

Mammography is good at detecting breast cancer, but it's not perfect, especially for women with dense breasts. Overall, it can accurately detect breast cancer about 84

percent of the time. But some studies estimate that mammography detects fewer than half of cancers in dense breasts. This is primarily because breast tumors and dense breast tissue look similar on a mammogram, making it difficult to distinguish between them. In addition, women with dense breast tissue are more likely to have a false positive (incorrect identification of some breast features as breast cancer) finding on mammography, meaning that they are called back for additional testing for something that turns out not to be cancer. This can result in additional imaging tests, or even biopsies, for an accurate diagnosis. Additional diagnostic tests can cause increased anxiety for the patient, extra time in the clinic and increased medical costs.

Learn more about breast density and mammograms

<http://www.komen.org/BreastCancer/HighBreastDensityonMammogram.html>

**Breast density compares the amount of fat to the amount of tissue on a mammogram. A dense breast has more tissue than fat.**

Scientists and clinicians have been working for decades to develop better methods for breast cancer screening in women with dense breasts, but Komen-funded researcher Dr. Deborah Rhodes and a team at The Mayo Clinic in Rochester, Minnesota may finally have a solution by using molecular imaging, a technology already used for imaging the heart.

### Do you have dense breasts?

High breast density is common. Between 40 and 50 percent of women (aged 40 to 74) in the U.S. have dense breasts. Women with high breast density are four to five times more likely to develop breast cancer compared to women with low breast density. Even more, dense breast tissue can hide cancer.

### Screening Alternatives

Several studies have evaluated other screening tools used in combination with mammography to see if the detection of breast cancer can be improved in women with dense breasts. Addition of ultrasound to mammography can improve breast cancer detection by a few cancers for every 1000 women. However, screening ultrasound is associated with a high rate of false positives (incorrectly identifies some breast features as cancer). Some studies estimate that adding screening MRI to mammography can increase cancer detection by three-fold or more; however, MRI is very expensive (up to 10 times the cost of a mammogram), is complex to interpret, and, like ultrasound, is associated with a high rate of false positives. For this reason, screening breast MRI is typically reserved for women at high risk for developing breast cancer. While current screening methods (mammogram,

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ultrasound and MRI) are effective for many, some women with dense breasts may still have tumors that go undetected altogether. The limitations of these methods highlight the need for new screening methods that can accurately detect breast cancer in women with dense breasts.

Recognizing Dr. Rhodes' promising work in potentially answering this need, she and her colleagues at the Mayo Clinic received two consecutive research grants from Komen to evaluate the effectiveness of using molecular breast imaging (MBI) as a breast cancer screening tool in women with dense breasts.

**MBI began as a method for imaging the heart. It uses a small camera called a gamma detector and a radioactive tracer. Patients are injected with the radioactive tracer which travels to tissues that have high metabolic activity (like a tumor). Imaging takes up to 10 minutes per view and 2 views are taken of each breast. Gamma detectors offer a unique advantage: unlike X-rays (used in mammography), the image produced by the gamma detector is unaffected by tissue density. Therefore, detection accuracy is high even in patients with dense breasts.**

## A Simple Roll of Duct Tape

Working closely with nuclear physicist Dr. Michael O'Conner, who was instrumental in developing MBI, Dr. Rhodes and the Mayo team used an everyday engineering



*Original MBI Machine with Duct Tape*

marvel – duct tape – yes, duct tape – and a bit of ingenuity to modify an existing mammogram machine. They removed the X-ray detector and replaced it with a gamma detector. Using this device, they were able to image the breast and detect a tumor in dense breast tissue.

Rhodes' innovative team was later joined by a biomedical engineer, Dr. Carrie Hruska, and two radiologists, Drs. Katie Hunt and Amy Conners, to improve the device. Now, the duct tape keeping the prototype together is gone, and MBI has been commercially developed by Gamma Medica® under the market name LumaGEM®. The technology uses a radioactive compound that concentrates within the tumor cells. Two cameras

are used to take pictures, detecting the radioactive compound within the tumor cells and producing a clear image – regardless of breast density.

