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Welcome to Yale Cancer Answers with your host doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week it’s a conversation about the role of surgery with Doctor Tristen Park. Dr Park is an assistant professor of surgical oncology at the Yale School of Medicine, where doctor Chagpar is a professor of surgical oncology.

Why don’t you start by telling us a little bit about breast cancer? We know that it’s incredibly common, so tell us a little bit about how it’s found and how it’s treated.

So this is one of the reasons why I chose to go into breast cancer. I feel like breast cancer is one of the fields in oncology, especially the surgical treatment of it, that has evolved so drastically in a positive way that I
really wanted to take part in its care. So as of 2020, the treatment of breast cancer, actually has morphed to the point where a lot of these cancers are caught by screening modalities such as mammogram and ultrasound.

Many, many decades ago, before this was implemented, these types of cancers would be caught in a much later stage where the patient would be able to feel it. Fortunately, in this day and age, that’s a more rare occurrence, and we capture these cancers through screening modalities implemented by general practitioners and obese humans. And we catch them at very early stage where the patients generally can’t even feel it, and people will go for their regular mammogram.

I suppose one of the other questions is always controversial, is the question that many people may be asking themselves, which is when should I start having a mammogram?
guidelines are all over the place. I generally see patients and recommend patients to start getting their annual mammograms at the age of 40. There have been adjustments and different entities such as the USPSTF prolonged or delayed the age of screening up till the age of 50, but in general I see patients that have started screening at the age of 40, and that’s the general recommendation. And so you know people out there should know that getting mammograms are really effective in terms of finding these cancers early, which really allows them to be treated in the most efficacious way and actually improves survival. So let’s suppose somebody goes for a mammogram, and they find something that they didn’t otherwise feel. They felt absolutely fine, and then they are shocked and horrified that the radiologist wants to do a biopsy and does a biopsy, it comes back breast cancer. What is the conversation that you have with these patients at that point?
At this point, I tell the patient that the current cancer that was detected is generally very small and in the average patient this happens to be a generally favorable receptor profile or the blueprint of the cancer is quite favorable. It's generally estrogen receptor positive, lower grade, and this is generally more in the older population, so I at this point I usually tell them that this is not a death sentence by any means, and that this is treated on a routine basis. Most commonly and most likely, the bulk of the patients I see, particularly as a surgical oncologist, will not die from their breast cancer, but will die of other natural means outside of their cancer. And you know, breast cancers are really well treated these days. Tell us a little bit about the modalities by which breast cancer is treated. I mean, you’re a surgeon, so clearly surgery is one of the mainstays of treatment of breast cancer. What are the surgical options that patients have these days? In this day and age we’re
very lucky to have several modalities, surgical modalities available for the treatment of breast cancer. Way back in the day, back well over 50 plus years ago, there was only one option which is removing the whole breast, otherwise known as mastectomy. But now with modern surgical and multidisciplinary management we’re able to do something called Breast Conservation Therapy where we just remove the tumor if it’s small enough and the ratio of the breast and the tumor is favorable and supplement that local resection of the tumor with something called whole breast radiation therapy. Which can give you a cancer free result that’s nearly identical to what we would traditionally have to do, which is remove the whole breast. So how do you do breast conserving surgery if you can’t see or feel this tumor? I mean, these women wouldn’t have been able to feel this tumor. It just got picked up incidentally, on a mammogram. So how do you know that you’re getting out the spot that actually
had the cancer?
So this is one of my favorite elements of my job is we get to use all this wonderful technology to help us find this tumor in a situation where otherwise my naked eyes, my hands and the patient wouldn’t be able to tell me where it is. So basically we use a combination of imaging as well as localizing technologies to help us pinpoint exactly where it is. The most classical one is something called a wire, which basically the patient comes in and my radiology colleagues using either a mammogram or an ultrasound can pinpoint exactly where it is and place this little wire that basically points to exactly where the tumor is, and I use this wire to help me in the operation and find exactly where to resect. And then I get to use another very fun high tech machine, which I call it a mini mammogram machine inside the operating room where I could place the specimen inside and confirm with all of that technology that I indeed took the suspicious area out.
