Hello. I am Marita Lazzaro, an adult nurse practitioner and women’s health nurse practitioner in the Cancer Prevention Center at [The] University of Texas MD Anderson Cancer Center. And I am going to be presenting today on Breast Cancer Survivorship: the Diagnosis of Calcifications.

The objectives of this lecture are upon completion participants will be able to understand the correlation between mammary calcifications and benign proliferative and pre-invasive breast disease; also identify the mammographic terminology associated with the benign and suspicious mammary calcifications; and to realize the importance of the concordance of imaging and pathology.

Let’s start with what exactly are calcifications. The term calcification is used to describe the calcified debris from cellular activity. In the breast this can be due to benign fibrocystic activity in the stromal fibrosis tissue or the glandular lobules, or due to a malignant process, in the ducts. Occasionally skin or vascular calcifications can be seen, but these tend to be easily recognizable and of benign etiology. Let’s discuss some of the concerning --- some of the facts concerning calcifications. First, the maj --- majority of calcifications are benign. They are considered a mammographic finding, are not palpable, and are not seen on ultrasound or MRI. A significant --- this is a significant reason why mammograms remain the gold standard of breast screening. Calcifications can be found on mammograms of women of any age, but are most prevalent in postmenopausal women. Calcifications can help identify pre-invasive breast cancer. And that’s why the mammograms continue to be our first line of testing and screening.

Calcifications are -- can be of benign etiology. These include breast cysts filled with debris, hyalinizing or involuting fibroadenomas as they age they can form calcified areas. Fibrocystic changes, sclerosing adenosis, ductal hyperplasia without atypia are all forms of active fibrocystic breasts. Secreting lesions include papillomas, duct ectasia filled with debris. Trauma to the breast can also cause calcifications. This is usually in the form of fat necrosis. And, therefore, evid --- evidence of trauma needs to be documented in the chart as much as possible for future clarification. Radiation therapy can also cause calcifications to the breasts as the tissue ages. Again, vascular and dermal calcifications can be seen in the breast, but are usually not concerning for malignancy, as they are easily read as benign.

Next, you have suspicious etiology. In this, we get into the proliferative breast disease. This includes atypical proliferation or hyperplasia of the glandular cells of the mammary ducts. This is where you’ll hear people say, “I am very fibrocystic.” Or, multiple biopsies need to be done to determine if the findings on mammogram are benign or not. Flat epithelial atypia is the new terminology that has been --- come out within the last few years, and is felt to be a pre-cursor to the next level, which is atypical ductal hyperplasia or commonly called ADH. In some cases, it is felt that flat epithelial atypia and atypical ductal hyperplasia are actually one in the same.
Finally, we get into malignant etiology. This is what is commonly called ductal carcinoma in situ, or DCIS. This is a pre-invasive disease. It is intra-ductal carcinoma. And its stage is Stage 0 or Tis, which stands for in situ or still contained within the duct. Usually DCIS is not palpable. It can be felt if there are a number of ducts that have the DCIS present. A cluster of ducts with the DCIS will feel as a vague thickening or mass on the breast exam.

Malignant Etiology: Pre-invasive disease is a dynamic process. Flat epithelial atypia if unchecked will turn into atypical ductal hyperplasia. Fifteen to 20% on biopsy through recent studies have shown that when excised DCIS was found in place or beside the atypical ductal hyperplasia. As you move on, if left alone, DCIS will then become evident. Twelve to 20% of excisions were upgraded to invasive disease. Focal invasion may also be present, and is noted as T1a. It is a dynamic process as stated above. That means it has time to move between the atypical ductal hyperplasia and the focal invasion. An area --- a mass about the size of a pea may take anywhere from one to five years to actually present. DCIS is a pathologic diagnosis. We do not diagnose this by imaging. We just identify areas of concern. Biopsy must be done.

