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Medscape Medical News

MRI More Sensitive Than Mammography in Women at High Risk of Breast Cancer CME

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Physicians - up to 0.25 AMA PRA category 1 credit(s)

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July 28, 2004 — Magnetic resonance imaging (MRI) was more sensitive than mammography for detecting early disease in women at high risk of breast cancer, according to the results of a large study published in the July 29 issue of the *New England Journal of Medicine*.

"The value of regular surveillance for breast cancer in women with a genetic or familial predisposition to breast cancer is currently unproven," write Mieke Kriege, MSc, from Erasmus Medical Center-Daniel den Hoed Cancer Center in Rotterdam, the Netherlands, and colleagues. "In a diagnostic setting, MRI is a sensitive method of breast imaging, and it is virtually uninfluenced by breast density, but the specificity is variable and the costs are high."

The investigators screened 1,909 women who had a cumulative lifetime risk of breast cancer of at least 15%, using clinical breast examination every six months and annual mammography and MRI with independent readings. Of 1,909 eligible women, 358 women were carriers of germ-line mutations. Median follow-up was 2.9 years.

Of 51 tumors detected, 44 were invasive cancers, including six ductal carcinomas in situ, one lymphoma, and one lobular carcinoma in situ. The sensitivity of clinical breast examination, mammography, and MRI for detecting invasive breast cancer was 17.9%, 33.3%, and 79.5%, respectively, and the corresponding specificities were 98.1%, 95.0%, and 89.8%. Compared with mammography, the overall discriminating capacity of MRI was significantly better ($P < .05$).

Compared with two different age-matched control groups, this surveillance group had a higher proportion of invasive tumors that were 10 mm or less in diameter (43.2% vs. 14.0%; $P < .001$ and 12.5%; $P = .04$). The combined incidence of positive axillary nodes and micrometastases in invasive cancers was 21.4% in the surveillance group, and 52.4% ($P < .001$) and 56.4% ($P = .001$) in the two control groups.

Tumors larger than 2 cm in diameter were found more often in the women with *BRCA1*, *BRCA2*, *PTEN*, and *TP53* mutations than in

the other two risk groups, suggesting that more frequent screening is needed for women with these mutations.

"MRI appears to be more sensitive than mammography in detecting tumors in women with an inherited susceptibility to breast cancer," the authors write. "A drawback of MRI screening is that it has a lower specificity than mammography, and as a result, MRI will generate more findings judged as uncertain, which require short-term follow-up or additional investigations."

In this study, MRI screening led to twice as many unneeded additional examinations as did mammography (420 vs. 207) and three times as many unneeded biopsies (24 vs. 7).

The Dutch Health Insurance Council supported this study.

In an accompanying editorial, Laura Liberman, MD, from the Memorial Sloan-Kettering Cancer Center in New York, NY, notes the "important contributions" of this study, while calling for randomized, controlled trials.

"MRI can detect otherwise occult breast cancer in high-risk patients and is probably most beneficial to those at highest risk.... No data support the use of MRI in screening women at normal risk," Dr. Liberman writes. "Ideally, breast MRI should be performed at facilities that follow technical and interpretive guidelines and that can perform biopsies of lesions detected by MRI alone. Whether the excellent results reported in the literature can be achieved in practice remains to be determined. Further outcomes research is essential to develop evidence-based recommendations for methods of breast-cancer screening that are tailored to the specific needs of women at various levels of risk."

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Learning Objectives for This Educational Activity

Upon completion of this activity, participants will be able to:

- Identify breast-cancer risk and screening methods for women with BRCA mutations.
- Compare the sensitivity and specificity levels of MRI vs. mammography screening in women at high risk for breast cancer.

Clinical Context

Inherited mutations of the *BRCA1* and *BRCA2* gene predispose women not only to an increased risk of breast cancer but an increased risk of ovarian cancer as well. According to an editorial by Liberman that accompanies the current article, mutation of the *BRCA1* gene is associated with a 3.2% cumulative risk of breast cancer by age 30 years, a 50.8% risk by age 50 years, and an 85% risk by age 70 years. Breast cancers associated with this genetic abnormality usually have a high nuclear grade and are estrogen-receptor negative.

