

# MRgFUS Could Be New Wave in Breast Ca Ablation

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SAN ANTONIO — Magnetic resonance-guided focused ultrasound shows great potential as a totally noninvasive means of ablating breast cancer, Dr. Yukiko Yasuda reported at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Indeed, results of a published phase II 30-patient trial conducted by Dr. Yasuda and her coinvestigators were so favorable that a phase III Japanese trial is ongoing (*J. Am. Coll. Surg.* 2006;203:54-63). In addition, a 600-patient multinational study to include the Mayo Clinic, Rochester, Minn.; Johns Hopkins University, Baltimore; and Brigham and Women's Hospital, Boston, is on tap, according to Dr. Yasuda of Breastopia Namba Hospital, Miyazaki, Japan.

MR-guided focused high-intensity ultrasound (MRgFUS) is a logical extension of the trend toward using breast-conserving therapy to lessen impact on quality of life.

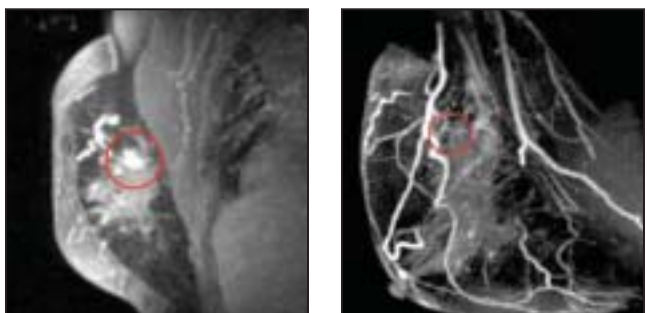
The treatment achieves thermal tumor ablation by concentration of ultrasound pressure waves inside the breast without physical penetration. When applied properly, there is no clinically significant heating of skin or other tissues along the ultrasound beam's path. Using real-time, closed-loop contrast MR feedback to monitor temperature changes at the target site, the operator can deliver destructive energy to a given point within 1 mm of accuracy.

In theory, this approach should result in less anesthesia, fewer infections, and faster recovery than with conventional surgical excision—and with no scars. Those are the potential pluses. The procedure's disadvantages are the expense of the technology and the lengthy treatment session. In the phase II study, a single 2-minute sonication

destroyed 0.16-0.67 mL of tissue. Complete tumor ablation required an average treatment time of 2 hours, 20 minutes.

However, this is a young technology, and two major technical advances to be introduced in the near future will speed treatment time and accuracy. One is a boost in the number of focused ultrasound transducer elements from the current 208 to 2,000. The other is upfield high-spatial-resolution MRI. These developments will permit three-dimensional treatment planning and therapy, she said.

Dr. Yasuda reported on 22 Japanese breast cancer patients who underwent

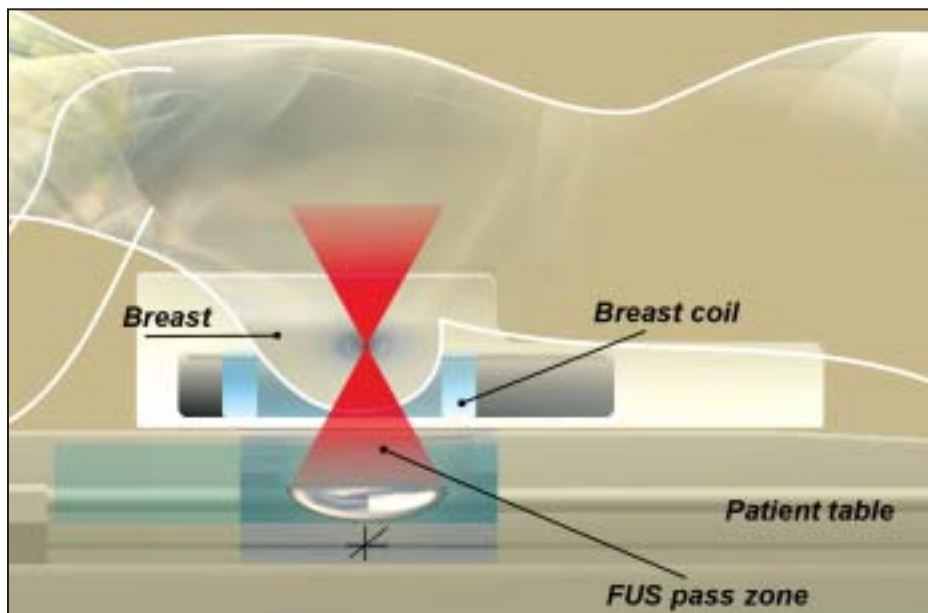


Contrast-enhanced images show a tumor (red circle) before treatment (left) and 2 weeks post treatment.

