Hello. I’m Dr. Kelly Hunt from the University of Texas MD Anderson Cancer Center. This afternoon, I’m going to talk with you about surgical approaches to the treatment of breast cancer.

The objectives that I want to cover are first, to discuss surgical treatment of the primary tumor and then oncoplastic techniques that we use for partial mastectomy reconstruction. I then want to cover the integration of reconstruction for patients undergoing total mastectomy; and finally, talk about nodal staging for breast cancer.

So, the factors that we typically consider in surgical planning are numerous. In fact, we look not only at the tumor size or the clinical stage of the primary breast cancer. But, we also consider the patient’s breast size and try to achieve a reasonable tumor size to breast size ratio for breast conservation. We look at the location of the tumor in the breast and also consider the family history or any suggestion of a familial breast cancer or a predisposition to breast cancer, such as a BRCA1 or BRCA2 mutation. We look at contraindications to the use of radiation therapy. And of course, consider the patient’s preference for treatment of the breast cancer and the overall health status of the individual patient.

In terms of pathologic assessment, there are a number of factors that are important in the individual tumor. One is the histologic subtype, the nuclear grade, and typically, we use a modified Black’s nuclear grade staging I, II or III, estrogen and progesterone receptor status, and the status of the HER2/neu oncogene either by immunohistochemistry or fluorescence in situ hybridization.

The primary objective in approaching the tumor in the breast is to excise the tumor with adequate margins. And, in general, our approach to the margins in both invasive and noninvasive breast cancer is to achieve a 2-mm margin in all directions around the tumor. This helps to minimize local recurrence and, again, we look at the expected cosmetic outcome. And that’s where, again, the tumor size to breast size ratio comes into play.

For early stage breast cancer, we generally consider breast-conserving treatment and mastectomy to the equivalent. There are a number of randomized trials that were done several decades ago showing that survival outcomes were equivalent in women with early stage breast cancer who were treated with lumpectomy and radiation versus mastectomy. In terms of the components of breast conservation, not only are we removing the primary breast tumor with a segmental or partial mastectomy, but we’re also including axillary staging as appropriate for the patient. So, those with invasive breast cancer would have nodal staging and those with noninvasive breast cancer would not require any axillary staging. Radiation therapy, of course, is also an important component of breast-conserving surgery. For mastectomy, this generally is a total mastectomy. Again, axillary staging, where appropriate, for those individuals with
invasive breast cancer, and then the integration of reconstruction which we’ll cover a little bit later.

So, the surgical options for a patient with early stage breast cancer generally will be segmental mastectomy. Again, there’re several ways to call a segmental mastectomy. There can be lumpectomy, partial mastectomy. In the past, the term “quadrantectomy” has been used, although typically we do not attempt to excise the entire quadrant when we’re excising the primary breast tumor. A total mastectomy can also be called a simple mastectomy or complete mastectomy. The goal is to remove the entire breast. Skin-sparing mastectomy is essentially a total mastectomy that’s performed with preservation of the entire breast skin envelope. And then finally, there’s nipple-sparing mastectomy where not only are we trying to preserve the entire breast skin envelope, but we’re also trying to preserve the entire nipple-areolar complex. And skin-sparing mastectomy and nipple-sparing mastectomy are always done with immediate breast reconstruction.

So, the sequencing of treatment is something that comes into play more frequently now as chemotherapy and other systemic therapies are utilized in the management of breast cancer patients. In the past, we would always do surgical treatment as the initial treatment. But, now that we know that systemic chemotherapy or systemic endocrine therapy may be used in an individual patient, we can sometimes use that treatment prior to any surgery in order to improve the surgical outcomes. And so, giving the treatment – the systemic treatment before surgery is often called neoadjuvant therapy. It can also be called primary systemic therapy or induction therapy. The indications that we typically use for neoadjuvant chemotherapy are to downsize the tumor in the breast to achieve breast conservation. So, in women with relatively large tumors in relationship to the size of the breast, where we know systemic chemotherapy is warranted in the management of that individual, we would consider doing the chemotherapy before surgery to shrink that tumor and require less volume of breast tissue to be excised at surgery. We also look at nodal involvement. So, women who present with metastatic disease in the lymph nodes that’s proven by fine needle aspiration biopsy are also candidates for systemic therapy prior to surgical intervention. And part of this is to assess the response to therapy because we know that after we’ve completed surgery and removed all evidence of the primary tumor and any regional nodal metastases, we can only wait in follow-up to see if there’s any recurrence. We don’t have any direct assessment of the response to that systemic therapy. If the tumor is still intact and we give the treatment prior to any surgery, we can measure the response clinically, radiographically. And then also at pathology, we can see how much residual invasive cancer is left and how much residual noninvasive breast cancer and get the pathologic response rate to that individual regimen. So, the indications for adjuvant chemotherapy are based on the size of the primary tumor, any evidence of nodal involvement, estrogen receptor status, the age of the patient, and then also, other considerations, such as overexpression of the HER2/neu oncogene. And these are the factors that we look at when considering, if we know the patient is going to be a candidate for adjuvant chemotherapy, we might move that chemotherapy to the preoperative setting and give it prior to any surgical intervention.
Now, the other factor to consider in breast conservation, as I mentioned before, is any contraindications to radiation therapy. And so, in some cases where the patient has already had radiation treatment, perhaps for Hodgkin’s disease in --- when they were a teenage or an early or young adult, or radiation treatment to the chest wall for other medical conditions, we might not be able to do breast conservation because of overlapping treatment of the radiation fields. In breast --- the indications for radiation therapy in the management of breast cancer patients are listed here on this slide. In --- in pretty much all cases of breast-conserving surgery, we’re going to recommended postoperative adjuvant radiation therapy when the patient has invasive breast cancer. Some exceptions are those elderly patients with strongly hormone receptor positive tumors where you might be able to avoid radiation. And in some cases of noninvasive breast cancer where we have a low grade tumor on pathologic assessment with widely negative margins, we might consider avoiding radiation. But, in general, when we’re doing a partial mastectomy or segmental mastectomy, radiation will be indicated. If the size of the tumor is a T3 tumor, that being greater than 5 cm in size, radiation therapy is generally indicated even if the patient is planned for a mastectomy for management of the primary tumor. And then these are the other indications for the use of radiation – those patients with T4 disease, nodal involvement where there’s more than four positive axillary lymph nodes, and in cases where there’s positive margins after mastectomy or evidence of extensive lymphovascular space invasion.

