

Digital Mammography Best for Some Women

BY ROBERT FINN
San Francisco Bureau

A large, head-to-head comparison of digital and film mammography found no overall difference in diagnostic accuracy, but digital mammography appears to have better diagnostic accuracy in some subgroups of women.

Digital mammography was significantly more accurate among women aged under 50 years, women with heterogeneously dense or extremely dense breasts, and premenopausal or perimenopausal women, according to the study by Etta D. Pisano, M.D., of the University of North Carolina at Chapel Hill, and colleagues.

The study involved a total of 49,528 women recruited over a 2-year period at 33 sites in North America. The final analysis included data from 42,760 women for whom the investigators had all relevant information (N. Engl. J. Med. 2005;353:[Epub ahead of print] doi 10.1056/NEJMoa052911, www.nejm.org).

All women underwent both digital and film mammography, and these were independently interpreted by two readers. Readers rated the mammograms on a seven-point malignancy scale and used the classification of the Breast Imaging Reporting and Data System (BIRADS).

Biopsy or aspiration of the suspicious

lesion was performed if either reader recommended it. These patients received follow-up mammograms an average of 455 days following their initial screening. A total of 335 cancers were detected among the women enrolled in the study.

Investigators used five digital mammography systems from four manufacturers. No statistically significant differences were found among the different mammography systems.

The investigators noted that the cancers detected by digital mammography but missed by film mammography included many invasive and high-grade in situ cases, precisely the lesions that must be detected to save lives.

The study found no advantage in the diagnostic accuracy of digital mammography for women aged 50 years and older, women with fatty breasts or scattered fibroglandular densities, and postmenopausal women.

But digital mammography has other advantages, the investigators noted. These include easier access to images and to computer-assisted diagnosis; improved means of image transmission, storage, and retrieval; and the use of a lower average dose of radiation without compromising diagnostic accuracy.

Conversely, the cost of digital mammography systems, which the investigators place at 1.5-4 times higher than film systems, provides a barrier to the universal use of this modality. ■

Gabapentin May Help Control Hot Flashes in Breast Ca Patients

BY DOUG BRUNK
San Diego Bureau

A 900-mg daily dose of gabapentin was associated with significant decreases in hot flash severity and frequency, but a 300-mg daily dose of the drug was not, results from a randomized, double-blind, placebo-controlled trial have found.

"We believe gabapentin can be added to the list of nonhormonal agents for the control of hot flashes in women with breast cancer, and the effects of doses higher than 900 mg/day merit further study," wrote the investigators, led by Kishan J. Pandya, M.D., of the University of Rochester (N.Y.).

In a study funded by the National Cancer Institute, he and his associates randomized 420 women with a mean age of 55 years to receive placebo, 300 mg/day of gabapentin, or 900 mg/day of gabapentin.

The women, the majority of whom were white, were enrolled at 18 different sites of the university's community clinical oncology program. Each of them recorded the severity level of hot flashes and 10 other symptoms experienced in a 1-week self-report diary at

baseline and during the fourth and eighth weeks of treatment (Lancet 2005;366:818-24).

Posttreatment analysis revealed that the reduction in hot flash severity score was only 15% for those in the placebo group, compared with 31% for those in the 300 mg/day gabapentin group and 46% for those in the 900 mg/day gabapentin group.

The differences between groups were statistically significant, but only the 900 mg/day dose of gabapentin was associated with significant decreases in hot flash frequency and severity, the investigators said.

No differences were observed among the three treatment groups with respect to the 10 other symptoms, which included fatigue, nausea, and shortness of breath, suggesting that gabapentin was well tolerated.

Gabapentin is approved for the treatment of epileptic seizures. But the medication also is used as a treatment for migraines, restless legs syndrome, and bipolar disorder.

Drug manufacturer Pfizer Inc., which is based in New York City, provided the gabapentin and placebo used in the trial. ■

BRCA-Negative Breast Cancer Does Not Raise Ovarian Risk

BY DIANA MAHONEY
New England Bureau

Women from families with hereditary breast cancer who do not carry the *BRCA1* or *BRCA2* genetic mutations are not at increased risk for ovarian cancer, a prospective study has shown.

