Breast Tomosynthesis May Reduce Recall Rates

BY PATRICE WENDLING
Chicago Bureau

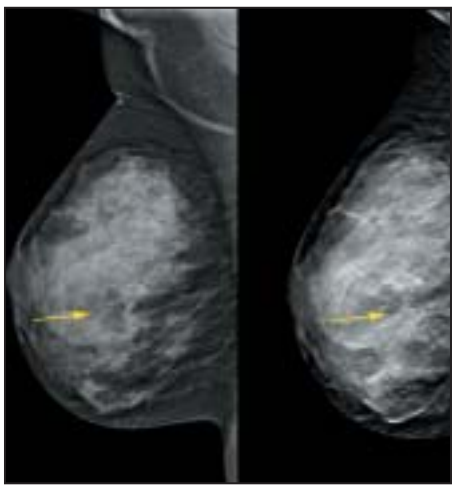
CHICAGO — The addition of digital breast tomosynthesis to digital mammography at screening could improve diagnostic accuracy and reduce recall rates by about 40%, according to results of a multicenter study.

Tomosynthesis creates a single three-dimensional image of the breast by combining data from 11 projection two-dimensional radiographs acquired during a single sweep of the x-ray tube around the patient.

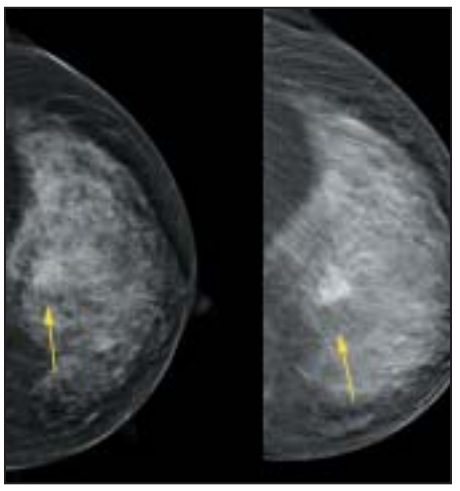
The technique improves breast visualization by reducing the overlap of normal breast structures, Dr. Elizabeth Rafferty reported during a late-breaking session at the annual meeting of the Radiological Society of North America. The total radiation dose of 1.5 mGy is about half that of a single mammographic exposure.

The technique is neither clinically available nor approved by the Food and Drug Administration, but based on findings from a data set of 316 women, Hologic Inc. (Bedford, Mass.) has petitioned the FDA for approval of the combined modality of tomosynthesis and digital mammography.

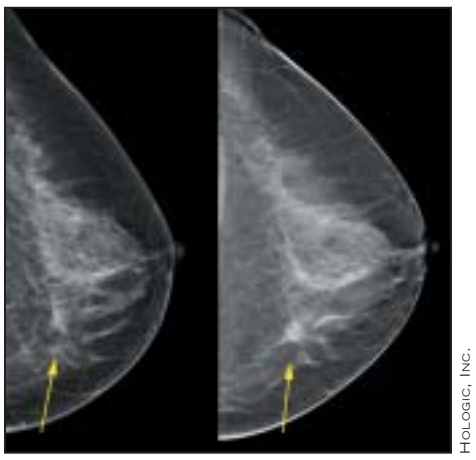
The data set was derived from a study in which 1,083 women, age 18 years or more, underwent two-view, full-field digital mammogram (FFDM) and digital tomosynthesis exams at five U.S. centers. The 316 women in the study included 100 women who presented for diagnostic examinations and 216 women who presented for screening exams, of whom 141 were recalled for additional imaging and 75 had normal exams. In all, 96 women underwent biopsy; 48 lesions were benign, and 48 were malignant.



Architectural distortion is clearer in tomosynthesis slices (right) than on digital mammography (left).



A spiculated cancer is better seen in the tomosynthesis slice (right) than on digital mammography (left).



HOLOGIC, INC.

Spiculated cancer with microcalcification is more apparent in the tomosynthesis slice (right) than on digital mammography image (left).

Twelve board-certified radiologists trained on 200 tomosynthesis imaging cases scored the digital mammography images as Breast Imaging Reporting and Data System (BIRADS) 0, 1, and 2. For the cases scored as a BIRADS 0, the radiologists were asked to give a forced BIRADS score of 1-5 showing the likelihood of disease in that patient and assign a probability of malignancy score rating from 1 to 100.

The combination of FFDM and tomosynthesis resulted in highly significant improvements in the radiologists' performance, as shown by receiver-operator curve analyses, said Dr. Rafferty of the radiology department at Harvard University Medical School in Boston. The performance benefits were seen primarily in the analysis of masses, architectural distortion, and focal asymmetries. A receiver-operator analysis showed that for all the readers, the combined modality of tomosynthesis and FFDM was superior to FFDM alone when using the forced BIRADS score and the probability of malignancy scale.

Using multicase and multireader analyses, the diagnostic accuracy (area under the curve) improved significantly for the forced BIRADS score from 0.83 with FFDM alone to 0.90 with FFDM plus tomosynthesis, with 0.5 representing a worthless diagnostic test and 1 a perfect test. The area under the curve for the probability of malignancy scale also significantly improved from 0.82 to 0.89 with the combined modality.