This is a general algorithm for our approach to the patient presenting with an early stage breast cancer that has a small or medium breast size. In general, if we anticipate a small parenchymal defect because it’s a small tumor in the breast, and the defect --- and the tumor is in a favorable location, that being a superior location in the breast or in the lateral aspect of the breast, we will usually proceed with segmental resection and local tissue rearrangement. In some cases, for a patient who has a very small breast, we might consider a composite flap. If the tumor is in an unfavorable location, and we generally consider this to be anywhere in the inferior aspect of the breast below the nipple-areolar complex, we look at whether there’s significant ptosis or not in the breast. And, so, for the patient who does have ptosis, we would consider doing a vertical reduction mammoplasty or mastopexy at the same time as resection of the primary tumor. For those patients who do not have any significant ptosis and we anticipate needing to resect skin in addition to the primary tumor, we would consider using a latissimus flap or a TAP flap or, in fact, proceeding with a mastectomy because, again, we anticipate that there would be a poor cosmetic outcome with breast-conserving surgery. Also, if the patient initially presents with a very large parenchymal defect or we know that there’s going to be a significant amount of skin resection at the time of surgery, we might consider going directly to mastectomy or doing a partial mastectomy with a latissimus flap or a TAP flap. Or, again, this is a consideration where we might do neoadjuvant or preoperative therapy prior to doing any surgical intervention.

In the patient who has a very large breast size or is an obese patient, we look at the size of the parenchymal defect. As listed here, we basically assess less than 15 percent of the breast, 15 to 30 percent of the breast, or greater than 30 percent of the
breast to resect the primary tumor with a negative margin. If we anticipate a small parenchymal defect, that’s an individual where we would proceed to breast-conserving therapy. But, if it’s a 15 to 30 percent parenchymal defect, we know that this will cause significant deformity in the breast and will also cause asymmetry with the contralateral breast. And, so, this is where we would consider local tissue rearrangement or reduction mammoplasty. And for women with very large ptotic breasts, reduction mammoplasty is done bilaterally and this is a very useful tool for them. And then, for a very large parenchymal defect, we would definitely consider reduction mammoplasty or insertion of a latissimus flap or consider a mastectomy.

So, the primary components, then, of breast conservation...

...are removing the primary tumor with a negative margin, but we also look at several other factors. We prefer that this is a unifocal lesion in the breast because we know that historically, data suggest that patients who have multifocal or multicentric disease in the breast have a higher rate of in-breast recurrence. We also look at the mammogram to assure that there’re no extensive microcalcifications that would make it difficult to follow that patient after surgery and radiation therapy. Again, we look at the breast size to tumor size ratio, the tumor location, and, then, look at whether or not preoperative therapy might be indicated. So, if for patients who have a high nuclear grade, estrogen receptor negative tumor and lymphovascular space invasion, those are considerations for chemotherapy. And we might consider the chemotherapy preoperatively. For women who have strongly estrogen receptor positive tumors, we might consider preoperative endocrine therapy in a postmenopausal patient that would typically be with an aromatase inhibitor. And we know from clinical trials that we can achieve breast conservation in a significant portion of those women who have strongly estrogen receptor positive tumors. Finally, we look at the family history and any need for BRCA testing. Those individuals who are BRCA mutation carriers are at much higher risk for developing additional primary breast cancers in their lifetime. That’s in the treated breast and in the contralateral breast. So, in general, we would not consider those individuals to be good candidates for breast-conserving therapy. Although we do discuss the options with them, and some patients may choose to go to go that route, but we are --- we make sure that they are aware that the expected risk of re --- in-breast recurrence is much higher than what we would typically consider to be an acceptable risk. Patients who have a strong family history where they’ve not been tested for BRCA mutation status may also fall in this category and they should be counseled accordingly.