If validated by additional studies, the findings by Noah D. Kauff, M.D., and colleagues at New York's Memorial Sloan-Kettering Cancer Center may allow physicians to better tailor ovarian cancer risk-reduction strategies.



Using records from the Sloan-Kettering clinical genetics service, investigators identified more than 1,700 patients who underwent genetic testing for *BRCA* mutations from August 1996 through July 2002 and who had consented to participate in follow-up studies. Those kindred with site-specific breast cancer who were *BRCA* mutation-negative and who had a living female proband received detailed questionnaires to provide clinical follow-up information and information on new cancers in themselves and their first- and second-degree relatives.

For the study, probands were defined as the youngest living *BRCA* mutation-negative women with breast cancer whose lineage included at least three cases of breast cancer—at least one of which must have been diagnosed before age 50—and no ovarian cancer, the investigators said (J. Natl. Cancer Inst. 2005;97:1382-4).

Probands whose heritage was exclusively Ashkenazi Jewish were included if they tested negative for the three Ashke-

nazi founder mutations because such testing has been shown to identify approximately 95% of detectable *BRCA* mutations, Dr. Kauff and associates stated.

Of 207 living female probands identified, 165 completed the study questionnaires. During a mean follow-up of 40.6 months, 19 new cases of breast cancer were diagnosed in the families, which included the 165 probands and 583 first- or

second-degree female relatives. The disease incidence was more than three times greater than expected in a general population of women from the general population.

During the same follow-up period, one case of ovarian cancer was diagnosed, which is consistent with expectations for an average-risk population.

Dr. Kauff and associates advised caution with respect to revising ovarian cancer risk-reduction strategies for women from families with site-specific hereditary breast cancer kindred and mutation-negative status until the findings can be confirmed through additional studies.

The authors wrote that "two-thirds of the women in the cohort were Ashkenazi Jewish, and it is possible that *BRCA* mutation testing in this group more effectively excludes the possibility of a deleterious mutation than in non-Ashkenazi populations."

Also, the study was powered to detect a 3.5- to 4-fold increase in ovarian cancer risk, compared with the general population, but detection of a 2.5- to 3-fold increase would require 3,800-7,600 women-years of follow-up, compared with the 2,534 women-years of follow-up represented by the current study. ■

If validated, the data may allow better tailoring of ovarian cancer risk-reduction strategies.

DR. KAUFF

Addition of Herceptin to Chemo Is Linked to Increased Cardiotoxicity

The Food and Drug Administration and Genentech Inc. are notifying physicians of new data demonstrating a significant increase in cardiotoxicity in patients randomized to receive Herceptin (trastuzumab) along with standard adjuvant chemotherapy, compared with patients who received chemotherapy alone.

The data come from the National Surgical Adjuvant Breast and Bowel Project (NS-ABP) study (B-31), a phase III trial involving 2,043 women with operable HER2 overexpressing breast cancer (immunohistochemistry test score of 3 or greater or a positive fluorescence in situ hybridization test score).

Preliminary analysis of safety data from this trial and the North Central Cancer Treatment Group (NCCTG) study (N9831) revealed a statistically significant increase in the 3-year cumulative incidence of New York Hospital Association class III and IV congestive heart failure and cardiac death observed in patients who re-

ceived the Herceptin-containing regimen (4.1%), compared with the chemotherapy-alone group (0.8%). No cardiac deaths were observed in patients who received the Herceptin-containing regimen; one cardiac death occurred in the control arm. Final analysis of the cardiac safety data collected in these two studies is ongoing.

Herceptin as a single agent is indicated for the treatment of patients with metastatic breast cancer whose tumors overexpress the HER2 protein and who have received one or more chemotherapy regimens. Herceptin in combination with Taxol (paclitaxel) is indicated for treatment of patients with metastatic breast cancer whose tumors overexpress the HER2 protein and who have not received chemotherapy.

For additional information, contact Genentech Inc.'s medical communication department by calling 800-821-8590 or by visiting www.gene.com/gene/contact/.

—Kerri Wachter