Ultrasound Can Detect Cancers Missed by Mammography: WHRY Research at Center of National Debate

The American Cancer Society recommends yearly mammography beginning at age 40. This is because a mammogram, an X-ray picture of the breast, is the only screening method proven in clinical trials to reduce the number of deaths from breast cancer through early detection. When caught early, most tumors are still small and highly treatable.

Yet mammography is an imperfect screening tool that can miss breast cancers in some women, particularly those with dense breast tissue. In fact, mammograms can miss up to half the cancers in women with dense breasts. Moreover, having dense breast tissue increases breast cancer risk and approximately 40 percent of women have dense breast tissue.

Mammography’s limitations led to a debate in recent years about whether other imaging technologies should supplement mammography to improve the early detection of breast cancer. One technology at the center of this debate is screening with ultrasound, which uses sound waves to produce an image of the breast.

Connecticut became the first state to enact a law mandating that radiologists inform women who undergo mammography if they have dense breast tissue and that they may benefit from supplementary screening tests.

Even before the Connecticut law took effect in October 2009, Dr. Regina Hooley, M.D., Assistant Professor of Diagnostic Radiology and a clinician at the Smilow Breast Center, knew she wanted to study the performance of screening ultrasound to begin exploring the key question for both patients and scientists: Can breast ultrasound screening after mammography effectively improve the cancer detection rate and find cancers missed by mammography?

“When I decided to do the study, I had no idea there was going to be a national movement,” Hooley said.

At least 10 other states – Alabama, California, Hawaii, Maryland, Nevada, New York, Oregon, Tennessee, Texas and Virginia – have enacted laws requiring breast density notification after mammography. As more women become aware of breast density and opt for ultrasound screening, the need for research data on the technology’s usefulness increases.

Against this backdrop, Hooley was awarded a 2012 Women’s Health Research at Yale Pilot Project Program grant to study the performance and value of supplementary breast screening with ultrasound, following mammography. Given Connecticut’s head start on experience with supplemental ultrasound screening, compared to other states, Hooley’s WHRY-funded research is at the forefront of a heated medical debate that has spilled into legislatures across the country.

Critics of the notification laws say that the breast density information requirements are premature because supplemental screening with ultrasound has not been proven to be beneficial. They point to a high rate of false positives with ultrasound screening, leading to unnecessary biopsies.

Supporters of the laws say providing information about breast density and supplementary screening options are positive steps for women who want to...
know if they have cancer or reassurance that they do not. They say that finding cancers at a smaller size and stage can reduce breast cancer deaths, and say that false positives with ultrasound can be reduced.

Hooley had mixed opinions initially and now is among the supporters, though she remains committed to following her research data wherever it leads.

Specifically, Hooley’s study is designed to determine the rate at which ultrasound screening can detect breast cancers not found through mammography screening, patients’ opinions about ultrasound screening, and Connecticut physicians’ referral patterns related to ultrasound screening after mammography.

She expects to survey 1,000 patients about their opinions on ultrasound screening after mammography. So far, questionnaires completed by more than 200 women indicate:

- 91 percent said ultrasound screening was important in finding cancers that were not detectable with mammography.
- 45 percent reported anxiety due to awareness of breast density.
- 89 percent said they chose ultrasound screening despite the increased chance of needing additional testing after the ultrasound.

Hooley is circulating a questionnaire to 500 physicians locally and about 800 physicians across the state through the Connecticut Medical Society, and is waiting for an adequate number of responses.

The central component of her study is a review of the records of nearly 4,000 women who underwent mammography and supplementary breast ultrasound screening in the first three years, 2009-2012, after Connecticut’s mandate took effect. Hooley is exploring breast ultrasound’s weaknesses as well as strengths, and seeking ways to improve its medical effectiveness. Although the study will not be completed until next year, Hooley’s preliminary conclusion is that supplementary ultrasound screening after mammography can benefit women with dense breast tissue.

