Breast MRI Shows Promise for High-Risk Women

BY GINA SHAW
Contributing Writer

NEW YORK — Breast MRI may have difficulty keeping up with the "potentially logarithmic demand" for its use as a cancer screening tool, experts said at a cancer symposium sponsored by New York University and by the Lynne Cohen Foundation for Ovarian Cancer Research.

The technique represents a vast improvement in sensitivity over traditional mammography and ultrasound, but it "may have been oversold" as a screening tool, said Linda Moy, M.D., of the university.

"MRI isn't suitable for use as an annual cancer screening tool for most women," she said, noting that it is too expensive (at about 10 times the cost of a mammogram) and too time consuming (at about 45 minutes per exam) to replace the more than 30 million screening mammograms performed annually.

But MRI remains the most promising of all breast screening modalities for one group of patients: *BRCA* mutation carriers. "MRI is the clear winner in every screening study undertaken to date in high-risk women," said Ellen Warner, M.D., of the University of Toronto.

In six large, prospective, nonrandomized studies that have compared screening tools for high-risk women, MRI's sensitivity was considerably higher than that of mammography, with ultrasound and clinical breast exam trailing far behind. Overall, Dr. Moy noted, most studies have found a sensitivity rate of 86%-100% for MRI in high-risk women, with reported sensitivities of only 33%-55% for mammography.

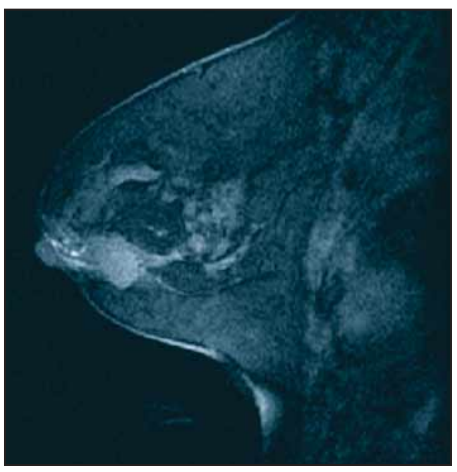
"This stands in sharp contrast to the excellent sensitivity of screening mammography for detecting [ductal carcinoma in situ] and early invasive breast cancers in the general population," Dr. Warner said. The difference, in part, can be attributed to the younger age—and greater average breast density—at which mutation carriers present for screening; MRI is far less influenced by breast density than is mammography.

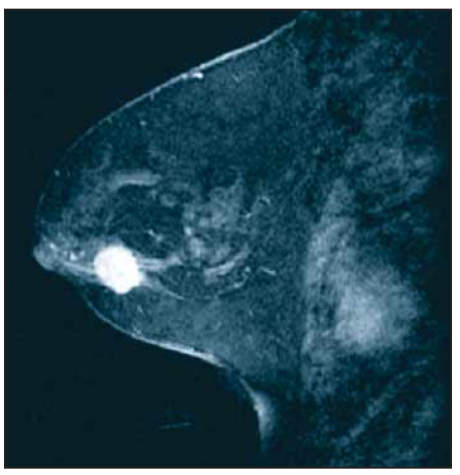
But while MRI is the undisputed sensitivity champion for screening high-risk women, it does have its drawbacks. First, it's not nearly as specific as it is sensitive. In the Dutch National Study, which followed 1,909 women, including 358 mutation carriers, MRI had a recall rate double that of mammography (10% vs. 5%), and triple the biopsy rate (5.8% vs 1.7%).

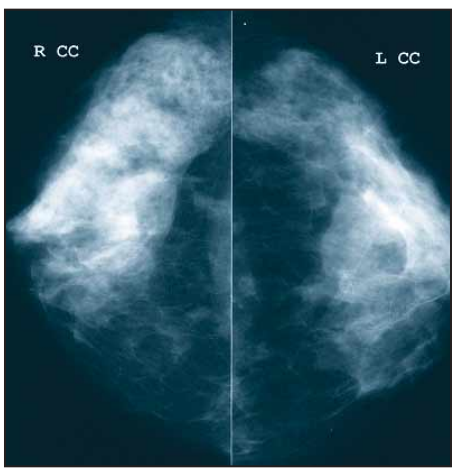
"The price of MRI's greater sensitivity is more false positives," Dr. Warner said. "MRI researchers are now working on protocols that we hope will slash recall and biopsy rates."

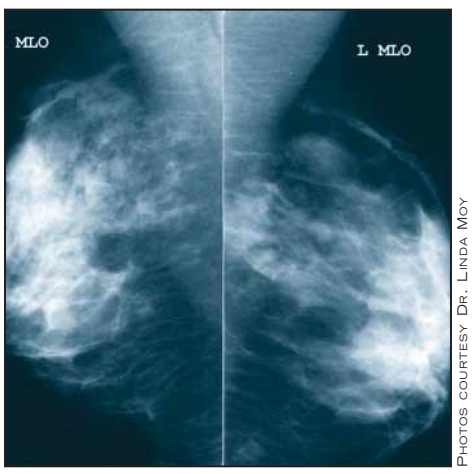
And no one yet knows whether MRI is actually saving women's lives. "To date, no study has proved that any screening regimen can actually increase survival rates," she said.