Now that’s the wire that kind of physically points to where the tumor is being replaced by these other non wire localization methods. This includes little gadgets that are the size of like a grain of rice that uses different either radioactivity or radio frequency or magnetic waves to help us detect it. And I get to use something that’s in the similar vein as like a Geiger counter, and I get to use that to tell me exactly where to go. So as of two 2020 we have all these wonderful modalities to find exactly where these tiny tumors are and bring minimal harm to the patient and so for many of these patients who have very small cancers, you can use technology to help you to find exactly where the cancer is and remove it. Sometimes patients may have, you know, widespread calcifications or calcium spots that show up on their mammogram, that may in fact be pre cancer, but if that is all over the breast, is there still a role for mastectomy in these patients? Certainly if they have large areas of
calcifications that we generally confirm with additional biopsies that these are either early stage cancer or pre cancer. I would definitely recommend the patient to have a mastectomy, but fortunately in this day and age we could also have wonderful reconstructive options working side by side with our plastic surgery colleagues and have results where it looks much better. Or if not, it looks just as good as we started. Tell us a little bit about how that works. I mean, do you operate with the plastic surgeons all at the same time? Do they use implants? Do they use people’s own tissue? How does that work? Generally we work at the same time and sometimes start at the same time and we work as a big team, so that’s actually a lot of fun and the way that the plastic surgeons can reconstruct the breast once I’ve removed it includes using implants, and in some cases some patients could also use their natural tissues that are found either in the belly area, the leg area, or the bottom area to
reconstruct a breast that’s actually made from their own tissues. This is a much longer procedure obviously, but has a lot of benefits, including feeling more natural. Accordingly, as the patient ages as well, a lot of times we partner with the plastic surgeons really to get an optimal aesthetic result. There’s now a concept that has come about called oncoplastic surgery where people are kind of combining oncology and plastic surgery. Even when doing these smaller resections. Do you do that? Tell us a little bit about that concept. I think this is a developing concept in America. I think it’s done more so in certain parts of America as well as I think it’s done more so in Europe. But I’m a big proponent of it and I try to incorporate oncoplastic techniques in my surgeries, particularly since I feel like as of 2020 as a surgeon, I’m able to treat these patients and resect their cancers and hopefully they’ll be living for another 20 to 50 years. And I want them to be happy.
0:11:07.842 –> 0:11:09.62 with how they look.
0:11:09.62 –> 0:11:11.882 So this includes more minor things
0:11:11.882 –> 0:11:13.929 such as very strategic incision
0:11:13.929 –> 0:11:16.249 placement where it’s well hidden.
0:11:16.25 –> 0:11:19.378 It could be in areas of the breast
0:11:19.378 –> 0:11:22.038 where there’s like a natural crease,
0:11:22.04 –> 0:11:23.98 or there’s a natural shadowing
0:11:23.98 –> 0:11:27.01 so that the scar is quite hidden.
0:11:27.01 –> 0:11:29.08 This also could include once
0:11:29.08 –> 0:11:31.15 you remove the actual tumor,
0:11:31.15 –> 0:11:33.694 the tissues or the breast tissues
0:11:33.694 –> 0:11:35.76 that are surrounding it are
0:11:35.76 –> 0:11:38.511 moved around a bit so that the
0:11:38.511 –> 0:11:41.47 cavity that’s left behind is not as
0:11:41.47 –> 0:11:44.02 obvious, not completely filled up,
0:11:44.02 –> 0:11:46.26 and there’s another wonderful option
0:11:46.26 –> 0:11:48.924 called oncoplastic reduction where if
0:11:48.924 –> 0:11:51.444 the patient starts off quite large breasted,
0:11:51.45 –> 0:11:54.341 we could remove a tumor and then
0:11:54.341 –> 0:11:56.967 the plastic surgeon could do a
0:11:56.967 –> 0:11:59.147 classical style reduction of that
0:11:59.147 –> 0:12:01.972 breast and then also do a reduction
0:12:01.972 –> 0:12:04.67 of the other breast so that she
0:12:04.67 –> 0:12:07.16 ends up both with the tumor
0:12:07.16 –> 0:12:09.482 removed and both breasts that
0:12:09.482 –> 0:12:12.07 look quite symmetrical and a lot of
0:12:12.07 –> 0:12:14.014 times in these larger breasted women
0:12:14.02 –> 0:12:16.547 it also has the added benefit of
0:12:17.18 –> 0:12:19.7 the relief of back pain and the other
0:12:19.77 –> 0:12:22.32 issues that occurred with that
0:12:22.32 –> 0:12:24.847 prior.
As you said, is not necessarily a death sentence. There are many surgical options for women, especially when they present early. Now, you mentioned some of the adjuvant therapies that we also use in the importance of a multidisciplinary team. One of the things you talked about was radiation therapy after breast conserving surgery. Can you tell us a little bit more about that and what things people might have to look forward to in terms of the side effects of radiation, how long it is and so on?