“There is increasing demand for improved breast cancer detection by both patients and their physicians,” Hooley said. “Mammography has its limitations, especially for women with dense breast tissue. Screening ultrasound is a reasonable supplemental screening tool that can detect breast cancer at a rate of 3.5 new cases per thousand (women screened).”

While this detection rate may seem low, it is close to the cancer detection rate for screening with mammography, approximately 5 new cases per 1,000 women screened, Hooley said.

Smilow Breast Center, the clinic where Hooley practices, did not offer ultrasound screening before Connecticut’s breast-density notification requirement took effect. With the law’s implementation, the clinic immediately began offering ultrasound screening by trained technologists using hand-held devices. Radiologists review the images. Connecticut is one of the few states requiring health insurance to cover the cost of supplemental breast cancer screening, and demand for ultrasound screening has kept the clinic very busy, Hooley said.

In the first year after the law took effect, 953 women who were informed about their dense breast tissue after mammography chose to have the extra ultrasound screening and were included in Hooley’s study population. The supplementary screening with ultrasound detected three cancers that were not found by mammography, for a cancer detection rate of 3.2 per 1,000, in this first year population.

Hooley is now reviewing the records of 1,046 women who underwent supplementary ultrasound screening in the third year after the law took effect. She will eventually review the records for the second year, but decided to review the third-year records first. This is because, in the third year, the clinic began

(Continued on page 3)
using a new, more sophisticated mammography (tomosynthesis mammography, which provides three-dimensional images) in conjunction with regular mammography.

Hooley wanted to immediately investigate whether this change would affect the rate at which supplementary ultrasound screening detects cancers not seen in mammography. As she expected, the 3-D mammograms revealed cancers at a higher rate than regular mammograms, so the detection rate for supplementary screening with ultrasound not surprisingly decreased from 3.2 to 2.0 new cases per 1,000, in this third-year population.

As radiologists in her clinic gain more experience looking at and interpreting ultrasound images, according to Hooley, the rate of false positives that require follow up tests or biopsies is being reduced. When she and her colleagues first started using ultrasound, they were seeing cysts and other masses that had not been detected with mammography. These findings initially caused concern. However, with more experience the clinicians are learning to recognize benign masses that do not need additional testing, Hooley said.

While she continues to gather evidence about the value of supplementary screening with ultrasound, Hooley thus far views the technology as beneficial, despite limitations and a need to continue improving its effectiveness. Ultimately, she said, research data will help clinicians identify which patients will benefit the most from supplementary screening, and which patients will not need follow-up tests.

“The bottom line is that, with the state notification law in place, patients want to know their options if they are informed they have dense breast tissue. Supplementary screening with ultrasound is a test that can actually give patients more reassurance that they don’t have cancer, or the test can find cancers missed by mammography,” Hooley said. “And this pilot study is helping us understand and improve the use of the technology.”

Q & A with Dr. Regina Hooley

Q: Why is screening with mammography an imprecise tool for detecting cancers in dense breast tissue?
A: Breasts consist of fat and glandular tissue. On mammography, fat is grey while glandular tissue and cancers are white. If a woman’s breast consists of mostly fat, it is easy to see the white cancer in a background of grey fat. However, if a woman’s breast consists of mostly glandular tissue, it can be very difficult to see a white cancer surrounded by white glandular tissue, like searching for a polar bear in the snow. With dense breast tissue, the mammogram is less accurate and can miss more cancers compared to non-dense breasts.

Q: Although your study is not completed, your preliminary conclusion is that supplementary screening with ultrasound after mammography can benefit women with dense breast tissue. Which of your findings lead you to this view?
A: Early results show the cancer detection rate of supplemental screening ultrasound in the general population is approximately 3 per thousand women screened, similar to the cancer detection rate of mammography. Some of these cancers are not seen with the new 3D tomosynthesis mammograms and are generally small, invasive tumors with very good prognoses. As screening with ultrasound is optional and controversial, it is important to be aware of women’s knowledge and opinions regarding this test. Early patient survey results indicate that women are amenable to screening ultrasound because it provides additional information regarding their breast health.