

Welcome to Yale Cancer Center Answers with your hosts doctors Anees Chagpar, Susan Higgins and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert on Myelodysplastic Syndromes. Yale Cancer Center Answers features weekly conversations about the research, diagnosis and treatment of cancer and if you would like to join the conversation, you could submit questions and comments to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can leave a voicemail message at 888-234-4YCC. Tonight, you will hear a conversation about screening for dense breasts with Dr. Regina Hooley. Dr. Hooley is Associate Professor of Diagnostic Radiology at the Yale School of Medicine. Here is Dr. Anees Chagpar.

Chagpar Regina, let us start by talking about what exactly we mean when we say dense breasts?

Hooley Dense breast tissue is determined by the way the breast looks on the mammogram. It is not really determined by how the breasts feel on physical examination. All women have their own unique mix of fatty and glandular tissue and on the mammogram, the glandular tissue looks white and the fatty tissue looks grey or blackish and so we are always looking for small cancers which are white spots, and so in women with dense and white breasts, it makes the cancer harder to see. If most of the breast is made up of glandular dense tissue, we call them dense breasts. If the breasts are predominantly made up of fatty tissue, we call them non-dense.

Chagpar And is a person's breast density genetically predetermined at birth, that if they have dense breasts, they will always have dense breasts? Or is this something that fluctuates with the hormonal milieu?

Hooley Dense breasts can change over time. We do notice that dense breasts tend to run in families but we do not know for sure if there is a true genetic link. There are factors in life which can change breast density. Women, when they are pregnant, have more dense breasts, their glandular tissue proliferates and grows. Overtime, women tend to have less dense breasts and more fatty replacement of their tissue, so dense breast tissue is not as frequent in women in postmenopausal years, but overall, dense breast tissue is a normal finding and about 50% of all women in the United States have dense breast tissue.

Chagpar How do you know if you have dense breasts? If I understand you right, dense breasts make reading a mammogram, finding those cancers which look white on a mammogram, more difficult. How does a woman know whether her breasts are dense or not? Hooley She will know when she has her mammogram. Here in Connecticut, we have a breast density notification law where we must inform women if they have dense breasts. In our practice at Yale, we also tell women if they do not have dense breasts, so they do not have to wonder whether or not they were told, so once a woman is told that she has dense breasts, we

also are obligated to tell them that they could benefit from additional screening for breast cancer with ultrasound and/or

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Chagpar Tell us more about how ultrasound and/or MRI would help in those patients and how do you decide whether you should get an ultrasound or you should get an MRI, clearly, there is a cost differential there too?

Hooley We think that all women after the age of 40 should have a screening mammogram and if a woman has dense breast tissue and she is of average risk, she has the option of having an extra test in addition to the mammogram and that would be the ultrasound. Ultrasound works particularly well in women with dense breast tissue because the way the ultrasound technology works is that the cancers tend to be dark on ultrasound and the glandular tissue tends to be more white on ultrasound and so we have that contrast to detect these small cancers. There have been numerous studies that have shown that with ultrasound, we can detect an additional 3 cancers per 1000 women screened. You might say, 3 per 1000 is not very high but keep in mind that with screening mammography, we are detecting about 5 cancers per 1000 women screened and that is accepted as being beneficial.

Chagpar So ultrasound may be useful for women who have dense breasts because you can now see this contrast. Tell us about MRI. When should patients have an MRI? Hooley Breast MRI is useful in women who are at very high risk for breast cancer. MRI is probably the best test we have to detect breast cancer. It is very sensitive. The only problem with breast MRI is that it is very costly compared to a mammogram and also requires an injection of intravenous contrast, so it is a little bit more invasive of a screening test. Nevertheless, women who are at very high risk, more than 20% lifetime risk, can benefit and we do recommend that they have screening MRI in addition to their mammogram, but if a patient does have MRI, then she does not need the screening ultrasound.

Chagpar How does a woman know what her lifetime risk is? When you say they need to be more than 20% lifetime risk, how do you figure that out?

Hooley There are various ways of determining that. There are computer modules on the internet where you can plug in your history, various history and personal information that will give you your lifetime risk. There are also certain groups of women who are very high risk. Any woman who is a known BRCA gene carrier is by definition high risk, any woman with more than 2 first degree relatives with breast cancer or a first degree relative with a premenopausal history of breast cancer would qualify as being high risk. There are also some familial genetic diseases that can increase ones risk as well.

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Chagpar Let us suppose you go and you have dense breasts, does it just effect how easy it is for you to find these cancers, that you need this additional screening, and right now there is actually newer forms of mammography that might help to find other cancers too, right, the 3D mammography.