So, the breast-conserving treatment is a multidisciplinary team effort. The diagnostic imaging specialists are the ones who will define the extent of disease in the breast for us preoperatively, depending on whether there’re calcifications or mass lesion or architectural distortion. They will place localization wires to show the extent of the disease for us so that we can resect the full extent of the disease. And also image the regional nodal basins typically with ultrasound, preoperatively, so that we can approach the appropriate nodal basins as well. The surgeon is responsible for resecting the disease in the breast and assessing the nodal status. And typically, we prefer to do this with one operation. So, for diagnostic purposes, we always prefer a needle core biopsy
and --- so that we have the definitive diagnosis prior to proceeding with any surgery. The pathologist then assesses the margins for us intraoperatively and helps us to determine if we need to take additional tissue at that surgical procedure. And they also assess the lymph nodes for us so that we understand whether or not the patient needs a complete node dissection. Plastic surgeons are involved in providing optimal cosmesis for the individual patient and the medical oncologist for systemic therapy, the radiation oncologist for radiation therapy.

This is a diagram showing some of the placement of incisions that we consider for the individual patient. Typically, in the upper superior aspect of the breast and the lateral breast, we place the incision overlying the palpable tumor. However, when it’s relatively --- when the tumor is relatively close to the nipple-areolar complex, we do consider using circumareolar incisions as they’re less obvious than the ones placed directly on the breast. In the medial part or the middle aspect of the breast, we tend to use more of a radial type incision, either medially or laterally. And in the inferior breast, we typically use a radial type incision that might be able to be incorporated into a mastopexy incision or a reduction mammoplasty incision.

To talk about patients based on the breast size for partial mastectomy and local tissue rearrangement, those individuals that have a C-cup breast size that have a small tumor, no ptosis and minimal skin resection are the best candidates for local tissue rearrangement.

And there’re many different ways to approach local tissue rearrangement. I’m just going to show you a few examples today. One approach that we have used here at the MD Anderson Cancer Center is to make a circumareolar incision and completely release the nipple-areolar complex to raise the breast skin, much as you would do for a skin-sparing mastectomy, up to the level of the primary tumor, then to resect the tumor with a margin of normal tissue, and then re-close the nipple-areolar complex along with the breast skin envelope so that there’s no tension associated with the closure at the primary tumor site. So, it’s important to lift that skin completely off of the breast and do the resection such that they’re not tethered together, creating a defect when the --- when the healing occurs postoperatively.

Another approach is to use something called a batwing mastopexy. This has been popularized by several surgeons in the U.S. and the U.K., where you might have a tumor just above the nipple-areolar complex and need to perform a small amount of a skin resection with that tumor. And you can see the incision lines that are planned out here based on that. Once the tumor is resected, the nip --- the nipple-areolar complex is elevated into the space and then the closure takes place here. And at the final closure, you can see how the incisions medially and laterally are visible. However, this incision above the nipple-areolar complex heals quite well and is cosmetically much more acceptable.

This shows a patient who’s had a partial mastectomy with an incision placed directly over the primary tumor. And in this case, she’s had a good result. Basically, the --- the
--- again, one of things that we’re trying to achieve is to be certain that there’s symmetry with the opposite breast. And that there’s not significant deviation of the nipple-areolar complex once the healing has occurred at the primary tumor site and the adjuvant radiation therapy has been completed.

The breast reduction technique is something that we tend to use for patients who have a larger breast size, such as a D-cup breast size. Or those patients with a C-cup breast size where there is a small tumor, but there is a relative amount of ptosis --- significant amount of ptosis in the breast.

And so this shows many of the pedicles that we might use for the approach to the reduction mammoplasty. You can see that in these diagrams, the tumor is located in different areas of the breast. In this case, behind the nipple-areolar complex, you might even remove the nipple itself and you can do a free nipple graft in some cases. Or completely remove the nipple-areolar complex and then do a nipple reconstruction once the patient has completed radiation therapy. This works for patients with tumors in the inferior aspect of the breast and then, in other locations, as you can see noted here. And so, these are the vascular pedicles that are used for tumors in those different locations of the breast.