"If MRI is picking up cancers prior to distant metastasis that would have gone undetected until after metastasis with other screening tools, then it will have a favorable impact on survival. But we don't know that yet," Dr. Warner added. ■









PHOTOS COURTESY DR. LINDA MOY

At left, MRI without contrast hints at a mass near the nipple. At right, the mass that is seen on high-contrast MRI was found to be invasive ductal carcinoma. The invasive ductal cancer present in the patient's right breast is not visible in a craniocaudal (CC) mammogram or a mediolateral oblique (MLO) mammogram.

Hot Flash Trials Compare Venlafaxine, Clonidine, and MPA

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO, FLA. — Venlafaxine controls hot flashes more effectively than clonidine, but not as well as a single dose of medroxyprogesterone acetate, according to randomized, controlled trials presented in posters at the annual meeting of the American Society of Clinical Oncology.

In a trial organized by the German Breast Group, venlafaxine (Effexor) reduced frequency of hot flashes by 62% and severity by 67% in breast cancer patients. Clonidine reduced frequency by 22% and severity by 48%, reported Sibylle Loibl, M.D.

In a North Central Cancer Treatment Group trial, venlafaxine reduced hot flash frequency by 52% and median hot flash scores by 57% in the first 185 patients evaluated. A single 400-mg dose of medroxyprogesterone (MPA, Depo-Provera) achieved an 85% drop in frequency and reduced scores by 88%, reported Charles L. Loprinzi, M.D.

"The bottom line is, it [MPA] clearly works better. I think it is a reasonable option to give," Dr. Loprinzi, an oncologist at the Mayo Clinic, Rochester, Minn., said in an interview.

Dr. Loibl, a gynecologist in Neu-Isenburg, Germany, told this newspaper that the superiority of MPA was not surprising. "But we want to treat, especially breast cancer patients, without hormonal therapy," she said.

The double-blind German trial randomized 80 breast cancer patients (median age 53) from April 2002 to October 2004, and was able to evaluate 69. All had at least two hot flashes per day at baseline; none used medication to treat hypertension or depression.

During the 5-week study, 34 patients took two 0.075-mg clonidine pills per day; 35 patients took venlafaxine in 37.5-mg pills, also twice a day.

The primary end point was frequency of hot flashes at 5 weeks, but the researchers also reported that venlafaxine worked faster, reducing hot flashes significantly in the first week.

Side effects were comparable with both drugs and mostly occurred in the first week. Mouth dryness was most common in both groups. Tiredness occurred in 25% of the clonidine group and 33% of venlafaxine patients.

About 25% of the venlafaxine patients experienced nausea, but Dr. Loibl said the incidence dropped nearly to zero after the first week.

Four patients ended treatment because of side effects, and seven disappeared from follow-up.

In the North American trial, almost two-thirds (63%) of the women had a history of breast cancer. The remaining 37% were afraid to take hormonal treatments because of breast cancer risk, according to Dr. Loprinzi.

All patients enrolled had at least 14 hot flashes a week. None were on antidepressants. Median age was mid-50s for all three arms of the 6-week study. The poster report on the study included data on a total of 195 patients.

One group of 94 patients started on a 37.5-mg daily dose of venlafaxine, which increased after 1 week to 75 mg. A second group of 94 patients received a single 400-mg dose of MPA.

A third group stopped accrual with seven patients because of enrollment difficulties. These patients received 500 mg of MPA every other week for 6 weeks.

By the end of the trial, Dr. Loprinzi reported that 22 patients (24%) in the one-dose MPA arm were hot flash free compared with one patient (1%) on venlafaxine. In the MPA group, 90% reported residual hot flashes scores as 49% or less of baseline, compared with 63% of those on venlafaxine.

For the most part, MPA was better tolerated, with patients reporting less constipation, hot flash distress, abnormal sweating, and sleepiness.

Safety is the big unanswered question. The concern is whether MPA interferes with hormonal therapies such as tamoxifen and aromatase inhibitors, Dr. Loprinzi said. ■

Black Cohosh Fails Phase III Trial

Black cohosh, a popular herbal remedy, failed to reduce hot flashes in a randomized, double-blind, placebo-controlled, phase III crossover trial presented in another poster at the meeting.

Barbara Pockaj, M.D., and her colleagues reported that the average decrease in hot flash scores was larger in placebo users (27%) than in those who received 20 mg of black cohosh daily (20%).

At the end of the 9-week study, 36 (37%) of the 97 patients completing the study preferred placebo, 31 patients (32%) favored black cohosh, and 30 patients (30%) had no preference. The other 19 patients evaluated in the study were listed as missing. The study included breast cancer patients and women with a perceived risk of breast cancer.

Toxicity results gave a slight edge to black cohosh, with no adverse events reported by 87% of patients on the herbal remedy and 77% on placebo.

None of the findings reached statistical significance, Dr. Pockaj of the Mayo Clinic in Scottsdale, Ariz., said in an interview.

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