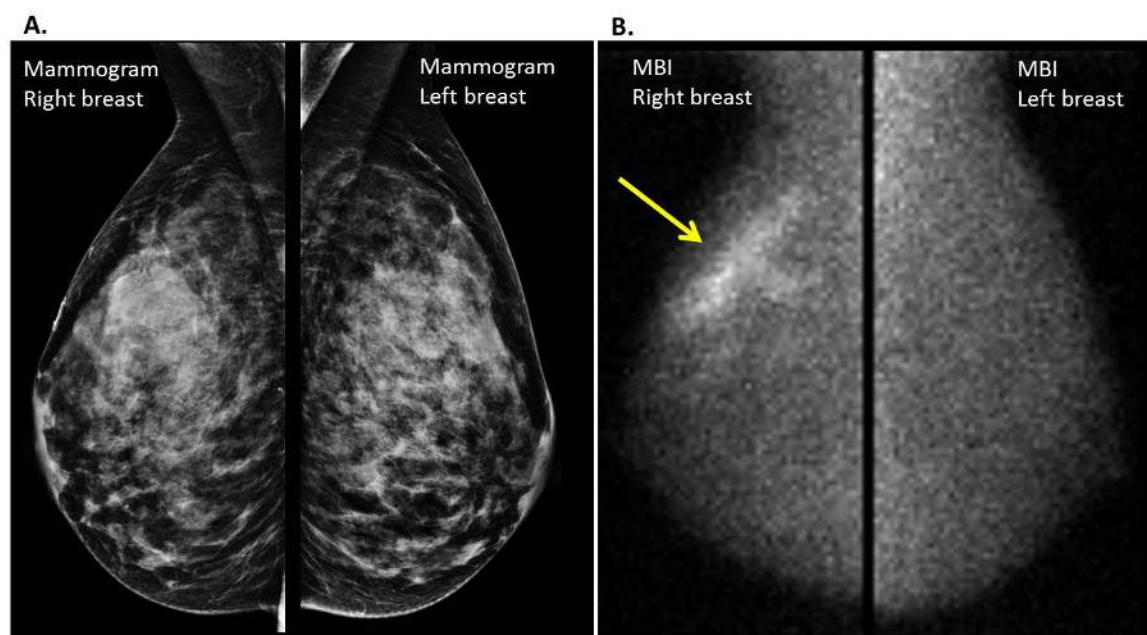
## A Big Boost in Accuracy

With her first grant from Komen, Dr. Rhodes and her Mayo colleagues were able to conduct a clinical trial to determine if MBI could detect cancer in dense breast tissue when used in combination with mammography. The study included 940 women who had dense breasts; Rhodes and colleagues found that MBI plus mammography was more sensitive than mammography alone, with a 91 percent

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chance of accurately detecting breast cancer compared to 27 percent with mammography alone. This study was a first step in moving MBI to the clinic. However, with a goal of developing a test that could be used repeatedly for screening, the Mayo team worked to modify the MBI system to allow for a lower level of radiation while still maintaining the quality of the image. Following these modifications, Dr. Rhodes received a second grant from Komen to conduct another clinical trial testing whether the performance of MBI was maintained at this lower radiation dose. Nearly 1,600 women participated in the study, and the research team showed that the lower radiation dose – comparable to what is used in mammography – still resulted in four times greater accuracy in the diagnosis of breast cancer when compared to using a mammogram alone.



*Breast cancer lesion undetected by a mammogram (panel A) was detected by MBI (panel B)*

## Benefits Beyond Accuracy

Rhodes says that, “the cost of MBI is comparable to the cost of mammography, but performing the two tests together does add expense.” However, her colleague, Dr. Hruska, found that the addition of MBI to the initial mammogram actually resulted in an overall drop in medical expenses by 15 percent for each cancer that was detected.

The research team hopes to demonstrate that by detecting cancers earlier than with mammography alone, MBI will allow for less-invasive and less-costly breast cancer treatments. The increased detection accuracy associated with this new technology highlights the impact MBI could have on routine breast health, in addition to the convenience and reduced anxiety patients may experience when a test is accurate the first time. Even more, patients found that MBI caused much less discomfort than a mammogram because it only requires light compression of the breast.

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## What's Next?

Dr. Rhodes' studies show that using MBI with mammography may improve the detection rate of breast cancer in patients with dense breasts, compared to using mammography alone. She believes that this new tool could be added to screening mammography in patients with dense breasts, thus improving accuracy. The next step is a clinical trial which would compare additional screening methods, such as MRI, whole breast screening ultrasound or digital breast tomosynthesis, with MBI to determine which one is the most effective at detecting a breast tumor in dense tissue.

***"When I consider the potential number of women who would be helped if we confirmed the best screening method, and the potential number of women who will be harmed by unnecessary testing or worse - a missed cancer - if we do not, I cannot think of a more important initiative in the field of breast cancer"*** says Rhodes.

## What it Means for Patients

Women with dense breasts are more likely to develop breast cancer than women with normal breast density. Even more,

mammography is not very effective at detecting breast cancer in women with dense breasts, enforcing the need for more-accurate screening methods for this population. Dr. Rhodes' study shows that MBI can detect breast cancer accurately, which may result in a faster diagnosis, earlier and less-invasive treatment and a better chance of survival. For the patient, the MBI screening method could reduce the anxiety associated with unclear results. Additionally, due to its increased accuracy, the overall costs of screening may be reduced. As a result, more patients could potentially gain access to affordable screening, increasing the number of women who receive an early diagnosis when the disease is most treatable. ***"MBI could give new meaning to early detection because it will reveal a significant number of cancers that would otherwise go undetected on [traditional] mammography - sometimes for years. This could have a large impact on breast cancer mortality, an endpoint that is important to study, but that will take many years and millions of dollars to assess,"*** says Rhodes. MBI equipment is now being installed at all Mayo sites, and is becoming available in more centers across the country so that it can be studied further.

