Ruth Adewuya, MD (host):

Welcome to Stanford Medcast, the podcast from Stanford CME that brings you the latest insights from the world's leading physicians and scientists. If you're joining us for the first time, be sure to subscribe on Apple Podcasts, Amazon Music, Spotify, or YouTube to stay updated with our newest episodes. I am your host, Dr. Ruth Adewuya. Dr. Jean Bao is a fellowship-trained breast surgeon and a clinical assistant professor of surgery at Stanford University School of Medicine. After earning her MD from the University of Chicago Pritzker School of Medicine, she completed her residency at the University of Texas Southwestern Medical Center and a fellowship in breast surgical oncology at Cedar Sinai Medical Center.

As a clinician, Dr. Bao is particularly interested in the management of breast cancer in older female, male and high-risk patients through procedures including skin and nipple sparing mastectomies, partial mastectomies, oncoplastic surgeries, and more. Dr. Bao additionally has strong research interest in lymph node staging for breast cancer, intraoperative 3D specimen imaging, localization techniques for non-poppable breast lesions, prophylactic mastectomy, and fertility issues in young women with breast cancer. Thank you so much for joining us today.

Jean Bao, MD (guest speaker):

Thank you, Dr. Adewuya, for inviting me on this podcast. I'm very honored to be here.

Ruth Adewuya, MD (host):

I'm really excited to dive into this very important topic of breast cancer, especially in light of October being breast cancer awareness month. But let's start with learning more about you. Could you share a little bit about your journey into breast surgical oncology? What drew you to specialize in this field and what aspects of your work do you find most fulfilling?

Jean Bao, MD (guest speaker):

Actually interesting that I went into medical school thinking I would be a pediatrician and I chose to do my surgery rotation first to get it out of the way. But I ended up loving surgery. I loved anatomy, I loved operating, I loved fixing problems with my hands. And as a breast surgeon, I really enjoy educating patients about their disease, cancer or benign and guiding the cancer patients through the cancer treatment journey. And I think as a cancer surgeon to be allowed to operate on someone, especially on a body part that really defines the female gender and to be able to tell them later on that you're cancer free. I just find that extremely humbling and that experience really rewarding.

And I also really cherish the long-term relationship that I develop with all of my patients and to hear their stories post-treatment, like getting more grandchildren or getting married or having children for the first time. And lastly, breast oncology is a very unique combination of clinical care and research in a multidisciplinary manner. A lot of what we do is so evidence-based and there are always new clinical trials, new research findings that end up becoming the new standard of care. I think that really sets it apart from other surgical specialties and make this feel really exciting.

Ruth Adewuya, MD (host):

That's an interesting path to where you are. You bring up some really important points around the field and the different aspects that are involved in surgical oncology and how you're really able to harness all of these different parts of being a clinician. And you practice that every day, and I'm sure in our conversation will unpack all of these pieces and how it shows up as you care for these patients. What are some of the most prevalent misconceptions about breast cancer that you encounter in clinical practice?

Jean Bao, MD (guest speaker):

The first things that come to mind are misconceptions around mammography, which is the cornerstone of breast cancer screening and early detection. Many people think mammography causes cancer, which is not true. The amount of radiation from a screening mammogram is very low, the same as being outside for eight weeks. Another mammography misconception is that people with breast implants cannot get mammograms, and that's also not true. It's extremely rare that mammograms cause implant rupture or cause problems around the implant. And mammography, if done correctly, should not cause any problems to the implant.

I think a common misconception around breast cancer is that it can only happen to women with a family history of breast cancer in older women or those who are unhealthy, but breast cancer can happen to anyone. It can happen to young women, it can happen to men as well. Many breast cancer patients don't have any major medical problems and carry a healthy lifestyle and don't have a family history. In fact, a very small proportion, five to 10% of all breast cancers are linked to a genetic mutation. So the rest is caused by a variety of factors that we don't completely understand. So I think if someone feels a breast lump in themselves, whether they're female or male, they should bring that to their doctor's attention.

Ruth Adewuya, MD (host):

What is the clinical decision-making process for managing benign masses and in what scenarios might surgical removal be warranted?

Jean Bao, MD (guest speaker):

Management of benign breast lesions can sometimes be less straightforward than cancer management because we don't always have clear guidelines. In general, if a benign lesion is thought to be discordant from imaging, meaning the benign pathology does not necessarily explain the suspicious imaging finding or if the benign lesion contains abnormal or atypical cells on pathology, surgical excision is usually considered to rule out any underlying cancer. Other indications for excision of benign lesions may be fast growth of a benign lesion, or if there are clinical symptoms like bloody nipple discharge in a setting of a papilloma or something. I also look at their age and family history. So older age and strong family history may sway me towards excising, probably benign or a high-risk lesion.

Ruth Adewuya, MD (host):

What defines high risk?