Hooley That is new technology. The tomosynthesis or 3D mammogram is revolutionizing, I believe, breast imaging. With tomosynthesis, multiple image slices are taken through the breast and it allows us to see cancers better because there is less tissue overlap due to the surrounding dense breast tissue, so with tomosynthesis not only can we increase our cancer detection rate but we can also decrease the number of false positives.

Chagpar Could you ever do tomosynthesis instead of an ultrasound as it helps to slice through the dense breast tissue?

Hooley You can, and I think we do not really know what the best screening protocol is. We have this new technology with improved ultrasound tomosynthesis and both of them can enhance the cancer detection rate in addition to conventional 2D mammography alone. Tomosynthesis can increase the cancer detection rate by about 2 per 1000, ultrasound increases it by 3 per 1000, some of the cancers seen on tomosynthesis are not seen on ultrasound, and some of the cancers seen on ultrasound are not seen on tomosynthesis, so we do not know which is better, either one will increase your cancer detection rate. Here in Connecticut, we often do both tomosynthesis and ultrasound in our patients. Again, due to the breast density notification law, it does not specify tomosynthesis as a screening option, so all women who undergo mammography and in our practice, all of our patients have tomosynthesis and also get breast notification and the option for screening ultrasound. C

hagpar Regina, when we started, you mentioned that all women over the age of 40 should get a screening mammogram and I know that that has been controversial with the United States Preventative Services Task Force and presumably women who are young in their 40s have dense breasts, so tell us more about why your recommendation is to get a mammogram when you are 40?

Hooley The United States Preventative Services Task Force recommendations are controversial and the American College of Radiology, the American Cancer Society and the American College of Obstetricians and Gynecologists still recommend screening women every year beginning at age 40, so breast cancer in women under the age of 50 is important. About 25% of all breast cancers occur in women under the age of 50 and these cancers account for about 1/6th of all cancer deaths and so it is important and these women are young and there are more years of life lost in these women, about 50% of years of life lost due to breast cancer occur in women under the age of 50. Moreover, the breast cancers in women under the age of 50 tend to be more aggressive, they grow faster, so we should be screening them every year beginning at age 50 and studies have shown that with screening mammography, there is a 15% reduction in mortality.

Chagpar All great points to get screened early. You know, some women may be concerned about the radiation exposure with mammography and how that builds up over time. Can you speak to that

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and how much radiation a mammogram actually has and how much radiation tomosynthesis has and how much radiation an MRI has?

Hooley Mammography does require low dose ionizing radiation but the dose is very low and it is thought to be not much higher than the natural background radiation that we all experience. We have to keep in mind that when we fly we get a little radiation as opposed to when we are on the beach at sea level and those people who live in the mountains get more radiation than those who live at sea level, so there is a certain amount of natural background radiation that we accept and having a mammogram is not much higher than normal background radiation. With tomosynthesis, the radiation dose does double in addition to what we have in mammogram but again the dose is considered to be quite low and the risk of having radiation induced cancer due to mammography is pretty negligible.

Chagpar So with ultrasound, there is no radiation right?

Hooley That is correct. Ultrasound does not require any radiation, so it is very safe and very well tolerated by patients and that is why in some respects it is a very good screening tool. MRI on the other hand does not require radiation but it does require an intravenous contrast injection and so it is a little bit more like I mentioned earlier, invasive.

Chagpar A lot of women when they come for their mammograms, they really do not love having their breasts pushed in a little machine, so what about ultrasound, if it is a great screening tool and if they can pick up cancers especially in women with dense breasts, do these women really need a mammogram? Can they just get an ultrasound instead?

Hooley That is a very good question Anees, and it is conceivably possible that we could use ultrasound instead of mammography. Certainly ultrasound will detect invasive cancers which we want to find. The only problem is that ultrasound is not as good at picking up calcifications. Sometimes microcalcifications can be an early sign of breast cancer and so mammography is excellent in that regard, so they are really complementary to each other, more over, there have been no randomized controlled trials to show the benefits of screening ultrasound.

Chagpar We are going to take a quick break for a medical minute. Please stay tuned to learn more information about screening for women with dense breasts with my guest, Dr. Regina Hooley.

Medical Minute The American Cancer Society estimates that over 1500 people will be diagnosed with colorectal cancer in Connecticut alone this year. When

detected early, colorectal cancer is easily treated and highly curable and as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Clinical trials are currently underway at federally designated comprehensive cancer centers such as the one at Yale Cancer Center and at Smilow Cancer Hospital to test innovative new treatments for colorectal cancer. Tumor gene analysis has

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helped improve the management of the disease by identifying the patient's most likely to benefit from chemotherapy and the newer targeted agents resulting in a more patient specific treatment. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at [yalecancercenter.org](http://yalecancercenter.org). You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Regina Hooley. We are talking about screening for women who have dense breasts. Regina, we talked a little bit about breast density and the fact that some women just have dense breasts and sometimes this gets less over time and it may be related to hormonal cycles or at least the amount of circulating estrogen and we know that that is in part related to breast cancers, so does breast density increase your risk for actually getting cancer on top of simply making it more difficult for you to find?