This is a nice drawing that I like to use with patients to kind of explain what DCIS is. Often our patients go on the Internet and --- when they hear about calcifications and they come in very frightened. I take them through what a normal duct looks like lined with glandular cells and sometimes these cells can proliferate and become a little bit thicker. This is called intraductal hyperplasia. Common forms of hyperplasia or thickening, is a scar, which is hyperplasia of the skin cells or a polyp, which is also hyperplasia of the glandular cells. Something, however, can trigger a change in those cells, and we are not even sure sometimes what it is, but they become atypical and they also proliferate. Atypical ductal hyperplasia is where we get small terminals at the end with these with these --- abnormal cells. Ductal carcinoma in situ is when this atypical ductal hyperplasia seems to take over more of the terminal ducts. If left alone, it will break out of the ducts and start forming a mass around itself, which then becomes the invasive ductal carcinoma.

Calcification Descriptors: Calcif --- Calcifications on a mammogram need to be described by two basic identities. Distribution describes the spacial orientation of the calcifications in the breasts and morphology describes the shape, clarity, and size. Without these two descriptors, the calcifications are not described well on a mammogram.

I’m going to take a minute here and review really quickly the BI-RADS® Breast Imaging System. More than likely you are all familiar with this. But I would like to go over it just in case you're not. BI-RADS® is an acronym for Breast Imaging Reporting and Data System. It was originally designed as a quality assurance tool for mammography. But it is now used for all imaging modalities of the breast including ultrasound and MRI. The BI-RADS® or comparable American College of Radiology, you’ll sometimes see it read as ACR, was developed to standardize the reporting system and force a decision as to the level of suspicion of the radiologist. This standardization helps us as the health care
provider to formulate a plan of care. BI-RADS® 0 is a no decision level. It designates that the level of suspicion cannot be rendered without additional information. This usually takes the form of imaging, magnification, or spot compression views, ultrasound, MRI, some other modality that can give more information to it. Pathology from a previous biopsy or even the level of clinical concern can sometimes be helpful in determining the final reading. BI-RADS® 1 is self-explanatory. A breast with normal breast tissue and an annual imaging is recommended. BI-RADS® 2 identifies findings in the breast that can be identified as benign. This usually occurs as cysts, milk of calcium calcifications, fibroadenomas, duct ectasia. These all fall into a fibrocystic nonproliferative breast tissue. BI-RADS® 3 is often tricky. And when I explain this to patients I sometimes leave this for the last. The term probably benign can easily be worrisome to some patients and will often require an explanation. This is used for breast findings that fit the criteria for benign with a confidence level of 98% that they are benign. The finding, however, may be new or noted on a first mammogram where stability cannot be confirmed. The interval check is rarely if less than six months for a mammogram. Anything sooner on a mammogram actually does not allow the breast to change if it is going to. And waiting six months does not will not change the treatment plan if it is a small cancer. Ultrasound is usually six months, but occasionally will be repeated in three. Several years ago benign-appearing, but new or increasing calcifications were often followed for a series of six months to show stability, sometimes every six months for two years. But with the advent of the minimally invasive and affordable stereotactic biopsy, calcifications in question now are rarely followed. Biopsy is usually recommended as a definitive diagnosis, and, therefore, reduces the risk of extra radiation, okay, to follow something that is benign. BI-RADS® 3 is now frequently used to show stability of asymmetric tissue on mammograms or benign findings, and is followed with the same imaging modality, such as mammogram follows mammogram in six months, if it is a mammogram finding. And ultrasound follows ultrasound in six months if it is an ultrasound finding. We usually don’t mix the modalities when we are doing stability. BI-RADS® 4 is described as a mammographic finding that requires additional imaging, such as diagnostic mammographic views, ultrasound, MRI, and/or biopsy to clarify the level of concern. BI-RADS® 4 carries a reasonable probability of malignancy ranging from 3-94%. As you can see, the range is fairly wide. Therefore, subdivisions of BI-RADS® 4a, b, or c are being proposed by the American College of Radiologists to help clarify for the health care provider what the true level of suspicion is. BI-RADS® 5 is simply a finding that by imaging suggests a cancer with a confidence level of greater than 95%. It should be viewed as a cancer unless proven otherwise. As you know, the diagnosis of malignancy requires tissue sampling and cannot be made by imaging of the breast alone. This level, therefore, requires a biopsy. A benign pathology on biopsy will require either additional biopsies or should be presented in a multiply a multiple disciplinary review to because it is discordant. The last category, BI-RADS® 6 is used when a cancer has been verified by tissue sampling and monitoring or additional imaging is required. It’s often used for staging to show the extent of the disease in the breast, or to assess treatment response.