This shows an example of a patient who has a relatively large breast size, but she has significant ptosis in the breast. And she’s planned for segmental resection. We anticipate that because of the resection in the in --- in the medial aspect of the breast and the use of radiation therapy, that the patient will have significant lifting of that breast, which causes asymmetry with the contralateral breast. So, of course, it’s important to consider both breasts in the treatment. So, in this case, the segmental resection has been completed here. You can see the planned incisions of the Wise pattern that have been marked out by the plastic surgeon. And in doing the segmental resection, we used that planned incision so we don’t make a separate incision overlying the tumor even though it’s located in the upper aspect of the breast. We go through the planned incision. You can see here where the plastic surgeon has de-epithelialized this and raised the nipple-areolar complex and this pedicle up. And it will be rotated into the defect that was created by the partial mastectomy.

And this shows the final result postoperatively. The patient’s had good healing of her incisions here and you can see that she has good symmetry of the breast. So, this is a very useful procedure for those patients with a larger breast or those that have a significant amount of ptosis.

The key to par --- to successful partial mastectomy is anticipating the cosmetic outcome. Again, as I talked about, the location of the tumor in the breast, the breast to tumor --- to tumor size ratio, and also symmetry with the opposite breast. And these are important considerations because after radiation treatment has occurred, it’s much more difficult to correct a cosmetic deformity. And so, we try to anticipate the cosmetic outcome before the radiation and do any repair before the radiation has taken place. This avoids the need for using other myocutaneous flaps or latissimus flaps to repair a
defect that has occurred after radiation treatment has already been completed. The repair, again, is based essentially on the breast size and relationship to the tumor size, and in considering other factors, such as the need for chemotherapy. In a patient with a smaller breast, even a very small tumor can sometimes create a significant defect. This is where we might consider neoadjuvant chemotherapy or insetting another flap or another amount of tissue like a latissimus flap. Using breast remodeling technique for the C-cup breast, as I showed you, or for using the breast reduction technique, design the pedicle based on the tumor location.

So, again, using preoperative chemotherapy as a strategy that we’ve employed over the past couple of decades here at the MD Anderson Cancer Center. It’s standard practice for those women who present with locally advanced breast cancer. And so, that we don’t take any stage III or stage IV patients directly to surgery until we’ve achieved maximal response with the appropriate systemic chemotherapy or endocrine therapy. Using this approach, we see excellent clinical response rates. And so, in general, 70 to 80 percent of the patients who have preoperative chemotherapy will have either a complete or partial response in the breast, so that does create a lot of room for different surgical options or different approaches to the surgical management of the tumor. We have not found that there’s any increase in surgical complications related to chemotherapy in the preoperative setting. And there’s no delay in patients receiving their adjuvant therapy such as radiation or other adjuvant endocrine therapy and other things such as this --- of this nature. So, it does not create any difficulties, and very few patients will have any progression of their disease while on preoperative therapy. And in fact, this is a very important thing to discern, if the patient has any progression of disease while on therapy, then we have the opportunity to switch to a different type of therapy and see if we can get improved response. But, it helps us to understand the biology and the nature of that tumor. We know that there’s no significant difference in survival whether we deliver the chemotherapy in the neoadjuvant or the adjuvant setting. And --- and yet, the neoadjuvant setting offers us many more opportunities for improving surgical options.

So, the patient who is treated with preoperative chemotherapy who starts out with a relatively large tumor in the breast or even a locally advanced breast cancer is somewhat different from that individual with early stage breast cancer. We need to consider some other factors so that we have the best local regional control in that patient. So, what we consider is that if the patient had any skin edema prior to initiating chemotherapy, we want to see resolution of all of that edema before we do breast conservation after chemotherapy. Ideally, the residual tumor size should be less than 4 cm in size. We found that with relatively large tumors after chemotherapy, that there is a higher local failure rate. And we prefer not to see any lymphovascular space invasion, especially not extensive lymphovascular space invasion, no extensive microcalcifications on mammography, and no evidence of multicentric disease on their baseline imaging that they had before chemotherapy.

At the time of the surgical resection, we typically will have the pathologist ink the segmental resection specimen with six different colors to mark the different margins,
superior, inferior, medial, lateral, anterior, and posterior. They will then section through
the segmental specimen. And you can see that in this case, grossly there is not any
significant defect that’s obvious grossly or even by palpation to the radiologist. They will
then radiograph those segments of tissue and then what you can see is that we are able
to identify areas of calcifications or density that might suggest areas of residual tumor.
And that makes it much easier for the pathologist to assess microscopically. And this
helps us to re-resect any close margins at the time of their initial surgery.

Next, moving to skin-sparing mastectomy and immediate breast reconstruction.

The use of breast reconstruction has increased significantly over the past two decades.
Initially, we --- we would tell patients that they should wait at least one to two years
before having any breast reconstruction because we wanted to see if there was any
evidence of recurrent disease before proceeding with breast reconstruction. Now, we
know that patients, especially those with early stage breast cancer have excellent long-
term outcomes. And we expect improvements in survival with our systemic agents that
we are using now. And so we would much prefer to do the reconstruction at the initial
surgery. We know now from a few decades of exploring the use of skin-sparing
mastectomy and immediate breast reconstruction that doing immediate reconstruction
does not compromise the primary operation. We’re still able to achieve negative
margins, assess the margins of the primary tumor, and also assess the nodal basins.
We know it does not alter survival to do immediate reconstruction. And importantly, the
reconstructed breast mound does not interfere with detection of any recurrent tumor in
the breast or any treatment for recurrent breast cancer.

