Good afternoon. It’s my pleasure to be discussing Diagnostic Breast Imaging over the next half hour. I’m Wei Yang, Professor of Diagnostic Radiology and Chief, the Section of Breast Imaging as well as Medical Director of Ben and Julie Rogers Breast Diagnostic Clinic at The University of Texas MD Anderson Cancer Center in Houston, Texas.

The objectives of this presentation are to help the participant understand the major imaging modalities available today including mammography, high resolution ultrasound, magnetic resonance imaging and their respective indications and role in breast cancer diagnosis, staging, and management; second, to be familiar with common benign and malignant breast conditions that are appropriately worked up with imaging; and third, to be familiar with the indications for imaging-guided biopsy.

The areas of emphasis during this discussion will include breast imaging evolution from screen-film mammography through breast intervention and high resolution sonography, right up to digital mammography setting a platform for future advances in digital imaging, dynamic contrast enhanced MR imaging with magnetic resonance spectroscopy and diffusion-weighted imaging, as well as emerging nuclear medicine tools that include positron emission tomography computer tomography, also known as PET/CT; positron emission mammography, known as PEM; and breast specific gamma imaging, known as BSGI.

Screen-film mammography involves an x-ray source that is used to image a structure that is then --- allows for data to be collected on film that requires film processing and then has to be viewed on a film viewer.

Here are examples of bilateral analog mammograms from the same patient including CC and MLO projections.

And here is an example of microcalcifications that were detected on the mammograms in two views,…

…seen as the highlight by the arrows. Seventy percent of all screened detected cancers present with calcifications.

And here is a small, tight cluster of heterogenous calcifications that were assigned and rated as BI-RADS® 4 suspicious finding, biopsy recommended.

This image is the stereotactic scout view in preparation for a stereotactic-guided core needle biopsy.

Here are the pre-fire images which show the calcifications at 15-15 degree projections.

And here is the post-fire image where the trough of the needle is directly over the calcifications.
Here are specimen radiographs after the core specimens were obtained and demonstrate appropriate sampling of the calcifications.

And this is the final image showing the post-biopsy clip at the site of the targeted calcifications with appropriate removal of calcifications. The final histopathologic diagnosis was fibroadenomatoid changes, which is benign. And the patient appropriately returns to annual follow-up.

The next indication for imaging using high resolution breast ultrasound is in the evaluation of a palpable finding. Additional indications are in the evaluation of abnormal mammographic findings; evaluation of young or pregnant patients; facilitation of image-guided biopsies and clip placement; and the staging of breast cancer including regional lymph nodes as well as monitoring of response to neoadjuvant therapy.

Here is an example of a patient who presents with an abnormal mammographic finding that comprises architectural distortions higher in the left breast and a second abnormality comprising calcifications in the lower left breast.

This is the corollary view showing the architectural distortion as well as the calcifications.

The architectural distortion presented as an irregular hypoechoic mass on ultrasound that was hypervascular…

… and was subjected to ultrasound-guided core biopsy.

Here is the clip marker placement on ultrasound, the CC view and on the lateral view.

And the histological diagnosis for this mass was a radial scar, part of a complex sclerosing lesion with associated microcalcifications.

Next, was the separate area of abnormality defined by calcifications…

… in the lower outer aspect of the left breast.

Stereotactic biopsy performed of this area showed ductal carcinoma in situ modified black’s nuclear grade 3.

The patient went on to surgical excision. And final histopathology from segmentectomy showed DCIS as well as the radial scar. And the DCIS is present in the background of a radial scar and these findings are concordant with the imaging findings.

The second patient demonstrates abnormal mammograms where we see a dominant hyperdense mass in the breast and a second smaller isodense mass both anterior to the patient’s in situ implants.
On ultrasound, the dominant mass is solid, hypoechoic with a thick echogenic rim and enhancement. And this is a suspicious ultrasound finding, in contrast to the second mass which is circumscribed, oval, and completely anechoic with enhancement. This mass is benign, consistent with a cyst BI-RADS® 2, and the larger mass is suspicious BI-RADS® 4C and requires core biopsy.