As stated previously, subcas --- subclassifications of BI-RADS® 4 is proposed to clarify the level of radiology suspicion. 4a is low and considered a less than 10% probability of
malignancy.  4b is to suggest intermediate with a 10-49% probability of cancer. And 4c is of moderate concern carrying a 50-95% probability of cancer. 4c is usually taken to biopsy. Greater than 95%, you jump into BI-RADS® 5 and is considered as highly suspicions. Expect all these calcification --- all these classifications to be finalized and in use by sometime this fall. BI-RADS® reports identifying calcifications should always address the distribution and morphology of the calcifications.

Let’s take a look at benign distribution. When you receive a mammogram report, benign eti --- terminology is such as diffuse, scattered, global. Global means scattered around and not clustered together. Clustering means that they may be actually formed inside a duct. Random calcifications throughout the breast is often used in the mammogram report. It’s usually bilateral and can be minimal to extensive. Usually annual imaging is recommended on these --- these benign --- these calcifications.

Benign Morphology: You’ll see terminology such as coarse or popcorn-like. This tends to be the sclerosing adenosis or the stromal fibrosis. Punctate or round usually tends to be more the milk of calcium, which is also called layering. Dystrophic calcifications tend to go along again with fibrocystic changes, maybe related to injury or trauma. Egg shell or rim, lucent centered, all of these with the distribution as benign go for or end up recommending an annual mammogram.

Here is an example of benign ka --- report and what it looks like. Distribution is diffuse and scattered. As you can see, there’s multiple calcifications all around. Here you will see a lucent centered and that’s morphology, or egg shell or rim calcifications. This tends to be a fat necrosis or cystic area and use --- is read as a BI-RADS® 2 requiring annual imaging.

Let’s talk now about the intermediate probability distribution terminology. This you will see terms --- terms such as clustered or group, especially if they are shown as tight grouping of calcifications. This easily could be benign, such as a fibroadenoma or fat necrosis, or even a cyst filled with debris, such as an inspissated cyst. Regional is another term. And it --- this looks at more than one quadrant of the breast and not conforming to a ductal distribution. Anytime you get it into one section of a breast or one quadrant, you need to question whether or not that duct group is actually under suspicion. It does require morphology to determine the level of suspicion. Sometimes annual imaging may be done to confirm this, especially if it’s regional. Biopsy may not be indicated if it is regional but scattered, or there isn’t a tight group to biopsy. It can also be read as BI-RADS® Category 4.

Morphology associated with the intermediate level is amorphous or distinct. Amorphous or distinct calcifications carry a probability of about 60% being benign and 20% proliferative disease, such as the flat epithelial atypia or the atypical ductal hyperplasia. DCIS can be found in at least 20%. So you can see that 40% of the ar --- of these amorphous or indistinct calcifications would benefit by biopsy. It requires this distribution descriptor to determine the level of suspicion. Again, “Is it tight or is it scattered?” Biopsy is recommended usually with this terminology and it’s a BI-RADS® Category 4.
Here is a mammogram showing this. The distribution is grouped. It is very tiny in this area. It’s also amorphous, very faint. Stereotactic biopsy was performed of these calcifications. And the pathology was benign sclerosing adenosis. The final deci — and the --- and the patient was taken back to annual imaging.

We come to the highly suspicious distribution or terminology. This you will hear things like “linear.” Anytime we have a linear area of calcifications, you have to suspect that it is intraductal follow --- following along the duct line. It may be branching as if the ducts are branching off more into a segmental area. It may be confined to a segment of the breast. It is suspicious for a specific group of ducts and their branches. The most suspicious terminology is segmental linear. This is read usually as a BI-RADS® 4 or 5 and will need a biopsy.