MRgFUS outside of a clinical trial. No adjuvant radiotherapy was used. The patients were subsequently followed with contrast-enhanced MRI and diagnostic ultrasound every 3 months for a median of 15 months.

During that time, one patient developed a local recurrence of pure mucinous carcinoma. Playback of stored treatment records revealed the explanation: insufficient temperature rise in the treated primary tumor, probably because of the dampening properties of the mucus. Armed with this information, operators can induce a higher temperature spike in patients with this subtype of carcinoma and avoid repeating the problem.

Treatment was performed using Insightec's ExAblate 2000 ultrasound system integrated into a 1.5-Tesla GE Healthcare MRI scanner. The ExAblate 2000 is Food and Drug Administration-approved for treatment of uterine fibroids. ■



In MR-guided focused ultrasound, a beam of focused ultrasound energy emanates from the transducer through the skin and breast to a focal point on the tumor.

# Take Family Structure Into Account in BRCA Screening

SAN ANTONIO — Consider lowering the threshold for BRCA mutation testing in patients with early-onset breast cancer who have fewer than two first- or second-degree female relatives older than age 45, Dr. Jeffrey N. Weitzel advised at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Patients with this sort of family situation, which he terms a "limited family structure," were 3.5-fold more likely to carry a deleterious BRCA mutation than were early-onset breast cancer patients with an adequate family structure, in his observational study.

Selecting appropriate candidates for BRCA mutation testing can be a challenge.

Current guidelines agree that testing is not appropriate for women without breast cancer in the general population. But the guidelines are less clear regarding what to do about women who develop breast cancer at a young age in the absence of a family history of breast or ovarian cancer.

Consideration of family structure provides a quick, useful aid in this decision making, according to Dr. Weitzel, director of the department of clinical cancer genetics and the cancer screening and

prevention program at City of Hope National Medical Center, Duarte, Calif.

He reported on 1,097 women who underwent BRCA mutation testing in the center's clinic for genetic cancer risk assessment. Of these women, 210 had breast cancer prior to age 50 and no family history of breast or ovarian cancer in first- or second-degree relatives. Half of these 210 women had a limited family structure.

A BRCA mutation was found in 17.3% of the women with early-onset breast cancer and a limited family structure, and in 5.7% of those with early-onset disease and an adequate family structure.

Family structure taken as a predictive factor for BRCA mutation had a sensitivity of 75% and a specificity of 54%.

Family structure's positive predictive value of 18% and negative predictive value of 91% were superior to the commonly used models for estimating the probability that a woman has a BRCA mutation—the Myriad Genetics, Couch, and BRCAPRO models.

None of those models proved sensitive to family structure as a risk factor, so consideration of family structure brings additional clinically relevant information to the table, Dr. Weitzel said. ■

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# Breast Cancer Prognosis Tied to Patient's First-Degree Relatives

SAN ANTONIO — Breast cancer prognosis appears to have a strong and previously unrecognized inherited component, Dr. Mikael Hartman said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

His study of 2,787 Swedish mother-daughter and 831 sister pairs with breast cancer showed that 5-year breast cancer-specific mortality was 60%-80% greater among first-degree relatives of a woman who died of the disease within 5 years of diagnosis than in those whose affected mother or sister had a good prognosis.

"We conclude that information about the outcome of breast cancer among affected first-degree relatives may be relevant for optimal clinical management of women with newly diagnosed breast cancer," said Dr. Hartman of the Karolinska Institute, Stockholm.

Among the 831 pairs of sisters, each with breast cancer, 5-year breast cancer-specific survival was 88% if the older affected sister was alive within 5 years of diagnosis, but only 70% if she was not.

After adjustment for potential confounders, including age at cancer diag-

nosis, treatment era, nulliparity or age at first live birth, and socioeconomic status, the risk of dying because of breast cancer within 5 years after diagnosis was 80% greater in women whose sister died of breast cancer less than 5 years following her diagnosis than in those whose sister had a good-prognosis form of the disease as defined in a multivariate model.

Similarly, the adjusted risk of breast cancer-specific mortality was 60% higher in the daughters of mothers with a poor-prognosis form of breast cancer, compared with mothers with a good prognosis, he continued.

Concordance with regard to prognosis was strongest among mother-daughter pairs in whom the mother was diagnosed before age 40.

The determinants of this newly recognized inherited component of breast cancer prognosis are likely to turn out to be genetic.

Their detailed identification could provide important new biologic insights into the disease. Similar multigenerational studies of other types of cancer deserve to be a research priority, Dr. Hartman said. ■