Hello. My name is Isabelle Bedrosian. I'm an Associate Professor in the Department of Surgical Oncology at The University of Texas MD Cancer Center. And today I'll be discussing the late effects of breast cancer surgery.

The objectives of this program are to understand the workup and diagnosis of the common late effects of breast cancer surgery and to discuss the management of these common late effects.

So the late effects that I'll be discussing with you today are the following: lymphedema, delayed breast cellulitis, chronic seroma, and chronic pain syndromes.

Lymphedema remains among the most feared complications of breast cancer surgery. Lymphedema is the disruption of the lymphatic transport system. And the subsequent sequelae occur in several phases, first, with a phase that involves swelling followed by inflammation, and finally, if not managed appropriately, a phase of fibrosis. It can involve any part of the extremity. But it can also involve the trunk and not uncommonly breast cancer patients will have lymphedema that involves the preserved breast, the chest wall, the supraclavicular area. And while treatment-related risk factors are well recognized, such as radiation and surgery, we're increasingly identifying patient risk factors that may be pertinent as well, among these obesity and genetics.

The risk of lymphedema is estimated to range from 6-70% after axial lymph node dissection and 1-17% after a sentinel node biopsy. These are very wide ranges clearly. And really speak to the fact that there is no consensus regarding how one defines lymphedema. And they can range anywhere from a clinical definition of lymphedema to very objective and highly technically sophisticated methods of measuring lymphedema and change in lymph volumes. However, the most commonly used diagnostic tool is a change in arm circumference. Key to treating lymphedema is early detection and treatment to minimize the morbidity of this condition.

It's also important to consider other possible etiologies. Not every swollen limb is lymphedema. Occasionally, one can have infection. One can have venous thrombosis. And these can also present with a similar clinical picture. For women who do have lymphedema, the core of treatment really is manual lymphatic drainage and compression bandaging and garments. And this actually can be folded into a larger complex program called complex decongestive therapy, or CDT, which is a multiphase treatment to help both decrease lymphedema, increase lymph drainage, decrease the long-term fibrosis of the limb, and improve the skin condition. The first phase of this is essentially the manual lymphatic drainage and compression garments to really bring down the size of the arm. And then a maintenance phase in Phase II which involves exercise programs, skin care, continued compression garment use, and lifestyle interventions, in particular maintaining optimal weight. There is, unfortunately, no cure for lymphedema. But as I tell patients that the good news is
that with these efforts, one can really maintain a limb that is normal in size and allow women to remain fully functional in their activities of daily living.

Just as there is no cure for lymphedema, there really is no proven means to prevent lymphedema either. Historically, we have recommended avoiding things like venipuncture or trauma to the ipsilateral side, to avoid the wearing of tight garments, to avoid exposures to extreme cold or extreme heat. Wearing compression garments has often been recommended as well when --- when patients are --- are taking a flight, particularly long flights but the data on this is evolving. It appears that perhaps wearing these garments may be more important for women who already have a diagnosis of lymphedema. Its role is becoming less clear in women who are at risk and who are trying to prevent the development of lymphedema.

Another area where there has often been confusion is the relationship between exercise and lymphedema. And fortunately, on this point, the data is becoming available. And this is one study, although small in nature, certainly a very important one published a few years ago. And what this study did was take women who were at risk of developing lymphedema and randomize them to one of two treatment interventions, either weight lifting or no --- no active therapy whatsoever, just sort of standard of care recommendations. And they defined lymphedema in two ways, either objectively by a 5% or greater increase in swelling of the arm at 12 months after --- after randomizing the study, or a clinically defined onset of lymphedema. And as you can see, when they looked at their outcomes --- lymphedema outcomes at 12 months, when lymphedema was dev --- was defined objectively, in fact there was less lymphedema that had developed amongst women in the weight lifting intervention arm, only 11%, compared to 17% lymphedema onset at 12 months in women in the control arm, a statistically significant difference.  And actually, this difference was magnified in the women considered to be at greater risk for lymphedema development because they had five or more lymph nodes removed. And here you can see in that weight lifting intervention arm, 7% developed lymphedema, compared to 22% who developed lymphedema in the control arm; again, a highly statistically significant difference. But speaking to this issue of how one defines lymphedema, if you look at the same outcome, but define it by clinical onset of lymphedema, there was not a statistically significant difference between the two trial arms.  So the bottom line from this study is that exercise is not harmful. It does not cause lymphedema and perhaps may actually even help reduce the onset of lymphedema.

Moving on, now to the topic of delayed breast cellulitis, this is actually not the cellulitis that we some --- sometimes see in the --- in the days and weeks immediately following breast surgery. But really, this is the cellulitis that develops months after completion of lumpectomy and radiation therapy. The incidence of such delayed breast cellulitis ranges from about 2-12%, so not terribly common. Its presentation, though, as one would expect, erythema, warmth, tenderness, patients may or may not have systemic symptoms at the same time. Risk factors for such delayed breast cellulitis includes obesity, lymphedema, as well as aspiration of prior seromas, perhaps introducing a nidus of bacteria that later spread to give the infection.
Management, again, is fairly standard, with the use of oral antibiotics. Most patients will resolve. Occasionally, IV antibiotics may be necessary for women who have systemic symptoms and if --- if there is a failure for this cellulitis to resolve after one to two rounds of oral antibiotics, and if the woman has a seroma present as well, one should consider opening and draining the seroma cavity. It’s important that --- that drainage of the seroma cavity is not necessary at the outset, but really can be deferred and an attempt given at just --- just conservative management with antibiotics before something more invasive such as an I and D is performed. About 20% of women will have recurrent episodes of cellulitis, al --- although it is rare that --- that this process becomes so intractable or so repeated that one has to convert to a mastectomy to control the situation. And as always, it’s important to consider a biopsy to rule out a local recurrence in cases that are not --- that are --- that --- that --- that are fairly atypical and not responsive to --- to appropriate interventions.