Jean Bao, MD (guest speaker):

High-risk patients are patients at a higher risk or an elevated risk of developing breast cancer due to a variety of reasons, family history or abnormal biopsy or having a genetic mutation. So an average woman has about 10 to 12% chance of getting breast cancer in their lifetime. A high risk is usually defined as more than 20%, but to put that number in perspective, on the other end of the spectrum, BRCA1 mutation carrier has up to 60 to 70% chance of getting breast cancer in their lifetime. So I see a lot of women in my clinic wanting to discuss breast cancer risk and what kind of imaging they may need for screening. So the first thing I do is actually to calculate their risk. And even though someone may have a strong family history or they think they may be high risk, but maybe the calculator will say that their risk is rather average.

So there are different calculators on the internet and different risk models. With the Gail model and the Tyrer-Cuzick model being the common list that I use and they're available on the internet, I encourage people and providers to play around with them on their own or when they're seeing patients, they can just pull it up and do it while they're seeing the patient. Now, a lot of women who have a strong family history or abnormal biopsy showing things like atypical hyperplasia may have a risk in that low 20s to 30% range for the lifetime risk.

Ruth Adewuya, MD (host):

That's very helpful. And so how has the approach to diagnosing breast cancer evolved, especially when we're talking about high risk patients? What are some imaging modalities that are available or are now available to improve cancer detection?

Jean Bao, MD (guest speaker):

When the lifetime risk exceeds 20%, I usually will discuss breast imaging in addition to mammography. So usually that's in the form of breast MRI. So breast MRI is the most sensitive breast imaging, meaning it hardly ever misses a cancer. So it's highly sensitive and it does not have radiation and the gadolinium contrast is overall very safe, but it can give false positives, which is a potential downside, and that's why we don't use it on a general population, not to mention the cost and the time for the test. But for people who are at high risk or elevated risk will need more vigilant screening and then MRI can be very helpful as they can detect more cancers than regular mammogram. Now another imaging modality is automated whole breast ultrasound. It's offered in Palo Alto and at the Stanford Cancer Center in Pleasanton in the East Bay. It's not invasive, it's just an ultrasound scanning both breasts, much quicker than MRI, can be helpful for women with dense breast tissue, but who don't quite meet the risk level for MRIs, but they still want some additional screening.

But like MRI, can have the false positives as well. Generally the more we look, the more we may find and not everything we see is going to be a cancer. Now the newest kid on the block is contrast enhanced mammography, which uses iodinated IV contrast with a standard mammogram, and that's offered in Palo Alto. Contrast enhanced mammo has better cancer detection than regular mammography, actually maybe similar to an MRI, but with fewer false positives. So I would use contrast enhanced mammography on high risk patients who cannot get or do not want MRIs, or maybe those women with dense breast tissue who want additional screening.

So it's faster than an MRI and patients with metal implants can get mammography and can get contrast enhanced mammo. The radiation dose is a little higher than regular mammography, and some people may have allergic reaction to the contrast that's used. So we're still learning a lot about contrast enhanced mammography. We're studying contrast enhanced mammo, comparing to contrast breast MRI to learn more about how it could characterize cancer cases, but it's a very promising tool in cancer detection in the screening setting as well as in disease characterization in cancer patients.

Ruth Adewuya, MD (host):

I think this is really exciting and to hear that there are these tools that are being developed to expand what is in the toolkit of oncology to be able to detect these things. There are a couple of things that I wanted to clarify that I heard. A couple of times you talked about the term dense breast tissue. Can you elaborate on what you mean by that?

Jean Bao, MD (guest speaker):

Yeah, that's a common topic of discussion in my clinic as well. Half of the women in the US have dense breast tissue. So when you do a mammogram, one of the things that radiologists look at is breast density. So there's four categories of breast density A, B, C, and D, so ranging from very fatty to extremely dense. The significance of density is that the denser the breast tissue, the more difficult it may be to detect a small mass on mammography because it can be obscured by the dense breast tissue. So hence the different supplemental breast imaging that we have to allow better detection of cancer in dense breast tissue. At baseline, many facilities are doing breast mammography with tomosynthesis. So pretty much all the Stanford mammography centers use tomosynthesis, which is 3-D mammography, and that's been shown to be more effective in cancer detection in dense breast tissue as compared to a regular 2-D mammography.

Ruth Adewuya, MD (host):

That's a great lead up to my next question. You talked about new technology that is available in our institution, and I'm curious about what data you might be aware of on a national scale in terms of access to these types of imaging techniques.

Jean Bao, MD (guest speaker):

I think more and more mammography centers are using the 3-D, mammography, tomosynthesis. I don't know the proportion of centers that do by. I would like to think that the majority of mammography centers are utilizing tomosynthesis now. MRI and ultrasounds are also fairly common, although an automated whole breast ultrasound, which Stanford has, is not as common as a handheld targeted ultrasound. Now, contrast-enhanced mammo is new, and I think that is something that many places are still studying and learning more about, but I think it will definitely see a lot more of that in the future.