Learn more about breast density and breast cancer risk

<http://www5.komen.org/KomenPerspectives/Breast-Density-and-Breast-Cancer-Risk.html>

## Committed to the Cure

Dr. Rhodes' training and innovative ideas have undoubtedly helped bring MBI technology to the clinic. She received a B.A. degree in history and literature from Harvard College and an M.D. degree from Cornell University Medical College. Her medical training was followed by an internship and residency in internal medicine and a Robert Wood Johnson Clinical Scholars Fellowship at Johns Hopkins Hospital. After years practicing in the clinic, she was inspired to focus her research

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on improving screening methods, because she strongly felt that patients with dense breasts were not receiving the most accurate results.

### **Question and Answer with Dr. Rhodes**

*Q: What made you decide to go into scientific research and focus on cancer biology, specifically breast cancer?*

A: This has been my passion for a long time – I devote nights and weekends to this. I am so driven because I feel that the focus of federal funding at the present time has moved away from screening. However, screening is important for early detection, and early detection could eliminate metastatic disease from ever developing in the first place.



**Dr. Deborah Rhodes, Associate Professor of Medicine at the Mayo Clinic in Rochester, Minnesota**

*Q: What made you decide to focus your research on Molecular Breast Imaging (MBI)?*

A: I decided to focus on MBI because I am a practicing clinician in a Breast Clinic and I felt we were providing false reassurance after a negative mammogram in women with very dense breasts. I knew that the sensitivity of mammography was reduced in these women, but we did not have a good alternative to offer. MRI is simply too complex and expensive to use as a screening tool in the sizable population of screening-eligible women with dense breasts unless they qualify for MRI screening on the basis of other risk factors. We developed MBI as a tool to screen women with dense breasts who are not otherwise high-risk.

*Q: How important was Komen funding for conducting this research?*

A: This work would not have happened without Komen funding. Komen took a chance on a very “out-of-the-box” idea that has lived up to its early promise.

*Q: Can you describe the ultimate outcome of this Komen-funded project?*

A: There is currently no standard recommendation for supplemental screening in women with dense breasts. It is very heartening to realize that an imaging test that we developed ten years ago and have been able to evaluate rigorously due to generous Komen funding has reached the clinical realm and is detecting important cancers missed by mammography. MBI equipment is now being installed at all Mayo sites, and is becoming available in more centers across the country – University of Pittsburgh, MD Anderson, and other academic centers are now studying MBI, and some community radiology practices have acquired it.

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***Q: Do you see MBI becoming a standard of care tool used in clinics across the globe? If so, when?***

A: I think MBI could become a routine part of breast imaging. It takes considerably less time to interpret than an MRI or ultrasound which generates hundreds/thousands of images vs. MBI with eight images. Also, MBI is more straightforward to interpret compared to most mammograms because it is not complicated by the need to distinguish density from tumors. Furthermore, it is a less-expensive test (at least at the Mayo Clinic) than a screening mammogram. Additionally, it is relatively easy and fast for radiologists to learn how to interpret this test, in contrast to MRI which is a highly complex test to interpret. However, what is really needed to convince those outside our institution is a multicenter trial comparing MBI to tomosynthesis in women with dense breasts. I am convinced MBI would detect considerably more cancers than tomosynthesis. The advantage of MBI is that it is a functional imaging tool, meaning that it exploits differences in tumor cell function relative to non-tumor cells in order to detect tumors. In contrast, tomosynthesis, like 2D digital mammography, relies on the visual distinction between tumors and background breast tissue, which can often be difficult to discern in a dense breast. The problem is that the cost of doing such a large, multicenter trial is in the many millions, and there is very little appetite currently for funding more screening trials – in part because I feel that the federal funding agencies have given up prematurely on new approaches to screening as a means of further reducing death from breast cancer.

***Q: Do you think MBI could be improved further? How?***

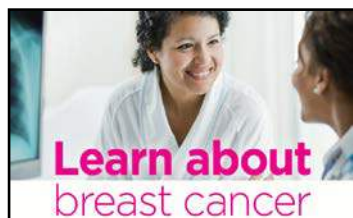
A: I think the best way to improve MBI further is to make it more available!

***Q: Anything else that you would like to share with our readers?***

A: Thank you, thank you, thank you, Susan G. Komen!

Dr. Rhodes' MBI studies were published in the American Journal of Roentgenology in June 2015:

<http://www.ajronline.org/doi/abs/10.2214/AJR.14.13306?journalCode=ajr&>.



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