So, the decision making in terms of whether to do an immediate breast reconstruction or
a delayed breast reconstruction is based on multiple other factors. As I said, we prefer
immediate reconstruction basically because we can achieve a better aesthetic result for
the patient. We can spare the skin and achieve what looks much more like their normal
and natural breast. There’s less emotional and psychosocial trauma when we do an
immediate breast reconstruction. There’re fewer operations for the patient, fewer
anesthetics, and it’s more cost effective. And it does not affect their cancer treatment.
So, we know that doing a med --- immediate breast reconstruction does not delay the
initiation of adjuvant chemotherapy. But, we do prefer to delay the reconstruction when
the patient is ambivalent about breast reconstruction. So, if the individual is not sure if
she wants it, or if she’s planned for postoperative radiation therapy for advanced breast
cancer, then we prefer to delay the breast reconstruction. Other considerations are
those patients who are active heavy smokers because that interferes with the blood
supply to the skin-sparing flaps or any rotational or free flaps that we might perform.
And also, patients who are morbidly obese, they definitely have a higher rate of
complications. So, if there’re any medical contraindications for that individual or some
of these other factors, we would also think about a delayed breast reconstruction.

There’re what --- many different ways to reconstruct the breast. Typically, what’s been
used in the past is an implant-based reconstruction. So, a tissue expander is placed
behind the pectoralis muscle after the breast has been removed and then either a saline
or silicone implant can be placed at a later time once the expansion has been complete. This is obviously less surgery, it’s a shorter recovery time for the patient, and there’s no other incisions anywhere else on the body, so there’s no donor site morbidity. But, typically, with time, patients will get contractures, sometimes infections or other considerations that require removal of the implant and additional surgeries. We generally will consider autologous tissue when appropriate for the patient that has enough of her own tissue to make a breast mound, and that’s typically going to be from the abdominal area or the back, using a latissimus flap. It does provide a more natural shape and feel with the reconstructed breast. It’s more complex surgery and does take a longer recovery time but long-term, there’re fewer complications. And in general, it provides a better aesthetic outcome.

For the skin-sparing mastectomy, the definition that we use for this is an en bloc resection of the nipple-areolar complex with any biopsy scars and the underlying breast tissue, and axillary contents as appropriate. It provides a much better cosmetic outcome, it’s oncologically safe, and --- but it is technically more demanding for the individual surgeon.

This is a diagram showing several different incisions that we use for skin-sparing mastectomies. The most common one is to make an incision around the nipple-areolar complex and remove the breast tissue by lifting up the breast skin and removing any axillary contents through a separate axillary incision. But, as you can see, there’re other approaches. This is sometimes called the tennis racket or lollipop incision. Also, for patients who have significant ptosis in the breast, you can use a Wise pattern incision much as you would if you were doing a reduction mammoplasty. You can also remove a more --- a larger skin ellipse and be --- and close this primarily.

This shows a patient who’s had a bilateral skin-sparing mastectomy with a nipple reconstruction. You can see her lateral incisions here the --- that lateral approach was used in this case. And you can see the incision from her abdominal flap here. So, the cosmetic outcome is quite good in that this looks much more like her natural breast. It feels much more like a natural breast, and long-term, there are very few complications that would lead to need for further surgery.

In terms of nipple-areolar preservation, this is something that’s become more popular over the last five to seven years. And this is mo --- most common in women undergoing prophylactic mastectomy, so those patients who are BRCA1 or BRCA2 mutation carriers. There’s some concern that we might be leaving more ductal epithelium behind the nipple-areolar complex and this may increase cancer risk. But, most of the studies that were done a couple of decades ago using subcutaneous mastectomy where there was a significant amount of breast tissue left behind the nipple-areolar complex, those individuals had more than a 90 percent reduction in the development of breast cancer. So, this nipple-areolar preservation is probably a safer approach. There’s left --- less tissue left behind than there is with the subcutaneous mastectomy. In patients who are undergoing mastectomy for cancer, there have been a lot of retrospective studies published in the literature looking at the incidence of occult cancers in the nipple-areolar
complex. So, in other words, the mastectomy was performed for a lesion somewhere else in the breast. And then the pathologist looked at the nipple-areolar complex and identified a cancer there. And this ranges anywhere from 8 to 50 percent. So, there’s certainly a lot of variability there. But, now, with improved imaging, it’s very uncommon to find an occult cancer in the nipple-areolar complex.

This shows a patient who’s undergoing a bilateral prophylactic mastectomy. She’s a BRCA mutation carrier. And what you can see is the --- in the lateral projection here, the breast was removed through a radial incision in the lateral aspect of the breast so that the nipple-areolar complex was completely maintained. No incisions are placed around the nipple-areolar complex and she had a bilateral implant-based reconstruction with a good cosmetic outcome.