Hooley Yes, breast density is known to be an independent risk factor for breast cancer. When you compare women with extremely dense breast tissue to those women with fatty breast tissue, there is a 4 to 6 times increased risk for developing cancer. Also because the mammograms are harder to read, women with dense breasts have a higher rate of having an interval cancer, that is to say, a cancer that presents in between the time of having the yearly screening mammogram. It presents as usually a palpable mass and these interval cancers which can be detected at a much higher rate, up to 17 times increased rate in women with dense breasts, also tend to be more advanced stage, tend to be larger and are more aggressive, so those are some of the issues that we have with dense breast tissue.

Chagpar If you have dense breasts, you certainly want to get an ultrasound or another test, at least talk to your doctor about what you can do to really make sure that you are finding these cancers early if you can. So what happens if you go for your mammogram and your radiologists says to you, you have dense breasts, we are going to do additional imaging. Can you walk us through that process and what happens if they actually find an abnormality?

Hooley The first thing to remember is that if you get recalled from a screening mammogram whether or not you have dense breast tissue or non-dense breast tissue is not to freak out. The majority of screening recalls turn out to be nothing. About 10% of all women who have a screening mammogram get recalled

for an abnormality but very often these abnormalities are just superimposed tissue or something related to positioning of the breast or perhaps what turns out to be a normal finding. About 1 out of 10 women who are recalled require a biopsy and if we go on to do a biopsy, you need to remember that most of the time the biopsies turn out to be benign. Only about 20 to 30% of the biopsies we perform turn out to be breast cancer, so you have to remember that most of the time we are actually wrong when we recommend a biopsy but that is the national standard because sometimes we are not sure whether the finding is malignant or not so

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it requires a biopsy. If you go down that route and you need a biopsy, most of the time, the biopsies can be done with a needle and we do it in the radiology department. It takes about an hour or so to do. We use a local anesthesia like the dentist does and we use imaging guidance whether it is ultrasound or x-ray guidance or perhaps MRI guidance and we scan and make a tiny little incision. It does not need stitches and then we sample it and we are very accurate in our sampling. It takes about three days to get the results and once we get the results, if it turns out to be positive, then we refer the patients to breast surgery for more treatment.

Chagpar What happens if it is negative, are those patients still at increased risk? Some people will get called back and they will say, well we need to see you back in six months and that really freaks people out because they are thinking well if you are worried enough to do a biopsy and tell me that there is nothing there and if you are not worried, then how come I cannot come back in a year. What do you do about those six month people?

Hooley As breast imagers we are very cautious and traditionally, when we get a negative biopsy result, we do 6-month follow-ups because we always have a little doubt in our mind that perhaps we did not sample it accurately. Remember that before we did needle biopsies, all the patients, if they had a mammographic abnormality, went to surgery and then we replaced surgery with needle biopsy and it was much less aggressive, so we wanted to be cautious by doing that 6-month follow-up. There are new studies that are coming out now that we have 10-15 years of biopsy experience that for the most part we probably do not have to do a 6-month follow-up for these biopsies that turn out to be benign but we are all creatures of habit and it is hard to break that cycle because we also want to be very cautious so it takes a long time to make the radiologist change but I think we are just being overcautious in that regard.

Chagpar And it is better to be cautious than not. The other question that I think a lot of patients have is often times when you do a biopsy, you put a little titanium clip in the breast and many patients wonder why you do that and will it set off airport detectors and that kind of thing?

Hooley We use a little titanium clip. It is really not a chip. It is not electronic.

It is half the size of a staple and it is really inert. It does not set off any metal detectors and we use that clip to mark our biopsy site and it is useful for a couple of reasons, first of all, if the biopsy comes back positive, then we know exactly where we were and sometimes we remove most of the lesion with our needle such as with the small cancers and so if the clip is there, then the surgeon can accurately go and do the definitive surgery in the region of concern and be very accurate. If it is a biopsy, it marks the biopsy site, so say a patient moves to another state or goes to another radiology facility down the line and they may not have all of their prior medical records, well that biopsy clip is there and so everyone will know when they do the breast image exam that that little nodule was already biopsied and not to be concerned about it. Keep in mind that when you have standard general surgery, say you have a gallbladder removed or your appendix removed, surgeons typically leave multiple staples in the body and they historically do not tell the patient, it is just part of the surgery, so we have been using these clips and staples for many years and they are safe.

