Detecting Breast Cancer:
Komen-Funded Researcher Explores the Universe of Sound

Dr. Neb Duric, Professor of Oncology at Karmanos Cancer Institute in Detroit Michigan.

Mammography has been the gold standard for breast cancer screening over the last four decades, but it is not foolproof. It misses some cancers (false negatives) and incorrectly identifies some breast features as cancer (false positives), resulting in unnecessary biopsies, exposure to additional X-ray radiation, and discomfort for some women during the procedure(s). Many scientists have been working on improving breast cancer screening, but Komen-funded researcher Dr. Neb Duric, Professor of Oncology at Karmanos Cancer Institute in Detroit Michigan, decided to look to the stars for answers, and he has come one step closer to a real solution.

Looking into Space and Seeing Within

Twelve years ago, the Barbara Ann Karmanos Cancer Center invited non-medical scientists to a think tank workshop and tasked them with applying their knowledge to identify and improve a current medical issue. For Dr. Neb Duric, then Professor and Astronomer in the Department of Physics and Astronomy at the University of New Mexico in Albuquerque, the area for improvement was clear: medical imaging. “I knew there were things we used in [astronomy] imaging that could be used for diagnostics in early breast cancer,” Dr. Duric recollected. Taking pictures of very distant objects, such as stars, often results in blurry images. For that reason, there is a constant effort in astronomy to create and optimize methods aimed at increasing the quality of these images. Dr. Duric was no stranger to such efforts. With his imaging expertise and the opportunity at Karmanos to extend his know-how to medical challenges, Dr. Duric began his research in ultrasound (US) imaging for detecting breast cancer.

The Imaging Dilemma

While mammography can successfully identify breast cancer in many women, it is particularly inefficient for women with dense breasts who are at increased risk for developing breast cancer. In these women, false negatives could be as high as 50%. However, alternative screening methods do exist. Magnetic Resonance Imaging (MRI) can image the breast by using powerful magnets and radio waves to create up to dozens of pictures with just one scan; and, it is about 80% effective at imaging dense breasts, compared to mammography’s 50%. But, the scan is slow – 45 minutes to one hour – and because of the design of the machine – the patient must lie on a narrow table, which slides into a large tunnel-shaped scanner – the procedure can be uncomfortable for some women. In addition, the technique requires the injection of a contrast agent, which can produce adverse reactions in some patients. Even more, MRI is costly for the hospital and patients – up to $2,000 per test. Computed Tomography (CT scan), another X-ray imaging technique like mammography, can better image dense breasts, but it still exposes patients to radiation.

> Breast density is a feature that reflects the ratio between dense tissue and fat in the breast. Breasts that contain more dense tissue than fat are referred as dense. In a mammogram, dense breast tissue can look white or light gray, which is also how cancerous tissue looks and is identified. Ultrasound can do a better job imaging tumors in dense tissue.

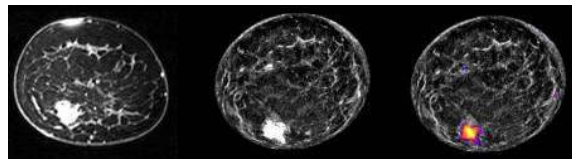
The Sound of Imaging

Dr. Duric has been exploring a lower-cost, innovative way of screening for breast cancer called ultrasound tomography (UST), which combines the low-cost advantage of mammography with the superior imaging performance of MRI. “The fact that mammography fails in [women with dense breasts] is the reason why alternatives are needed” says Dr. Duric. And, “MRI is not a viable option for screening the general population, from an economic perspective,” he adds. UST uses high frequency sound waves to measure differences in breast tissue stiffness to generate images of the breast. However, US imaging is not new to medicine; it has been routinely used for the last 30 years.

Unlike traditional US, which generates 2-dimensional images as the sound waves reflect off body structures, UST records a series of images that can be re-constructed into a 3-dimensional image, providing a much more complete picture of the breast. What makes UST particularly appealing is its lack of radiation exposure and its low price tag. There is also no need to compress the breast to image it, as in mammography. Instead, the breast is simply submerged in water, which allows for higher quality transmission of sound waves than air. In addition to increasing the comfort of the patient, no compression also means that the technique is able to much better locate tumors very precisely.

Fighting Breast Cancer at the Speed of Sound

In 2007, with a 2-year, $300,000 grant from Komen, Dr. Duric set out to study the effectiveness of using UST to measure breast density. Dr. Duric, his student Carri Glide-Hurst and colleague Peter Littrup collected and analyzed nearly 300 patient images from UST and were able to show that the speed at which sound travels through the breast correlates with breast density – the denser the breast, the slower the sound waves travel through the tissue. Taking this a step further in a small clinical study, also supported by Komen, the research team was able to demonstrate that UST could successfully image dense breasts and had the potential to replace mammographic density as a measure of breast cancer risk.