And this just shows another patient who is planned for a bilateral skin spar --- or nipple-areolar sparing mastectomy, showing projection of the nipple.

And after the mastectomy has been performed, you can see the radial incision here. And she still has quite good projection of the nipple. So, there --- this procedure is possible for many patients to maintain the nipple-areolar complex and have a more natural appearance to the breast.

Right now, what we use as eligibility criteria for nipple-areolar sparing is patients who are undergoing prophylactic mastectomy or those with early stage breast cancer, so Stage 0, I, and II breast cancer, who have a primary tumor that’s at least two and a half centimeters away from the nipple-areolar complex. And also, we look for any evidence of microcalcifications extending toward the nipple, such that if there’s any evidence of ductal extension of ductal carcinoma in situ or another process toward the nipple, we would not perform a nipple-sparing mastectomy on these individuals.

We do not consider this procedure for smokers. As I mentioned, with skin-sparing mastectomy and immediate breast reconstruction, smokers have more complications. And they definitely have more incidence of nipple necrosis with nipple-areolar sparing mastectomy. We would also not consider this for patients with inflammatory breast cancer or breast skin involvement, those patients with collagen vascular disease, or those with Paget’s disease of the nipple.

And something that --- that we’re starting to explore here more and more at MD Anderson is the use of immediate breast reconstruction even in patients who require post-mastectomy radiation. This has been a very significant multidisciplinary --- multidisciplinary effort in that it requires significant coordination between the breast surgeon, the plastic surgeon, and the radiation oncologist. More and more, patients that have Stage II breast cancer, so those with a few positive nodes or a larger primary tumor, might be considered for post-mastectomy radiation. And this is why we’ve incorporated this strategy into our reconstructive algorithm. So, in patients where we think they might need post-mastectomy radiation, we do a skin-sparing mastectomy and place a tissue expander in the subpectoral position and then look at the final pathology,
both the assessment of the primary tumor and the nodal disease. And we have a postoperative consultation with the radiation oncologist. If the patient does not require any post-mastectomy radiation therapy, they can proceed to their definitive breast reconstruction, whether that’s an implant-based reconstruction or an autologous tissue reconstruction. But, in those patients where it looks like they will require radiation therapy, we try to get full expansion of the tissue expander within a few weeks and then deflate the expander before the radiation takes place. So, that there’s better geometry for the radiation oncologist in treating all of the areas at risk, the chest wall, and any regional nodal basins that need to be treated. We then reinflate the expander immediately after radiation and then, the patient ultimately, a few weeks to months later, will have definitive breast reconstruction. And typically, this is going to be with an autologous reconstruction, either a TRAM flap or a latissimus dorsi flap.

And this has helped us to save the breast skin for many patients who would otherwise have had a rad --- a modified radical mastectomy with removal of all the skin and then require a significant skin replacement using autologous tissue reconstruction. We look at patients who have clinical Stage I or II disease who we think they might need radiation. Sometimes, it’s difficult to tell if they will, especially in patients who have extensive microcalcifications on mammography or those who have multicentric disease on their imaging where we think that final pathology may lead us to incorporate post-mastectomy radiation. In these patients, they need to be able to withstand two anesthetic procedures, clearly their initial surgery and then their later reconstructive surgery.

This shows a case of a patient with a T2 N1 breast cancer where she had a skin-sparing mastectomy, placement of a tissue expander. And you can see that expander was fully expanded pret --- pretty rapidly in order to save as much of that breast skin as possible. And then, you can see the photo here where it’s been deflated to allow the radiation oncologist to treat all of the areas at risk.

So, skin-sparing mastectomy is a very oncologically safe tool we’ve studied now for several decades. And recurrence rates are no different than those patients undergoing a standard modified radical mastectomy. And a skin-sparing with immediate reconstruction is generally reserved for those patients who will not require radiation after surgery. But, we are exploring this approach of immediate delayed reconstruction for patients where we think they might need radiation, where we can place a tissue expander, deflate it, and inflate it as needed. And finally the role of nipple-areolar complex preservation is still under investigation. But, we think this is a useful tool especially for those patients undergoing prophylactic mastectomy for risk reduction.

The final area that I’m going to talk about, then, is axillary lymph node staging.

The goals of staging are, of course, to provide an accurate stage for that individual patient to allow for the incorporation of the appropriate systemic and adjuvant therapies. We also want to provide regional nodal control for the individual patient. But, we know there’s no benefit to removing healthy uninvolved lymph nodes. And there’s also
significant morbidity associated with the use of a standard axillary lymph node dissection.

