Molecular Imaging Helps in Detection of Breast Cancer

BY KERRI WACHTER
Senior Writer

A novel imaging technique seems to be better than standard mammography at detecting breast cancer in high-risk women with dense breast tissue, according to findings from a study involving 940 women.

Molecular breast imaging detected three times as many cancers as mammography did in this group of women, Carrie B. Hruska, Ph.D., said at a media briefing on Sept. 3 that was held in advance of the American Society of Clinical Oncology's annual Breast Cancer Symposium.

"Molecular breast imaging may be a promising adjunct to screening mammography for women with dense breasts and who are at increased risk," she said. It is estimated that roughly a quarter of women 40 years and older have dense breast patterns.

Molecular breast imaging (MBI) relies on increased uptake of the radiotracer Tc-99m sestamibi by cancer cells, compared with healthy breast tissue, to identify tumors that might go undetected by conventional mammography, according to Dr. Hruska, a research fellow in radiology at the Mayo Clinic in Rochester, Minn.

For the investigation, a total of 940 women underwent mammography and molecular breast imaging.

All of the participants had previously been determined to have mammographically dense breasts and had at least one cancer risk factor, including personal or family history, genetic mutation, previous precancerous finding, a history of chest irradiation, or elevated risk by Gail model.

For MBI, the women were injected with 740 MBq of Tc-99m sestamibi. The location of accumulated radiotracer was then detected using two opposing semiconductor-based gamma cameras. The novel dual-camera configuration was developed at the Mayo Clinic and the sestamibi tracer was supplied by Bristol-Myers Squibb Co.

Craniocaudal and mediolateral oblique views of each breast were obtained (10 minutes per view). The MBIs were read by two radiologists, who were blinded to the mammographic interpretation and all ancillary patient information.

Breast cancer status for each participant was determined using a combination of pathology findings and clinical and/or imaging findings within a 15-month follow-up period.

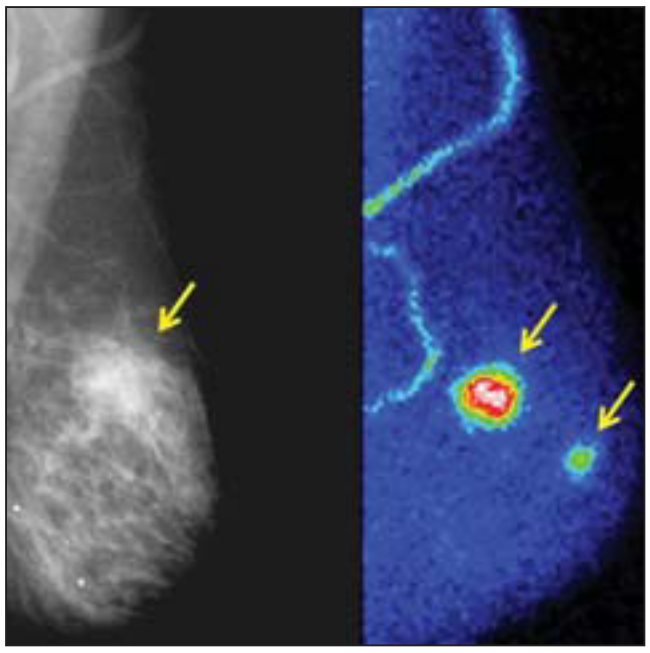
In all, 13 cancers were diagnosed in 12 patients. Eight cancers were detected by MBI alone, two by both techniques, and two by mammography alone.

In the subset of 375 patients for whom more than 15 months of follow-up had passed since they had MBI, the sensitivity of MBI was 75%, compared with 25% for mammography. The specificity of MBI was 93%, compared with 91% for mammography.

Of the 17 biopsies prompted by mammography in 1.8% of patients, 18% were found to be positive for cancer (positive predictive value).

In comparison, of 36 biopsies that were prompted by MBI in 3.5% of patients, 28% were found to be positive for cancer (positive predictive value).

"To put this in context, probably somewhere in the range of 10%-15% of all breast cancers are clinically occult on mammography. … That is a more common problem in women who have dense breasts," said moderator Dr. Eric Winer, who is the director of the Breast Oncology Center at the Dana-Farber Cancer Institute in Boston.



IMAGES COURTESY DR. CARRIE B. HRUSKA

Molecular breast imaging (right) found a tumor (bottom arrow) that was not seen on standard mammography (left).

MBI was developed based on incidental findings on myocardial perfusion scans, which use Tc-99m sestamibi.

"The reason that MBI [was investigated for] breast imaging is that during cardiac scans in women, people noticed that there was uptake in breast cancers," Dr. Hruska said.