Certainly so again, we’re very blessed in this modern times that this radiation treatment can be very seamless and incorporated to one schedule in a way that causes minimal disruption. I usually tell patients that it’s around 30 minutes door to door and that you could fit it in during your lunch hour. Or you could go before work, or you could drop by after work. It lasts about four to six weeks depending on the plan that the radiation oncologist maps out for you, and they basically radiate the chest.
wall of the side of the tumor. So we call it whole breast radiation therapy.

Most common side effects include during the time of the radiation, patients generally feel some level of fatigue, but most patients actually could work through it. They work full time and they do note that fatigue, but it’s not limiting. The fatigue goes away once the radiation stops. The other most common side effect would include changes to the skin and texture of the breast. This includes a darkening of the skin like you had a deep tan and also, the breast tissue could get more firm and slightly more contracted. Sometimes patients consider that a positive because it’s a more firm feeling which some people like. So it sounds like there are lots of options for breast cancer. We’re going to learn a little bit more right after we take a short break for a medical minute. Please stay tuned.

Support for Yale Cancer Answers comes
The beyond pink campaign aims to empower metastatic breast cancer patients and their loved ones to learn more about their diagnosis and making decisions. Learn more at lifebeyondpink.com.

This is a medical minute about survivorship. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience for cancer survivors. The return to normal activities and relationships can be difficult and some survivors face long term side effects resulting from their treatment, including heart problems, osteoporosis, fertility issues, an increased risk of 2nd cancers. Resources are available to help keep cancer survivors well and focused on healthy living. More information is available at yalecancercenter.org.

You’re listening to Connecticut public radio. Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Tristen Park. We’re talking about the role of surgery in breast cancer and right before the break we talked about many surgical options varying from breast
conserving surgery which we can do for even non palpable tumors all the way up to mastectomies that we can do with immediate reconstruction. And we talked a little bit about radiation, which is one of the ancillary adjuvant therapies that we use after breast conserving surgery that allows outcomes to be equivalent to that of a mastectomy, but one of the questions that people often ask is do I need chemo? Can you talk a little bit about who needs chemotherapy and who doesn’t in terms of breast cancer? Certainly. Chemotherapy is the systemic kind of treatment for breast cancer, and generally in patients that have larger, tumors or tumors that are higher grade, meaning at the cellular level that the cancer cells are more active, or if they have evidence that the disease has spread to either the lymph nodes or to other organs, chemotherapy is then recommended. And on this show, we’ve talked a lot about different kinds of chemotherapy, but before we get to that, you did mention before
The break that many of these cancers are what you called a favorable subtype, and you mention things like estrogen receptor. Tell us how those things impact whether a patient will need chemotherapy or not.

Breast cancer subtypes are dependent on the expression of three different receptors that were molecules found on top of the cancer cell that includes estrogen receptor, progesterone receptor and a 3rd receptor called HER-2 Neu. Depending on your combination of receptor expression that determines the blueprint of your cancer and there are certain combinations where we have specific or so-called targeted therapies available. If your estrogen receptor positive, you could have treatment that blocks estrogen receptor in the form of systemic undercurrent therapy. If you’re HER 2 Neu positive, you could have targeted therapy in the form of Herceptin. And if you were negative for all three, generally chemotherapy.