The investigators hypothesized that tomosynthesis would provide little gain in the assessment of clustered breast calcifications because calcifications are well seen on traditional mammography and aren't typically obscured by surrounding tissue. The data bore out this hypothesis, with only a slight, nonsignificant improvement from 0.80 to 0.84 observed in the area under the curve.

In noncalcified cases, the difference in the area under the curve for FFDM versus the combined modality was highly significant (0.82 vs. 0.92), representing good versus excellent dignostic accuracy. Dr. Rafferty has received research support from Hologic, the study sponsor. ■

Treatment Pearls for Common Breast Cancer–Related Symptoms

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — The flip side of the impressive decline in breast cancer mortality during the last several decades is the unprecedented number of survivors with tough-to-control chronic symptoms caused by the disease or its aggressive therapy, Dr. Charles L. Loprinzi said at the San Antonio Breast Cancer Symposium.

'Exercise is the answer, not more rest,' for patients who experience fatigue after chemotherapy.

DR. LOPRINZI

He focused on evidence-based therapies for five of the most common and problematic breast cancer survivorship issues: vaginal dryness, fatigue, chemotherapy-induced neuropathy, diminished libido, and hot flashes.

► **Vaginal dryness.** Pilocarpine (Salagen) shows enough promise that Dr. Loprinzi and colleagues have embarked on an ongoing randomized, double-blind, placebo-controlled trial of the oral drug at 5 mg once daily or b.i.d. in 192 women treated for breast cancer. Results should be available next year.

The impetus for the study was an anecdotal report a few years ago of marked clinical improvement in cyclophosphamide-induced vaginal dryness in four patients, along with a separate earlier report of significantly decreased vaginal dryness as a secondary outcome measure in a phase III trial of pilocarpine for oral and ocular dryness in patients with Sjögren's syndrome (Arch. Intern. Med. 1999;159:174-81). The drug is approved for that indication as well as for dry mouth caused by head and neck radiation therapy.

Estrogen therapy is effective for vaginal dryness and is worthwhile in some severely affected women, but there is concern that it could promote breast cancer recurrence. That concern extends to vaginal estrogens as well, said Dr. Loprinzi, professor of medicine and chair of oncology at the Mayo Clinic, Rochester, Minn.

► **Fatigue.** This is a major complaint for cancer patients across the full spectrum of disease, from those on adjuvant chemotherapy to patients with advanced, incurable cancer. Exercise is the intervention with the strongest evidence base. "Exercise is the answer, not more rest," Dr. Loprinzi stressed.

► **Chemotherapy-induced neuropathy.** Gabapentin is widely prescribed for this problem. However, the sole rigorous study to date—a multicenter, placebo-controlled, double-blind, crossover trial conducted by Dr. Loprinzi and colleagues in the North Central Cancer Treatment Group (NCCTG)—failed to show any benefit (Cancer 2007;110:2110-8).

Vitamin E (alpha-tocopherol) at a dose of 400 mg/day was reported to protect against cisplatin-induced peripheral neuropathy and ototoxicity in an interim analysis of a 50-patient randomized, placebo-controlled study presented at last year's American Society of Clinical Oncology meeting. The NCCTG has an ongoing randomized trial, also comparing vitamin E at 400 mg/day and placebo. Until the results are in, Dr. Loprinzi urged caution in using vitamin E for prevention of chemotherapy-induced neuropathy.

"We haven't proved that it's helpful, No.1, and also there are some data suggesting that vitamin E can get in the way of cytotoxic therapy, particularly radiation therapy for the head and neck area," he said.

► **Low libido.** Sexual counseling is the only thing that can be recommended. Transdermal testosterone cream proved ineffective in a double-blind, randomized, placebo-controlled crossover trial by Dr. Loprinzi and the NCCTG (J. Natl. Cancer Inst. 2007;99:672-9).

► **Hot flashes.** Effective nonhormonal therapies are available. Dr. Loprinzi and his colleagues showed in a randomized, double-blind, placebo-controlled trial that venlafaxine at 37.5 or 75 mg/day reduced hot flash scores by 40% and 60%, respectively, from baseline (Lancet 2000;356:2059-63).

In a subsequent double-blind, placebo-controlled crossover trial, they showed that fluoxetine at 20 mg/ day also was effective for hot flashes in women with a history of breast cancer (J. Clin. Oncol. 2002;20:1578-83), although less so than venlafaxine.

Paroxetine at 20 mg/day seems roughly as effective as venlafaxine at reducing hot flashes, based upon randomized controlled studies by other researchers.

A couple of negative venlafaxine studies have been reported. However, neither featured adequate pretreatment baseline hot flash scores. That's a fatal methodologic flaw, according to Dr. Loprinzi, who noted that in his study that venlafaxine reduced hot flash scores by an average of 30% on day 1, compared with the baseline week.

Tamoxifen is metabolized by cytochrome P450 2D6 to a key active metabolite, endoxifen, believed to be responsible for the selective estrogen receptor modulator's efficacy in preventing breast cancer. Coadministration of paroxetine and tamoxifen has been reported to result in a significant decrease in plasma endoxifen levels (J. Natl. Cancer Instit. 2003;95:1758-64). But in another study, venlafaxine didn't reduce endoxifen levels (Clin. Pharmacol. Ther. 2006;80:61-74).

Another nonhormonal option is gabapentin, said Dr. Loprinzi. ■