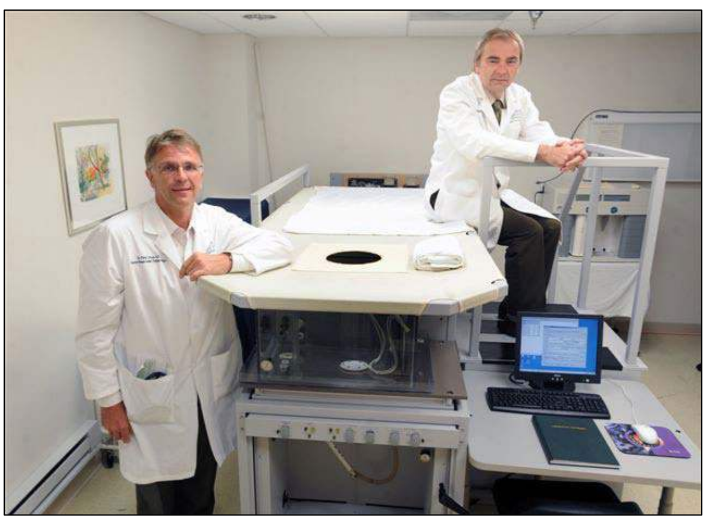


MRI UST color UST

UST has the ability to detect cancer as well as MRI, but without the high cost and intravenous injection of imaging dyes which MRI requires.

With this validation, Dr. Duric and his team began to focus on the software needed to optimize and potentially automate the detection of breast cancer with UST. In 2010, with another Komen research grant funded by Belk, Belk EDGE: A Susan G. Komen for the Cure® Grant for Early Detection and General Education, Dr. Duric began to perfect the statistical methods used to analyze the images generated by UST and identify regions that could potentially be cancer. After analyzing hundreds of UST images from patients, Dr. Duric and his team demonstrated that the technology was able to correctly identify cancer in 90% of all cases, regardless of breast density. The investigators estimated that up to 30% of unnecessary biopsies could be avoided by using UST.

From the Lab to the Clinic



Drs. Littrup (left) and Duric (right) present the UST clinical prototype. A patient lies in the prone position such that the breast is suspended inside a water tank (opening on the center of the device) that contains the ultrasound sensor.

During the 12 years that Dr. Duric was optimizing the use of ultrasound imaging to detect breast cancer, he also was working to create a commercial version of the device – one that could ultimately be installed in hospitals and help patients. Dr. Duric and Dr. Peter Littrup, M.D., his long-time research partner and collaborator on the Komen grants, were able to commercialize the ultrasound screening device under the name SoftVue*. The first machine was installed at Karmanos last November and is being used in a clinical study aimed at proving that the new version of the device maintains or exceeds the performance of the earlier prototype. Sixty patients have already been scanned and most reported that they found the exam more comfortable than mammography. They especially liked the speed at which the scan completes; about one minute per breast. Larger clinical studies are still required to support a broader, clinical implementation of SoftVue.

* In 2009, Drs. Duric and Littrup, and the Karmanos Cancer Center co-founded Delphinus Medical Technologies for the commercialization of SoftVue. The company, located in Plymouth, Michigan, currently employs 20 people, including Dr. Littrup as Chief Medical Officer and Dr. Duric as Chief Technology Officer.

What's Next?

Dr. Duric and his research team are focusing on improving the imaging and accuracy of SoftVue even more. They are now able to produce higher quality images with the device and are fine-tuning how the software "recognizes" cancer. These improvements will need to be validated in another 300 patients, and the results compared to MRI scans. Dr. Duric and his collaborators have requested FDA clearance of SoftVue as a diagnostic device for breast imaging. A Future FDA application for screening approval will require the expansion of the current clinical studies, which will be costly as it will require participation of multiple testing sites and up to 25,000 patients. So far, Drs. Duric and Littrup have approached 10 different Centers, and are in the process of negotiating the agreements and building the machines that will be used at each Center.

What Does it Mean for Patients?

Women whose breast cancers are found early, when they are still confined to the breast, have a 5-year survival rate of 98%. However, these women account for only 61% of breast cancer cases. More than one-third of cases are detected at advanced stages or have spread to other parts of the body and have a survival rate of only 55%. These numbers illustrate the importance of early detection. There are many reasons why cancers are not detected early, including limited participation in breast screening – because of fear of radiation or discomfort – and the limitations of current detection techniques, particularly for women with dense breasts who are at high risk of developing breast cancer.

Dr. Duric's SoftVue system could provide a lower cost and more effective technology for finding more breast cancers early, with increased accuracy, safety, and comfort. In particular, the technology could provide a more effective tool for finding early disease among women at high risk of breast cancer because of dense breasts. Even more, the technology could improve breast cancer survival rates by detecting breast cancer at an earlier stage, when it is most curable, and by increasing participation in breast cancer screening programs by offering a more comfortable, accessible imaging method. Increased participation and improved breast cancer detection would have a significant impact on the nearly 1 in 3 women who are diagnosed each year with later stage breast cancer, totaling approximately 60,000 women per year in the United States.

Behind the Scenes

Astronomy has been a passion for Dr. Neb Duric since he was 8 years old. Born in the former Yugoslavia, he spent many nights looking at the sky and wondered what he was seeing. Following his passion, Dr. Duric received his PhD in Astrophysics in 1984 from University of Toronto, and he worked in astronomy for 20 years. Dr. Duric did his post-doctoral fellowship training in British Columbia before heading to Albuquerque where he stayed for 18 years. In retrospect, Dr. Duric never thought that he would have switched from astronomy. "Getting such a faculty position was a dream job" Dr. Duric recalled; however, through consulting, he found that there was an opportunity to directly help people with their medical needs and that became a new fascination. His father died of cancer around the same time, so the opportunity became even more appealing, and Dr. Duric decided to make the jump. The change was a risky one, as Dr. Duric had to abandon a tenured faculty position, one that guarantees employment at the University, to start from scratch. But his persistence and dedication has paid off. "I felt so strongly about the opportunity to help people directly that it was worth the risk," says Duric.

Dr. Duric's Komen funded work on the development of SoftVue was published in Medical Physics in January 2012.