And some evidence that immune based therapies, or therapies...
that target the immune system can provide benefit. I want to get to the immune therapy, because certainly that’s a hot topic, but just before we go there tell us a little bit about endocrine therapy. Is this really chemotherapy? I mean, should people be afraid that they’re going to lose their hair or those kinds of things? It’s not the same as chemotherapy, but it is systemic therapy, meaning that it will affect you from head to toe so any cancer cells that are floating in your body could be sufficiently targeted. But it definitely will not cause hair loss. It mainly blocks the estrogen receptor through multiple mechanisms. Then there’s different families of estrogen blocking modalities, generally it will not cause hair loss, and it’s a pill that you take like a vitamin, for instance, and generally it’s given from 5 to 10 years and it could result in the risk reduction of cancer.
0:19:27.289 –> 0:19:29.799 recurrence or the emergence of
0:19:29.8 –> 0:19:31.528 new estrogen receptor positive
0:19:31.528 –> 0:19:33.256 cancers on either breast.
0:19:33.26 –> 0:19:34.98 It sounds like
0:19:34.98 –> 0:19:38.004 for many people, especially if they have
0:19:38.004 –> 0:19:40.22 an estrogen receptor, positive cancer
0:19:40.22 –> 0:19:43.44 endocrine therapy with a little pill that
0:19:43.44 –> 0:19:46.644 you take once a day might be sufficient,
0:19:46.65 –> 0:19:48.71 but for some patients,
0:19:48.71 –> 0:19:51.285 particularly those who have larger
0:19:51.285 –> 0:19:53.704 cancers or who are lymph node
0:19:53.704 –> 0:19:56.403 positive or who may have a genomic
0:19:56.403 –> 0:19:59.175 profile that is a little bit worse,
0:19:59.18 –> 0:20:00.8 chemotherapy might be
0:20:00.8 –> 0:20:02.42 something that’s indicated.
0:20:02.92 –> 0:20:05.377 Yes, it will definitely be indicated in
0:20:05.377 –> 0:20:08.183 those types of patients and then after
0:20:08.183 –> 0:20:10.715 their course of chemotherapy is finished,
0:20:10.72 –> 0:20:13.352 they have the added benefit of having
0:20:13.352 –> 0:20:15.739 this additional treatment of the endocrine
0:20:15.739 –> 0:20:18.127 therapy that could provide further benefit
0:20:18.13 –> 0:20:21.25 in the last five to 10 years,
0:20:21.25 –> 0:20:24.37 as long as they take the pill.
0:20:24.37 –> 0:20:26.2 So something really to think
0:20:26.2 –> 0:20:28.03 about now are the side effects
0:20:28.099 –> 0:20:29.827 of that endocrine therapy.
0:20:29.83 –> 0:20:31.885 You mentioned that it doesn’t
0:20:31.885 –> 0:20:33.94 make your hair fall out.
0:20:33.94 –> 0:20:36.898 Does it have other side effects
0:20:36.9 –> 0:20:40.352 that people should be aware of?
0:20:40.352 –> 0:20:43.796 Yes, it could cause some symptoms of menopause,
Including hot flashes and fatigue.

Other common things include musculoskeletal pain, joint pain, and muscle aches, and then there’s very rare side effects which include clots in your lower extremities or in your lungs, and rare cancers, but those are quite rare and actually the risk benefit ratio for the average patient is to the point where we generally, if they could take the endocrine therapy, it’s a plus to take it.

OK, now getting into the chemotherapy and you mentioned that in some of these cancers, particularly those where the estrogen receptor is negative, so they can’t take endocrine therapy, they can’t take HER 2 directed therapy because, let’s say their HER 2 is negative, the chemotherapy might be of benefit because there is no other targeted therapy for these patients, and you mentioned specifically and you mentioned specifically immunotherapy.

Now I know that that’s something that you’re working on in your lab. Can you tell us a little bit more about these so-called
triple negative breast cancers?
The implications of that subtype, how they’re managed?
So triple negative breast cancers are considered the most poor prognosis.
An aggressive subtype of cancer. It’s negative for all three receptors.
There’s a possibility of treatment options for them.
As you know they’re not eligible for the estrogen or the HER 2 based targeted treatments,
since they’re not expressing those receptors.
And the interesting thing, though,
is that they happen to in multiple preclinical studies,
these tumors have shown to generate more mutations.
They’re called somatic mutations, the mutations are
only found in the actual cancer cells.
So they have a higher level of what we call mutational load,
and generally that’s correlated with more response to immune therapy.
The more mutations you have on your non normal cells,
the more likely your immune system could detect them or kind of seek them out and kill these cancer cells that have all these targets
that are not self and portraying themselves to yourself. So how come then your normal immune system given the mutational load of these cancers, doesn’t seek them out and get rid of them by itself?