The complications of an axillary dissection are most commonly lymphedema and this occurs in anywhere to 20 to 25 percent of patients with early stage breast cancer. And the rates are significantly higher in patients with more advanced breast cancer who have both surgery and radiation. There’re also a number of other things that occur after axillary surgery: shoulder dysfunction, paresthesias and pain from interruption of intercostal brachial nerves. And patients can also have persistent seromas and hematomas requiring aspirations and other interventions.

The use of lymphatic mapping with sentinel lymph node biopsy was first popularized by Donald Morton in the 1990s for patients with clinically node negative melanoma. And the sentinel node is defined as that first draining lymph node from the primary tumor. And it was found with melanoma and other solid tumors that the sentinel node was predictive of the status of the remaining nodal basin. So, that those patients with a positive node were more likely to require a node dissection. Those patients with a negative sentinel lymph node did not need removal of the remaining lymph nodes. It was David Krag and Armando Giuliano that first reported the use of sentinel node surgery for breast cancer patients in the early 1990s.

And it’s now become standard of care for patients with early stage clinically node negative breast cancer. Typically, a peritumoral injection of either a blue dye or a radioisotope, or a combination of those are utilized. And this travels through the lymphatic channels to the first draining lymph node, also called the sentinel node.

In the operating room, we can identify the blue dye within the axillary contents and when the blue lymphatic --- when the blue dye is passed through the lymphatic channels and accumulates within a lymph node such as this, it’s very easy to discriminate. But, we can also use, as I said, the radioisotope. And we have a handheld probe that registers radioactive counts, in this case, 22,000 counts that are easy to discriminate the uptake from surrounding lymph nodes.

Now, there’re several trials that have been performed to assess the safety and utility of sentinel lymph node surgery in breast cancer patients.

And the first large trial in the U.S. was the NSABP B-32 trial. In this case, the hypothesis was that sentinel lymph node surgery alone was safe compared with sentinel lymph node surgery with completion axillary dissection. So, patients that had clinically node negative breast cancer were stratified based on age, clinical tumor size, and the planned surgical procedure, and then randomized to either go sentinel lymph node surgery with a completion axillary dissection at the same surgery, or sentinel lymph node surgery alone followed by axillary dissection only in the case when standard H&E staining identified a positive sentinel node. So, those patients who had a negative sentinel node had no specific axillary treatment.
This trial was recently reported in *Lancet Oncology*. The overall accuracy was 97 percent.

And you can see the technical success rate here, based on tumor size, overall 97 percent, and basically the --- even in patients --- patients with larger tumors, even those with greater than 5 cm tumors, the success rate was quite good. Now, one thing that was somewhat unexpected with this trial was the relatively high false negative rate. It was almost 10 percent overall. It did not vary based on tumor size so it was stable across even larger tumors. But, what this tells us is that even in --- in very trained hands, all these investigators were trained in the use of sentinel lymph node surgery before the trial. Even in well trained hands, there is a relatively high rate of identifying a negative sentinel lymph node but the axillary nodes still harbored disease within them.

The factors that affected the false negative rate were the tumor locations. So, those tumors in the lateral breast were more likely to have a false negative event. Perhaps, because of shine through from the radioactivity in the lateral breast, it was hard to discriminate in the axilla. Patients who had had an excisional biopsy before surgery were more likely to have a false negative sentinel node. And those patients who only had one or two sentinel lymph nodes recovered were more likely to have a false negative sentinel node. This tells us, and the average number of sentinel nodes removed in most trials is 2.5 to 2.7, so this tells us that there is usually more than one sentinel node and that it’s --- it’s best staging when all of the sentinel nodes are recovered.

The American College of Surgeons Oncology Group also initiated some sentinel node trials at the same time as the NSABP trial. This was in the late 1990s. These trials all completed in the mid 2000s but were only recently published with long-term follow up. In the ACOSOG trial, patients with T1 and T2 tumors that were planned for breast conservation had sentinel lymph node biopsy. And if the sentinel node was negative, they had no further treatment of the axilla but they all had radiation treatment to the breast. If they had a positive sentinel node, they were eligible for the Z0011 trial. And in the Z0011 trial, patients with one or two positive sentinel nodes were randomized to have a completion axillary dissection as was the standard at the time, or axillary observations, so no further treatment. Again, they all had breast conservation and all had a standard tangential breast radiation to the intact breast without specific radiation to the axilla or the supraclavicular nodes.

In the Z0010 trial, there were over 5,000 patients enrolled. Twenty-four percent had a positive sentinel node by standard H&E staining.

And you can see the complication rate, relatively low. Only 7.5 percent of patients had a seroma that required any aspiration or other intervention.

The lymphedema rate, however, was higher than what we expected. As I said, with axillary dissection, it’s reported to be somewhere between 20 to 25 percent. In this trial,
sentinel node only, it was about 7 percent and this was based on arm measurements with a 2 cm difference with the ipsilateral treated arm versus the contralateral arm.

The predictors for those patients that develop lymphedema were those patients of older age. So with increasing decade, there was a higher rate of lymphedema. And also, with increasing BMI, so patients that had increasing BMI had a higher rate of lymphedema. So, this information is very helpful to us in counseling our patients.