Because breast cancers associated with *BRCA* mutations occur in younger women, screening with traditional mammography can have a poor sensitivity when compared with screening mammography used for older women. This may be because of the increased density of breast tissue in younger women or different pathologic features of the *BRCA* tumors. The authors of the current study compare the efficacy of traditional breast-cancer screening with the emerging technology of MRI in the evaluation of women at high risk of breast cancer due to *BRCA* mutation or family history.

Study Highlights

- Women participating in the study were recruited from 6 familial-cancer clinics in the Netherlands. All women were younger than 70 years and had a cumulative lifetime risk of breast cancer of at least 15%. Women with a personal history of breast cancer or presenting symptoms suggestive of breast cancer were excluded from participation.
- Study subjects had a clinical breast examination performed every 6 months. They also underwent screening and (if necessary) diagnostic mammography plus dynamic breast MRI with gadolinium contrast annually. Both mammography and MRI results were scored based on the Breast Imaging Reporting and Data System (BI-RADS). A BI-RADS score of 4 or 5 prompted an invasive biopsy.
- For statistical analysis, women were divided into one of three groups depending on their risk of developing breast cancer: a *BRCA* mutation group (cumulative lifetime risk, 50% to 85%), a high-risk group (risk, 30% to 49%), and a moderate-risk group (15% to 29%). These groups were compared with control groups comprising a general cohort of women with breast cancer and another group of unscreened women with at least a 15% lifetime risk of breast cancer.
- The main study endpoints were the sensitivity, specificity, and positive predictive value of the clinical breast examination, mammography, and MRI.
- 1,909 women were evaluated per the research protocol. The mean age of all subjects was 40 years old. 75% of the cohort was premenopausal.
- 358 women had a *BRCA* mutation, while 1,052 women were judged to be in the high-risk group and 499 in the moderate-risk group.
- For a median follow-up period of 2.9 years, a total of 44 invasive breast cancers and 6 ductal carcinomas in situ were diagnosed

in the entire cohort. The risk of all cancer was greatest in the *BRCA* group (26.5 cancer cases per 1,000 women-years), while the high- and moderate-risk groups had similar cancer risks (5.4 and 7.8 cases per 1,000 women-years, respectively).

- 32 breast cancers were detected by MRI, of which 22 were not visible on mammography. 13 cancers were missed by MRI, and 8 of these cancers were visible on mammography. 5 of these 8 cancers were ductal carcinoma in situ, and the authors note that mammography had a higher sensitivity in diagnosing this type of tumor.
- Mammography found 18 tumors but missed 27. Of the 27 cancers that mammography did not diagnose, 22 were visible on MRI.
- For all breast cancers, the sensitivity of MRI was 71.1% compared with 40% and 17.8% for mammography and clinical breast examination, respectively. The specificity was highest for clinical breast examination (98.1%) followed by mammography (95%) and MRI (89.8%).
- Positive predictive values of clinical breast examination, mammography, and MRI were 9.6%, 8%, and 7.1%, respectively. These values were for women with a BI-RADS score of 3 or more.
- MRI was shown to better discriminate between malignant and benign cases according to receiver-operating-characteristic curves. However, MRI led to twice as many additional diagnostic investigations and 3 times as many unneeded biopsies as mammography.
- In comparing the tumors found in the study group with those of the two control groups, the study group had more tumors that were node negative and without micrometastases than either control group. Other histologic features were generally similar between the study group and control groups, except that the study group generally had a higher proportion of tumors less than 10 mm than the general cohort of women with breast cancer.

Pearls for Practice

- *BRCA* mutations are related to a significant increased risk of breast cancer, but screening women with *BRCA* mutations using traditional methods can be difficult. This is especially true in younger women because of the increased density of breast tissue.
- MRI is more sensitive than mammography in breast-cancer screening in high-risk women but may require more diagnostic investigations and unnecessary biopsies due to the lack of specificity.

Instructions for Participation and Credit

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Target Audience

This article is intended for primary care physicians, radiologists, oncologists, surgeons, and other specialists who care for women at high risk of breast cancer.

Goal

The goal of this activity is to provide the latest medical news to physicians and other healthcare professionals in order to enhance patient care.

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