Tumor uptake of the tracer appears to be "somewhat related to mitochondrial activity, but nobody really knows the true mechanism," she added.

The researchers are also looking at alternative tracers. "One of them is very exciting. It actually is taken up in tumors based on their angiogenesis, so we think we can find even smaller cancers," Dr. Hruska said.

The researchers disclosed that they had no conflicts of interest relevant to their study. ■

DRUGS, PREGNANCY, AND LACTATION

Antirejection Drugs

BY GIDEON KOREN, M.D.

Stopping a medication during pregnancy because of potential risks to the fetus is not an option for women who have had an organ transplant, because they risk losing the transplanted organ. Despite considerable concerns about the reproductive safety of cyclosporine, by far the most commonly used antirejection drug for several decades, the data have been reassuring.

Several years ago, a meta-analysis of 15 studies looking at pregnancy outcomes in women after cyclosporine therapy suggested that the prevalence rate of major malformations was not substantially different from the rate usually reported in studies in the general population. The analysis did suggest a trend toward an increased risk (Transplantation 2001;71:1051-5).

The neurotoxic side effects of cyclosporine in adult and pediatric patients have raised concerns about the potential effects on brain development in children exposed to the drug in utero. At Motherisk, we recently completed a prospective study evaluating IQ, language, and development in about 40 children of transplant recipients who took cyclosporine during pregnancy and in controls, correcting for the maternal socioeconomic education level and IQ. Follow-up of the children to ages 3-8 years found similar achievement in those exposed to cyclosporine and the controls. (This study has been presented at meetings, but not yet published.)

Cyclosporine use has decreased, largely because of its nephrotoxic side effects and the availability of newer, highly effective immunosuppressants. However, there are far fewer reproductive safety data available on the newer drugs. For one, mycophenolate mofetil (Cellcept), the available data are worrisome.

To date, the data do not suggest that tacrolimus (Prograf) is associated with an increased rate of major malformations, but there are still no data on the drug's effect on the neurobehavioral development of children exposed in utero.

Because cyclosporine, tacrolimus, and sirolimus are associated with some serious adverse effects, particularly chronic kidney damage, new drugs are being used—particularly mycophenolate mofetil (MMF)—which have similar effects on preventing rejection, but with far fewer nephrotoxic effects.

But evidence is beginning to emerge that MMF is associated with an increased rate of major malformations. The drug's label states that treatment should not be started until the patient has a negative pregnancy test, and women of childbearing age should use two forms of contraception.

In recent years, reports of malformations in babies exposed to MMF during the first trimester include microtia, cleft lip and palate, hypoplastic fingers and toenails, diaphragmatic hernia, congenital heart defects, and micrognathia. These reports come from small case series and case reports and do not prove causation, but they have raised concerns about the drug's reproductive safety because of the clustering of similar defects, instead of the distribution of malformations seen in the general population.

In a National Transplantation Pregnancy Registry (NTPR) study of outcomes of pregnancies exposed to MMF or sirolimus, there were 26 pregnancies, including 11 that ended in spontaneous abortions, in 18 kidney recipients treated with MMF. Of 15 live births, 4 (26.7%) had a structural malformation, including hypoplastic nails and shortened fifth fingers, microtia with and without cleft lip and palate, and a death in a neonate with microtia and other malformations.

Among the seven transplant recipients who received sirolimus (Rapamune) during pregnancy, there were three spontaneous abortions. Of the four live births, three had no malformations and one baby whose mother had been treated with MMF during pregnancy but had changed to sirolimus late in pregnancy had microtia and a cleft lip and palate (Transplantation 2006;82:1698-702).

Motherisk recently published a precautionary note about this drug in women in which we advised that a woman who has had a transplant and is on MMF and planning a pregnancy should consider switching to cyclosporine for a short period (Canadian Family Physician 2008;54:1112-3).

In addition, many women transplant recipients are also on corticosteroids, which are known to increase the risk for oral clefts. Many are also on azathioprine (Imuran). A trial comparing pregnancy outcomes in 189 women in Europe, Asia, and North America who took azathioprine during pregnancy with 230 women who took nonteratogenic drugs in pregnancy found no evidence of an increased rate of malformations, but the drug was associated with lower birth weight, gestational age, and prematurity (Birth Defects Res. A Clin. Mol. Teratol. 2007;696:701).

DR. KOREN *is a professor of pediatrics, pharmacology, pharmacy, medicine, and medical genetics at the University of Toronto. He heads the Research Leadership in Better Pharmacotherapy During Pregnancy and Lactation at the Hospital for Sick Children, Toronto, where he is director of the Motherisk Program. He also holds the Ivey Chair in Molecular Toxicology at the department of medicine, University of Western Ontario, London.*