The morphology associated with this distribution is pleomorphic. That’s one of the most common ones that you’ll see. Heterogeneous or gran --- granular: The probability of malignancy ranges in this group from 40-80% and is dependent upon the distribution characteristics. Such as, if it is linear and segmental and pleomorphic, you are usually reading it as a BI-RADS® Category 5. Fine, linear, or casting is the highest probability for ma --- for malignancy of calcifications, and usually is associated with a high grade ductal carcinoma in situ.

Here is an area along this line of what we call segmental linear. It’s in the segment, one segment of the breast. It is in a line and it is very fine. This was biopsied and shown to be DCIS Category 5. Surgical excision was completed and segmental mastectomy and radiation therapy was obtained as on the segmental mastectomy borders showing DCIS were found.

As stated earlier, one of the most important things that we need to be concerned with as the health care provider reading this and explaining this and coordinating the plan of care for this patient is concordance of imaging and pathology. The majority of radiologists are as --- are assuming the responsibility, at this time, of addressing the concordance and documenting it on the addendum. However, you need to watch for this. Because if it is not present, then you may be the person to actually contact the pathologist or contact the radiologist as to whether or not, it is concordant or not. The provider must assure that this has been done before a plan of care can be created. If concordance is not there, it may need rebiopsy or you may need additional imaging. The following points will help guide you as to whether concordance is shown. First of all, “Was the sampling adequate?” That should say in the pathology report. “Were calcifications identified on the specimen radiograph?” This is very important and should be present on the films that you receive or have access to. “Were the calcifications identified on the pathology report?” So the calcifications have to be shown on the biopsy sample through mammogram, but they also have to be documented on the pathology report. If either one of them is not showing calcifications, then adequate sampling may not have been achieved. “Was adequacy questioned by the radiologist or pathologist?” Radiologists and pathologists are very sharp nowadays. And they will
be the first ones to say we question whether or not this biopsy is adequate and would recommend a repeat. “Is the pathology concordant with the level of concern on imaging?” In other words, if I have a BI-RADS® 5 mammogram with linear and branching calcifications and I have a benign pathology report, that is not concordant. And one of the first things you have to check is whether or not sampling adequacy was achieved. BI-RADS® 4; however, can yield either benign proliferative disease or malignancy. BI-RADS® 5 should always yield malignant pathology. If not, then it is discordant.

So what do you do with discordant? You check with a multidisciplinary discussion or a second opinion. At the cancer institutes, we are very privileged to be able to take cases to a multidisciplinary conference. And here at MD --- The University of Texas MD Anderson Cancer Center, we have a set conference to discuss these cases every week. And in this discussion, we have multiple radiologists, multiple pathologists. The surgeon is present and the provider is also present. And we discuss the case clinically through imaging and then also through pathology. And we come up with a final recommendation. It could be it is benign. It could be it needs excision. Or it could be we need more tissue.

This is a nice example of whether or not sampling adequacy was done with the calcifications on this stereotactic biopsy. As you can see, each one of these little worm-like tissue areas are --- is a core biopsy. So this patient actually got about 8 cores. You can see on this --- on this core sampling the calcifications were abs --- were actually obtained. This is an adequate sampling. The calcifications on the report --- on the pathology report were confirmed.

Imaging and pathology are concordant. It is a BI-RADS® Category 5 by terminology with segmental distribution and fine, linear morphology. It was DCIS on final excision.

In summary, imaging with mammogram can characterize calcifications and identify those patients at risk for pre-invasive disease before it becomes an invasive breast cancer. The majority of calcifications in the breast are benign, not what the patient reads on the Internet. The ability to identify high-risk terminology on mammogram reports will support an appropriate management and plan of care by you as the provider. Concordance between imaging and pathology is essential. And multiple --- multiple disciplinary discussion or second opinion on discordant findings is recommended. Thank you very much for your attention and we welcome your feedback on this lecture. Thank you.