There are multiple schools of thought for the reasons why cancer cells evade the immune system. So this includes the cancer cells could evolve ways to hide themselves from the immune system.

Overexpressing kind of inhibitory markers that blunt the immune system or makes the immune system weaker in that particular location. That’s the main one.

Are there therapies that have tried to unhide the cancer or make the immune system stronger against these particular cancers?

Tell us more about the immunotherapy. The Nobel Prize for cancer has been awarded recently to this concept called checkpoint inhibitors, so the checkpoint, the immune checkpoints are natural breaks that people have as well as the
cancer cells have kind of manipulated to make the immune system blunted, so normally if one of your immune cells recognizes let’s say a foreign antigen like the flu or something and it generates a response you want it generate enough of a response that it clears that problem, but you don’t want it to go crazy because then it could harm your normal tissues. And that’s actually the opposite side of that spectrum called autoimmune disease, so these immune checkpoints occur in nature and are also kind of taken advantage of by the cancer cells. So one way to selectively strengthen the immune system or make the cancers more visible include something called checkpoint inhibitors, which basically takes the brakes off these immune cells and makes the immune cells more prone to detecting the cancer cell that’s non self. And have there been studies looking at these immunotherapies and triple negative breast cancer? Does this concept really work? And the second part of that question is
if you take the brakes off the immune system and the brakes were put there so that you don’t go nuts as you said and get kind of autoimmune conditions do we find that in patients who are taking these immune therapies that they get these symptoms of autoimmune disease? Certainly.

In the past one year actually, the FDA has approved the first immune based therapy for triple negative breast cancer in the metastatic setting, meaning the patient has widespread disease outside of the breast and lymph nodes. This drug is called Atezolizumab, and it targets PDL1, which is one of these checkpoint markers. It’s shown benefit for overall survival in a specific cohort of triple negative breast cancer cells that express high levels of the PDL1 so that’s been an exciting milestone and also as a surgeon I’ve been eagerly following the use of these checkpoint inhibitors in the neoadjuvant setting, meaning we give the therapy prior to surgery and hopefully that will make the tumor shrink. Sometimes it makes it shrink to the point where it’s completely gone,
and by the time we take it out, the tumor has completely disappeared and results are something called a pathological complete response. So the latest trial that’s coming to my head is the Keynote-522 trial that was discuss at ESMO this past year and that had shown that when you add one of these checkpoint drugs called pembrolizumab with the traditional neoadjuvant chemotherapy setting, that this could increase or improve the complete response rate, meaning the cancer is completely obliterated and there’s no evidence of it. When we remove it from the patient, sometimes up to 70% in certain cohorts of patients that have expressed high levels of PD-L1, but in general it improves this surrogate of pathological complete response by almost 15 points, which is definitely very encouraging. So that sounds really exciting. But what about the side effects? I mean, do people get autoimmune conditions? Are those long lasting?
Is there a way to put on the brakes after you’ve taken the brakes off? Well, certainly with every new tool comes the negatives, so there are autoimmune side effect profiles seen with the use of these drugs. But in breast cancer, I think we’re fortunate in this Keynote-522 trial that the side effect profile or the autoimmune profiles was rather mild than in other disease processes. Other cancers that utilizes checkpoint inhibitors there could be more severe autoimmune effects, including pneumonitis. For colitis, requiring interventions and hospitalizations, but in the breast cancer setting, the most common side effects seen that’s autoimmune related is an affect on your thyroid gland, which can be alleviated in an outpatient setting with supplemental thyroid medication. But the more severe toxicity profile seen in other cancer types, including melanoma, that’s the most famous one, actually are not seen as much. That being said,
there are the occasional and quite rare severe side effects that sometimes could even cause death, so we have to be careful, cautiously optimistic with the use of these breakthrough drugs. Doctor Tristen Park is an assistant professor of surgical oncology at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at Yalecancercenter.org. We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut public radio.