Ruth Adewuya, MD (host):

That's really exciting that there are these innovations that are happening. Now we're talking about the diagnosis and we talked about all of these imaging modalities that are available. I want to pivot to management and to talk about generally the management of high-risk patients and what is happening in this space now and how has that evolved?

Jean Bao, MD (guest speaker):

Management of high-risk patients usually includes some form of regular breast imaging, so at the least annual mammography, and then we can add MRI or ultrasound or even replace the mammo with contrast-enhanced mammo, and we can sometimes consider hormone therapy for risk reduction. So hormone therapy would be something like tamoxifen to reduce the risk of a future cancer in either breast. And there has been an Italian trial that supports the use of baby-dose tamoxifen in the risk reduction setting and even in the treatment of DCIS and has been shown to be effective in reducing a future cancer risk as compared to a placebo. So we're really starting to use the baby-dose tamoxifen more and more now with a minimal side effect. And prophylactic mastectomy, so removing both breasts can be considered for some people, especially the very high-risk patients, and usually those are the mutation carriers. So I don't usually recommend that for in most elevated-risk patients.

Ruth Adewuya, MD (host):

We're talking about advancements that have happened in breast cancer surgery, but I do want to pick your brain a little bit more around surgery specifically because we've had some celebrities that have been in the news over the years identifying that they've had the BRCA gene or perhaps someone that they love has had the BRCA gene and they have proactively decided to have a double mastectomy. And that idea has sort of gone mainstream in some ways, and obviously we don't know their personal and medical history to evaluate whether that was right for them or not, but I think it has perhaps given people the impression that a double mastectomy is protective. Can you talk more about that?

Jean Bao, MD (guest speaker):

Another misconception about breast cancer I see frequently, that a double mastectomy, which is removing both breasts, it's better than lumpectomy or breast-conserving surgery. It's been proven over and over again in many, many clinical trials that lumpectomy is oncologically equivalent as a mastectomy and a double mastectomy really does not guarantee no recurrency. There is a lot of media attention on double mastectomies, and the Angelina Jolie's effect has been well studied. And it's interesting, after Angelina Jolie got her double mastectomy, revealed that she's a BRCA mutation carrier, she did the double mastectomy for preventative purposes, so she actually did not have breast cancer, and we can see that the

rates of double mastectomy after she increased, after she revealed that about herself, she brought up two separate points. One is a healthy patient with a genetic mutation, and then another scenario is a cancer patient trying to decide between saving the breast, doing a breast-conserving surgery versus doing a mastectomy to remove the cancer.

So let's take a look at that second scenario. First, in a cancer patient, there have been many randomized clinical trials studying lumpectomy versus mastectomy showing no difference in survival. And that's basically shown over and over again in many, many studies. In fact, if anything, I think people are happier after they get an lumpectomy if they get to keep their breasts and they're more satisfied with their body. And I think it's a little counterintuitive where you think, oh, double mastectomy or mastectomy by removing the whole breast should make you live longer. It should control the cancer better than just removing the lump itself. But I think our understanding of breast cancer has really come along when, this is where I think we know that tumor biology is really what drives cancer outcomes and not necessarily the extent of surgery. And we see that when it comes to axillary surgery, doing a big lymph node surgery does not improve survival compared to a small more selective surgery.

So that's again, that kind of de-escalation has been shown over and over again to not compromise cancer outcomes while actually maintaining or improving quality of life. But back to then healthy patient mutation carriers. So then the BRCA mutation carriers may benefit from a double mastectomy. There are some data suggesting there may be even a survival benefit to do a double mastectomy in young BRCA mutation carriers. They don't have to get a double mastectomy. If they choose to watch their breasts, that's perfectly reasonable as well. We can watch them very closely with mammography and MRIs. So if they ever develop a breast cancer, it can usually be detected at a very early stage at a very small size and can be treated very effectively at that time.

Ruth Adewuya, MD (host):

Thank you for clarifying that and highlighting the data that goes behind the decision-making between a double mastectomy and a lumpectomy. And I think what I heard from you is that this process is really one that should be driven by conversations between the patient and their clinician. Just one final question on this topic of prophylactic mastectomy. Can you share your thoughts on when this procedure would be appropriate or could be appropriate?