The suspicious mass is also shown to be hypervascular on ultrasound. And the final histologic diagnosis was chronic lymphocytic leukemia, metastatic to the breast.

Here is a third patient which illustrates the importance of lymph node evaluation. All patients who present with a diagnosis of breast cancer at MD Anderson have regional lymph node evaluation using ultrasound. And that starts in the left axilla where we see the normal fatty hilus being compressed with eccentric cortical thickening. This is a centimeter marker on the right. So this lymph node is approximately 7 mm thick.

Ultrasound-guided needle biopsy can be performed rapidly with low cost and immediately at the time of evaluation. This slide shows the needle with its tip within the cortical thickening of the node. And immediate assessment is possible with this procedure.

And lymph node evaluations are important in breast cancer staging. And this is an H&E slide of a paraffin section of a metastatic lymph node.

Moving on to the role of digital mammography and future advances that are possible with digital imaging.

In contrast to the analog schematic that we saw as the first slide in this presentation, in full field digital mammography, the x-ray source will hit a digital detector which allows for immediate assessment of the digital image on the workstation within the x-ray room. These images are then transferred to high resolution workstations in the reading rooms where physicians and radiologists can review the films in great detail for accurate assessment of abnormality.

These are two images obtained from the same patient. To your left is an analog right CC image. And to your right is a digital right CC image with a 50 micron pixel.

And images when they are transferred to the reading room workstations can be hung in several different protocols according to the operating radiologist's preferences, where you can hang CC with MLO or you can even review films as single images on the workstation.

Post processing is an additional advantage of digital mammography where an area of interest can be magnified or zoomed.

And this will allow for closer assessment of abnormalities including masses, architectural distortions and calcifications.
Here is an example of the role of digital imaging in a patient who presents for preoperative needle localization right through her surgery and assessment of her final excised specimen. This is a digital mammogram obtained during needle localization where two needles have been used to bracket an area of cancer that's marked by a post biopsy clip.

After the lesion is marked, the patient presents for surgery in the operating room and after excision of the specimen, an x-ray --- specimen radiography is performed in the pathology laboratory…

…and then images transferred immediately via teleradiology to the radiologist's interpretation room. This first digital image is of the en block surgical specimen with both wires in situ, the clip in the area of malignant or cancerous calcifications.

The second image is of the sliced histological specimens,…

…which are then again subjected to digital imaging,…

…and these sliced specimens are then teleradiographed to the interpreting radiologist.

In a different patient, here is a digital image of sliced specimens from a mastectomy specimen, comprising a total of 14 slices.

Using post processing and magnification,…

…the radiologist is able to determine the exact location of the cancer which has been annotated for direct radiologic pathologic correlation.

The additional advantage is to allow for assessment of margins so that the patients can achieve good margins and decrease the re-excision rate.

Moving on to an application of digital mammography. Computer-aided detection, or CAD, is a tool that is useful in the detection of abnormalities in a screening mammography setup. Depending on the experience of the radiologist, this had led to up to a 15% increase in cancer detection rates across multiple studies that have been published over the last decade. These computer-aided devices mark areas that are regarded suspicious, either in the form of calcifications and masses. The caveat to this technique is that there is a significant false positive rate which requires over-read by the radiologist in order not to workup excessively and add to the health care cost without attendant patient benefit.

So here is an example of the CC and MLO views that have been subjected to computer-aided detection, or CAD,…
…whereby the arrow illustrates an area of calcifications that have been annotated on this image.

And these calcifications are seen on both the CC and MLO projections and were finally proven to represent ductal carcinoma in situ.

Publications in the last five to ten years have shown that CAD versus double reading of radiographically visible lesions in baseline mammograms showed that for full field digital mammography and screen-film mammography, that the sensitivity was significantly different in full field digital with and without CAD. And the CAD marking of cancers not detected at prospective independent double reading was up to 36% on FFDM and 13% on SFM, concluding that CAD shows a potential to increase the cancer detection rate for FFDM and SFM, noting that this is a single institution study and across multiple studies, the incremental value of CAD is up to 15%.

The conclusion, then, is that full field digital mammography with CAD combination allows for a detection performance that is at least as good as that with screen-film mammography.