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Chagpar So the other question that people have with regards to these clips is sometimes people will say that the radiologist told them that the clip moved.

Hooley If the clip moves it makes it a little bit more challenging for us to go back and biopsy a small site that perhaps turned out to be positive and we cannot see the original lesion or the original mass anymore, it is challenging but there are usually ways of getting around it and working things out but yeah, like all things in life, some things are not perfect and sometimes the clips move.

Chagpar So again, this is the do not freak out message.

Hooley Yes.

Chagpar We have talked a little bit about a few different modalities for breast imaging. We have talked about standard mammography which sounds like is really being replaced by tomosynthesis, this 3D mammography. We have talked a little bit about ultrasound and a little bit about MRI. What is the future for breast imaging? What do you say about thermal imaging or all of these molecular imaging techniques? Is there a future to that, are we always going to have mammography?

Hooley That is another good question Anees. Mammography, again, is the gold standard and I think with tomosynthesis we are getting better. There is growing interest in contrast enhanced mammography where a contrast, similar to a CT or CAT scan, is injected into the breast and it can be very accurate, similar to MRI and the advantage of that is that the contrast enhanced mammogram can be done at the same time as the regular mammogram, all in one appointment as opposed to having a mammogram and having to come back at a different time perhaps and going to a different room, a different imaging suite to have the MRI, so that is something where there is growing interest. With ul-

trasound, there is also contrast enhanced ultrasound that is gaining popularity. Ultrasound contrast are microbubbles, they are air bubbles that can be injected intravenously and can show tumors to enhance, similar to MRI, so there is growing interest in microbubble contrast agents with ultrasound. There is diffusion weighted MRI which perhaps could someday eliminate the need for intravenous gadolinium contrast which we use for MRI, so that is also an attractive tool. Technology moves very quickly and there are a lot of technology advances. As you mentioned, there is thermography which is attractive because it does not require breast compression or any intravenous contrast and it measures the temperature of the breast, the theory being that cancers are warmer. Having said that, we do not believe that thermography is accurate. The Society of Breast Imaging and the American College of Radiology have looked at studies and although it is a comfortable exam for patients, the accuracy in detecting small early breast cancers has not been well proven so I would hesitate to recommend patients undergo thermography especially in addition to the mammogram, so there is a lot of technology, it moves very quickly, it takes a long time to get the right answer. I think medical science in some ways does not move as fast as technology moves and there are a lot of exciting things down the line and it is hard to say which is going to come out on top to be the best exam.

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Chagpar When you talked about the microbubble contrast agent with ultrasound, might it be concerning to some patients who say, you are going to put bubbles of air into my venous system, isn't that how people get air emboli that causes strokes and things, are you afraid of that?

Hooley That is an issue and that is why it has taken a long time for the FDA to approve it. It is FDA approved for cardiac, for echocardiograms here. In Europe and Asia, they have been using microbubble contrast agents for many years safely even in the pediatric population. These are very tiny, tiny microbubbles. They are associated with a sort of fatty substance to make them slippery and they do not last that long, so I think the adverse side effect which is significant, having a stroke is a significant adverse side effect, is very very minimal and it is believed to be safe, so we hope it is just a matter of time before the FDA will approve it for use in addition to cardiac echo.

Chagpar What about elastography? A lot of people have been talking about that as a new technique in ultrasound. Tell us more about that.

Hooley Elastography is a measure of tissue stiffness. It is a hi-tech measurement of how dense or how firm a lesion is. It is a hi-tech replacement for a physical exam. We know on physical exam that cancers tend to feel very hard and benign or noncancerous masses are soft, so elastography can measure tissue stiffness. Early studies have shown that it can improve the accuracy of ultrasound, but it is difficult to do. It takes a lot of experience to do it right and I think it is really early in its development and that has a lot of promise but we are not



quite there yet.

Chagpar What about PEM, a lot of people talk about PET scans, which is positron emission scans, and now there is something called positron emission mammography, do you think that that is going to be the new mammography of the future?

Hooley I do not think so at this point. With PEM, there is a high radiation dose. It is much higher than mammography and they have been trying to bring down the radiation dose over time but remember if you are doing a PET scan in a patient who is very sick or has a known cancer, then it is worth that single exposure but to do PEM screening in women who are otherwise healthy with high radiation doses is probably not safe.

Dr. Regina Hooley is Associate Professor of Diagnostic Radiology at the Yale School of Medicine. We invite you to share your questions and comments, you can send them to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written format at [yalecancercenter.org](http://yalecancercenter.org). I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.