So chronic seromas are another --- another long-term sequelae that we will sometimes see in Survivorship Clinic. And the chronic seromas should be distinguished from the postoperative seroma that develops immediately after surgery. A postoperative seroma is a collection of inflammatory exudates that is a normal response to surgical trauma. Within the preserved breast, this can actually help preserve normal breast contour initially and over time, this fluid collection will be replaced by scar. In women who have undergone a mastectomy and who have undergone node dissection, the fluid that collects can delay and hinder the --- the skin flap from adhering down to the chest wall. So in these cases, we will often place drains initially to collect this fluid and allow for healing process to complete itself.

The management really depends on the site of the seroma. Within the breast, if the patient is asymptomatic, no intervention is really needed. Only if the patient is symptomatic and is bothered by the heaviness of this fluid collection, would aspiration be necessary. Sometimes aspirations will need to be done repeatedly. And on rare occasion, a recurrent symptomatic seromas may actually require re-excision of the biopsy cavity to allow for this cavity to heal, close down, and prevent future fluid accumulation. For women who have a seroma in the chest wall or in the axilla, aspiration will be required, sometimes, again, multiple aspirations. Consideration should be given to drain catheters if recurrent aspirations have failed. And those catheters should probably be left in for some time until fluid has been completely drained out. And the flaps have sealed down to the chest wall. Some have also
advocated limiting shoulder abduction to about 90 degrees, again, to limit the flow of fluid and help resolve these chronic seromas of the chest wall.

The question sometimes arises whether --- whether the fluid that’s drained and aspirated from these seromas should be sent for cytologic evaluation. This is data from a small but representative study that was published some years back. Thirty-eight cases of seroma were aspirated. And as you can see, abnormal cells were found fairly routinely in these --- in these women. And in 11 cases these were clearly inflammatory cells. But in many cases, these cells looked quite atypical – some mildly, some highly atypical. In only two cases were there clearly malignant cells in the aspirate that were similar to the primary tumor. And core biopsy confirmed the presence of a malignancy. The presence of atypical cells alone, however, does not necessarily mean that there is, in fact, a tumor present. And so these women that have highly atypical cells underwent core biopsy but no tumor was found.

So, “What does this mean?” I think what this data suggests that, again, atypical cells are common in seroma aspirate fluid after a lumpectomy and radiation therapy. And so just the presence of atypical cells alone does not mean that the patient has had a recurrence of her cancer. It really is critical to perform a core biopsy to confirm recurrent disease before any further interventions, such as mastectomy, are planned. And I think a larger point is that --- that it really is not necessary to send breast seroma fluid for cytology on a regular basis unless there is clinical suspicion that the patient has a recurrence event.

Lastly, I’d like to turn to the issue of chronic pain syndromes. While lymphedema gets a lot of attention, chronic pain syndromes really are also a significant and unfortunately underappreciated and understudied problem. Pain and sensory changes are quite common after breast cancer surgery. In fact, a recent study that followed several thousand Danish breast cancer survivors notes that over half the patients are going to have these sorts of symptoms and complaints two to three years after completion of breast cancer treatment. With regards to pain, as much as 50% of patients will report some degree of chronic pain. These pain symptoms can be quite variable, both in terms of location, frequency, as well as severity. It’s not uncommon at the --- at the lowest end of the scale to have patients complain about an intermittent sharp, shooting pain that comes through the breast periodically. These sites of pain typically are in the breast, but can also involve the axilla, the arm, and the side of the body less frequently.

It’s important to note that patients with pain, a considerable portion of these patients, are taking analgesics and are seeking alternative treatments. And so these are important to inquire about at --- at follow-up visits. And predictive factors for chronic pain from this study included young age, axillary node dissection, speaking again to larger and more aggressive surgery and radiation therapy which may result in some degree of scarring and fibrosis that leads to these pain syndromes.
And in terms paresthesias, which is the other component of these pain syndromes, about two-thirds of women will --- will report some sort of sensory disturbance, again, two to three years out from breast cancer treatment. And these sensory disturbances really can be quite variable. They can range from burning to hypersensitivity to pure sensory loss. And the predictive factors for --- for these paresthesias are similar to that of chronic pain syndromes. Again, young age seems predisposed to this, as does the axillary lymph node dissection procedure.

What has become very clear is that these post-surgical pain syndromes seem to be associated with other pain syndromes as well. And they also seem to be associated with psychosocial status, things like depression, anxiety, and fatigue. And really, these kinds of associations has --- has resulted in a --- in the development of a multidisciplinary approach to these pain syndromes that draws in the expertise of oncologists, pain specialists, psychologists, psychiatrists, and rehab specialists. There are few randomized, placebo-controlled trials in these populations. And --- and, really, this lack of trial data further underscores the need to treat this patients in a multidisciplinary fashion.

As always, it’s also important to consider non-neuropathic etiologies. Although these are uncommon, they should be on the differential. And they include brachial plexus infiltration with tumor, radiation-induced ischemic plexopathy, and fibrosis, as well as lymphedema.

So in summary, we commonly will see late effects of surgery among breast cancer survivors. Lymphedema, although a--- a common problem, can be managed aggressively. And --- and, in so doing, it can help to minimize morbidity of our patients. Seromas are also common in the preserved breast. But importantly, they do not need to be always aspirated unless they’re symptomatic. And chronic pain syndromes and paresthesias are quite common and best managed in a multidisciplinary/multimodality setting. Thank you for your attention, and we welcome any feedback you may have on this program.