The next advance application of digital imaging is digital breast tomosynthesis which is an advanced imaging technique whereby the x-ray tube moves in an arc across the breast and allows for a series of low dose images that are acquired at different angles through the breast. And then allows for reconstruction of these images and at the same time allowing for total dose acquired during the syn --- tomosynthesis exam to be similar to a single view breast exam.

This schematic shows the gentle compression plates with the breast within the two paddles and the digital detector with the arc that will be traveled by the x-ray tube.

Here is the schematic showing the tomosynthesis gantry that has to be added on to the digital system unit.

And here are clinical images obtained with the digital breast tomosynthesis unit,…

…where multiple single institution study publications have been published over the last five to ten years.

This first clinical illustration shows that on the CC mammogram and on the initial tomogram, that there is no abnormality in the left breast. But during review of the multiple images…

…and in the tomosynthesis study, that there is a small, oval mass that finally showed to represent ductal carcinoma in situ and was occult on the Selenia digital mammogram.

In a different patient, an area of architectural distortion that was deemed suspicious on digital mammogram is seen here on the tomosynthesis exam.
And in scrolling through this study that was reported by tomosynthesis as a pseudolesion or a lesion that was not significant, the patient went on to biopsy which confirmed benign breast parenchyma or a pseudo lesion due to compression issues for this specific patient.

The next topic I would like to cover is dynamic contrast MR imaging including magnetic resonance spectroscopy and diffusion weighted image.

And the premise for DCE or dynamic contrast enhanced MRI study predicates on the detection of angiogenesis associated with malignant tumors. The providence of a cancer or a malignant tumor is that genetic mutations cause a cell to become cancerous. And when the tumor reaches a critical small size there are angiogenic vessels or leaky vessels that surround the growing tumor. And it is these leaky vessels that allow for extravasation of contrast agent locally and that can be captured by a dynamic contrast-enhanced MRI study to allow for depiction of the tumor location and facilitate biopsy for early diagnosis.

The requirements of DCE-MRI in the evaluation of patients for breast cancer are that this technique must be capable of detecting early breast cancer with high sensitivity, and that the high spatial resolution will provide information not only on structural abnormalities defined as morphology, but will be able to provide kinetic information using the dynamic contrast-enhanced method.

This single image in a dynamic sagittal contrast-enhanced MRI study shows a 7 mm enhancing mass.

And the kinetic curve for that mass was assessed and essentially the principles of interpretation are that a fast initial rapid enhancement followed by a quick washout of contrast is concordant or consistent with leaky vessels and supports a malignant diagnosis versus a slow initial enhancement and persistent progressive enhancement in the delayed phase supports non-leaky vessels and is more consistent with a benign lesion.

The indications for MR imaging in our institution include screening of high risk women; evaluation of an equivocal mammogram, ultrasound, or highly suspicious physical finding without attendant imaging abnormalities using mammogram and ultrasound; in a patient who presents with biopsy-proven axillary adenocarcinoma with an unknown primary; for assessment of response in patients who undergo neoadjuvant chemotherapy; and in staging of breast cancer in patients with dense breasts for whom the disease extent and specifically invasion deep to the fascia and chest wall invasion are excellently depicted by breast MR.

Here is an example of a 47-year-old patient with a gene mutation who presents for high risk screening, where the type 3 breast parenchymal pattern or BI-RADS® 3 breast pattern on the mammogram reveals no abnormality. Nonetheless, the sagittal dynamic
contrast study shows a 5 mm enhancing mass with rapid enhancement and washout. And this was a 7 mm invasive ductal cancer.

For a patient with equivocal mammogram,…

…ultrasound, or clinical exam, this right breast was interpreted as abnormal with a mass. And the left breast was reported as normal. Nonetheless, the patient presented with minimal nipple retraction on the left.

The MRI study on the left shows the nipple retraction with multiple irregular masses that are seen to be even more numerous on the sagittal scan with a normal right breast.

So this patient had biopsy-proven multifocal invasive lobular cancer.

Here are the kinetic evaluations that show these abnormal masses in a segmental distribution, and in this case, with fairly plateaued delayed kinetics.

So the role of MRI in staging patients with breast cancer who are candidates for breast conservation have been well-described over the last 10 years.