In terms of failure to identify a sentinel node, there were both surgeon factors and patient factors. So, the number of cases that the surgeon performed on this trial were important, suggesting that the experience of the surgeon is very critical, and the volume of cases that the surgeon performs is an important factor. And also, increasing age and increasing BMI were also factors that predicted for the failure to identify sentinel node at surgery.

Now, recently, the Z0011 trial was reported and this has created a lot of excitement in the surgical community. And in the breast cancer community, in general, because this suggests this trial --- the results of this trial suggest that axillary lymph node dissection is not needed even in all patients who have a positive sentinel node. So, again, in this trial, small tumors T1 or T2 tumors, if the patient had a sentinel lymph node that was positive, they were eligible to be registered in the trial. And they were randomized to undergo an axillary lymph node dissection or no further surgery. They all received breast radiation as standard for breast conserve --- conservation. And the systemic therapy, either adjuvant chemotherapy or endocrine therapy, was based on the primary tumor factors and individual physician treatment decisions.

If we look at the patients --- the characteristic patients that were enrolled in this trial, you can see that 65 percent were over age 50. So, this was largely a postmenopausal patient population. The majority had small T1 tumors, 80 percent were estrogen receptor positive, and only 38 percent had any lymphovascular space invasion. Most patients had only one positive sentinel node, although there were some with two or even three positive sentinel nodes. And the majority received syst --- systemic therapy, 60 percent received adjuvant chemotherapy, which is the standard in the U.S. at the time of the --- this trial.

Now, a completion lymph node dissection, only 27 percent of patients who had the completion node dissection had additional positive nodes in the axilla, and only 14 percent had four or more positive nodes. Now, despite the fact that the patients who did not have a node dissection would be expected to also have this amount of nodal disease in the axilla, there were no differences in local or regional recurrence rates between the two treatment arms. And you can see that they were very, very small numbers in --- in terms of axillary fail --- failures or regional recurrences.

So, when we look at the ACOSOG Z0011 trial results, again, all of the patients had positive sentinel nodes. But these are patients who all had breast conservation with whole breast radiation, tangential breast irradiation, and we know that that treats a
significant portion of the axilla, based on many different single institution studies. There were no differences in local or regional recurrences. And there were no differences in overall survival between the two treatment arms.

This suggests that axillary node dissection is not needed in all women who have a positive sentinel node. But, axillary dissection is still the gold standard for many cases. So, those patients who present with clinically positive nodes, those individuals should have an axillary node dissection. We still use axillary dissection in patients who have neoadjuvant chemotherapy and have a positive node after chemotherapy. And other considerations where we might still use axillary node dissection are those patients who are very young age. Again, in Z0011, the patients were largely postmenopausal and older patients. And those individuals with triple negative disease, where we know that local regional failure rates are higher in general. But, in patients and in --- and also in patients who wouldn’t otherwise need radiation. So, those women who are undergoing mastectomy who have one or two positive nodes that might not need post-mastectomy radiation therapy, so those low risk Stage II disease. So, there still are indications for the use of axillary dissection, but it’s important to note that many women undergoing breast conserving surgery who have small volume disease in the sentinel nodes probably do not benefit from an axillary lymph node dissection.

So, at the --- this time, the National Comprehensive Cancer Network Guideli --- Treatment Guidelines™ suggest that sentinel node biopsy is appropriate for those patients who have a clinically node negative axilla. The team should have documented experience. And in general, axillary node dissection is performed for those with --- when the sentinel node is positive or when the sentinel node cannot be identified.

The ASCO Guidelines suggest that axillary dissection is --- should be performed when sentinel node is identified on routine histopathologic exam. I would imagine that we’ll see some modification as these guidelines were published in 2005. And the Z0011 results were only published in just the last year.

So, in summary then, what I’ve presented today is --- is significant in terms of breast conservation and mastectomy in the treatment of early stage breast cancer. We know that there’re equivalent in terms of outcome for early stage breast cancer. But, breast conservation is also feasible for those individuals with locally advanced breast cancer or large primary tumors who have a good response to preoperative chemotherapy. Selection criteria are very important to achieve the optimal outcomes in these individuals. For those patients who require a mastectomy or elect to undergo mastectomy, we think that skin-sparing mastectomy provides the most optimal results with immediate reconstruction. And now, we’re considering nipple-sparing mastectomy in selected cases. And, finally, sentinel lymph node biopsy is a tool that is --- provides alternate staging to axillary lymph node dissection. So, it’s accurate, it’s safe, and it has less morbidity than a full axillary lymph node dissection. And in selected patients with a positive sentinel node, we can avoid the use of axillary lymph node dissection, especially those individuals who have breast conserving surgery with whole breast
irradiation. I want to thank you very much for your attention and we are certainly happy to hear any feedback from you. Thank you.