1909	q6m	q1y	–	q1y		
Sensitivity		18%	33%	–	80%		
Specificity		98%	95%	–	90%		
Warner et al. ¹⁴ 2004	236	q6m	q1y	q1y	q1y		
Sensitivity		9%	36%	33%	77%		
Specificity		99%	100%	96%	95%		
Lehman et al. ⁸ 2005	367		q1y		q1y		
Sensitivity			25%	–	100%		
Specificity			99%		94%		
Kuhl et al. ¹⁵ 2005	529	q1y	q1y	q1y	q1y		
Sensitivity			33%	40%	91%	49%	93%
Specificity			97%	91%	97%	89%	96%

Abbreviations: CBE, clinical breast examination; MRI, magnetic resonance imaging; Mam, mammography; US, ultrasound.

Role of MRI

Screening mammography has a low sensitivity in women with increased genetic risk, with a reported interval cancer rates as high as 46%.¹⁹ Several studies suggest that women at high risk would benefit from breast MRI screening.^{6,8–15} However, although combining MRI with mammography or any other imaging modality may increase the sensitivity for diagnosing familial breast cancer, it does not ensure reduced mortality. Studies suggest that MRI can detect an otherwise mammographically occult cancer, but its limitations prevent it from replacing mammography. Currently, MRI and MRI-guided biopsy are more costly and less available compared with mammography, ultrasound, and stereotactic and ultrasound-guided biopsy; the techniques and interpretation of an MRI examination are not standardized; and microcalcifications are better seen with mammography than with ultrasound or MRI.

Breast ultrasound retains some advantages and may be integrated into screening protocols. The advantages of ultrasound include its widespread avail-

ability, ready access for biopsy procedures, speed, lower cost, and the lack of ionizing radiation. Although its sensitivity is lower than that of MRI, ultrasound may be considered as an interim imaging modality.^{14,15} Many radiologists also have more experience with mammography and ultrasound than with MRI, and many providers in United States have issues with national reimbursement.

The impact of MRI screening on mortality is still not known. Clinicians should inform patients of the current data before offering MRI or adopting it into practice. The potential for false-positive findings that lead to additional imaging and biopsy can be

costly and may increase patient anxiety. Informing patients of the benefits and disadvantages of these imaging modalities involves considerable counseling, which may be impractical in many screening programs. The appropriate management strategy is best determined individually. No universal recommendation for the frequency of ultrasound or MRI in the screening protocol is currently available for screening high-risk women. However, the NCCN Breast Cancer Screening and Diagnosis Clinical Practice Guidelines in Oncology recommend that MRI be considered for genetic mutation carriers.

Conclusions

Studies have shown that MRI is effective in detecting cancer in patients at increased risk for breast cancer.^{6,8–15} The addition of MRI to mammography and CBE improves surveillance sensitivity for detecting early breast cancer in the high-risk population and therefore should be considered in genetically high-risk women. Whether intensified surveillance using combined mammography, MRI, and CBE reduces

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morbidity and mortality and impacts on survival is not known. The patient must be informed of the lack of evidence and the caveats related to breast MRI screening. Therefore, MRI should be considered an adjunct to mammography and CBE and not a replacement for mammography in the surveillance of high-risk populations.

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