The third category for utilization of breast MR includes axillary adenocarcinoma diagnosed with an unknown primary.

Here is a patient who presents with gross abnormal right axillary nodes…

…that are also seen on the evaluation with MR.

And here in the right breast are multiple masses representing the patient’s occult breast primary on conventional imaging.

“What about neoadjuvant chemotherapy and monitoring response of patients with MR?”

This is a 33-year-old patient with a large metaplastic tumor that shows rim enhancement and internal necrosis with a classic washout malignant kinetic pattern at diagnosis.

Three months after therapy, MR imaging shows interval decrease in size of the tumor and a more benign, or less malignant, kinetic curve where there is slow washin, slow initial enhancement, and progressive delayed enhancement.

This is a 3D MIP MR image of the same tumor.

And multiple publications have been reviewed in the literature over the last decade evaluating the role of breast MR in monitoring response.

Finally, the role of MR in staging patients with known breast cancer including the extent of disease and invasion of the chest wall.
Here is a dramatic case showing complete replacement of the left breast by a large inflammatory breast cancer that completely invades the posterior chest wall,…

…and on a separate slice, is also involving the contralateral internal mammary lymph node. We see the skin thickening in the multiple tumoral masses at this different plane on the axilla imaging.

In a different patient a palpable mass is seen on mammography as an area of architectural distortion with calcifications.

And this is the incumbent right breast cancer that is also seen at staging MRI on the top row. This represents the known palpable cancer also seen on mammograms. However, at a slightly lower slice there is a second round mass which was shown to represent multifocal disease.

But in the contralateral breast was an additional enhancing mass that required biopsy and was a benign fibroadenoma.

MRI-guided biopsy is essential for all practices considering utilizing breast MR. And this shows the MR gantry as well as the MRI-guided needle that is traversing the mass during a biopsy procedure.

Finally, I’d like to discuss emerging techniques in nuclear medicine.

And top on the list is a high resolution positron emission tool for the breast known as positron emission mammogram that has been approved by FDA as a high resolution PET scanner. Preliminary studies show encouraging results with a 90% sensitivity not only in the depiction of ductal carcinoma in situ, but also in invasive breast cancers and in cancers that measure 1 cm or smaller.

This is a portable unit with high spatial resolution that allows exquisite anatomical and molecular imaging with an approximate 10 minute scan time for each breast. The portable unit is compact and provides 3D tomographic PET images of the breast after the breasts are gently immobilized using the dual compression paddles which contain the detectors.

So here is a close-up view showing the compression paddles with detectors in situ that will then scan through the breast and allow for images…

…in both the CC and the MLO projection. The differences between high resolution positron emission mammography and PET/CT are multiple. The positron emission mammography unit, or PEM, is optimized for small body parts and is significantly lower in cost than a PET/CT.

The resolution of the PEM is significantly higher when compared with PET…
…and images obtained with a PEM scanner are slab images adding up to a total of 12 slices that are obtained of each breast separately. This image shows multiple abnormal areas of FDG uptake consistent with multifocal breast cancer.

And here is the comparison of the same patient with the PEM image compared with the PET/CT where the image is much less clear due to the lower spatial resolution.

The additional applications of this tool are in the assessment of post surgical change versus recurrence where PEM shows rim accumulation consistent with seroma and allowed for routine follow-up.

There is also a potential role for PEM to evaluate the lymph nodes in breast cancer patients. And these two images show that there is abnormal FDG uptake within the axilla of this patient with known multifocal disease in the lower inner quadrant.

In summary, this discussion has discussed the evolution of breast imaging methods from screen-film to digital mammography, which then provides a platform for future advances in digital imaging including computer-aided detection and digital breast tomosynthesis. The role of high resolution ultrasound in the evaluation of palpable masses as well as abnormal mammographic findings, and as a superb guide for intervention has also been discussed. The third imaging tool in the breast armamentarium is dynamic contrast MR imaging. And, finally, a few words on the evolving role of nuclear medicine imaging tools for breast cancer. On this note, I would like to thank you for your attention and would welcome further queries or questions regarding this presentation. Thank you very much.