Jean Bao, MD (guest speaker):

I usually do not recommend removal of the healthy breast. I don't recommend a contralateral prophylactic mastectomy in the absence of a high-risk genetic mutation. There is no survival benefit to doing that, and the risk of a contralateral cancer in the other breast, in the healthy breast, is quite low, much lower than what most women think. Now with that being said, I have done many contralateral prophylactic mastectomies only after a thorough discussion about the pros and cons of the procedure. Now, many women want that peace of mind, and that's probably the most frequent reason for wanting contralateral mastectomy at the end of the day. And I think interestingly, very few actually regret that decision, especially if that thorough counseling is provided before surgery. Now in the setting of a high-risk genetic mutation like a BRCA mutation, PALB2, TP53, the discussion's a little bit different. And in fact, I'm taking care of a 27-year-old woman with a BRCA1 mutation who has a triple-negative breast cancer.

She's only 27. She was told by everyone she should get a double mastectomy. She does not have children, not yet married, and she's just not ready to part with her breasts. And so we discussed that she will be at a higher risk for developing a new cancer if she decides to save her breast. And we really went over the benefits and risks of every surgical option, and she ended up choosing to save her breast. And she actually thanked me for empowering her to make that decision and not making her feel guilty for keeping her breasts. So I think that's the power of counseling, our job is not to tell them that you have to get certain surgeries, although some cases maybe more of a mastectomy case or a lumpectomy case, but usually women have that choice. So I think our job is to really cancel patients and provide those options.

Ruth Adewuya, MD (host):

With the evolution of breast-conserving surgeries, can you discuss some of the impact of skin and nipple-sparing mastectomies and oncoplastic surgeries on patient outcomes in quality of life?

Jean Bao, MD (guest speaker):

We really have come a long way in our understanding of breast cancer and the treatment of breast cancer. Breast cancer patients are living longer, and the focus of a lot of current research is on improving quality of life, such as reducing lymphedema risk and optimizing cosmetic outcomes without compromising oncologic outcomes. We have proven lumpectomy or breast-conserving surgery as an equivalent to a mastectomy, and then now we have skin-sparing and nipple-sparing mastectomies, skin-sparing mastectomy saves the entire skin envelope except the nipple areolar complex and nipple-sparing saves the entire skin envelope, so including the nipple. So the cosmesis of nipple-sparing mastectomy is usually better just because the nipple is preserved. And usually these procedures are done with breast reconstruction at the same time, so with a plastic surgeon and may take multiple surgeries to achieve the final reconstruction, but sometimes patients can have an implant placed at this time of the nipple-sparing mastectomy, so they're done with a mastectomy and reconstruction in one surgery.

The cancer outcomes between nipple-sparing and skin-sparing mastectomies are the same as a simple mastectomy with no reconstruction, but patient satisfaction with their body is generally better, especially after nipple-sparing mastectomy. He mentioned oncoplastic surgery. Oncoplastic surgery is a very trending topic in breast surgery. Basically it refers to reconstruction of the lumpectomy defect to minimize the contour deficit. I do my own basic oncoplastic surgery for small lumpectomy defects by rearranging the tissue within the lumpectomy to fill in the cavity, but for patients with a larger cancer, hence a larger lumpectomy defect, or those who desire a breast reduction or a breast lift, I will do these cases with our plastic surgeon.

I actually do a lot of oncoplastic surgery, a lot of oncoplastic reconstruction with a plastic surgeon. Many patients with a large area of disease who otherwise may need a mastectomy may actually be good candidates for a large lumpectomy with oncoplastic reconstruction if the disease is relatively localized to one part of the breast. We definitely have also done some more extreme oncoplastic reconstruction for much larger cancers, spanning more than five centimeters, even more than 10 centimeters in women with very, very large breasts. And we've had very good, excellent cosmetic results, and we were able to achieve a clear negative surgical margin. There actually is a fairly recent study that showed that these large oncoplastic surgeries have fewer surgical complications compared to a mastectomy, fewer number of revisions and less pain. And that has been my own experience as well.

Ruth Adewuya, MD (host):

It's incredible because I think what you just said about less pain, I think ultimately it's better outcomes for the patient, which is ultimately what we're aiming for. The one thing that I think maybe an innovation or an evolution also in this space has to do, I believe, with nodal staging strategies for breast cancer that have also changed. Can you expound on that a little bit and what that impact has been?

Jean Bao, MD (guest speaker):

Yeah. Nodal staging has come a long way as well in parallel to the management of the breast itself for the breast cancer. It's remarkable, for nearly 100 years, we did the same axillary dissection where we removed most of the lymph node tissue from the armpit for breast cancer, and that has a lot of problems, especially arm swelling. But now sentinel node biopsy, which is selective removal of the gatekeeping of the axilla is the standard of care. Lymphoedema rates are well under 5% for sentinel node biopsy as compared to 20% or higher for axillary lymph node dissection. And in some women with small favorable cancers, especially in older patients, we're not even checking lymph nodes anymore. We work with

plastic surgeons to do the lymphovenous bypass or lympha surgery when we do an axillary dissection where they can reroute or reconnect with lymphatic channels to reduce the risk of lymphedema if we have to do an axillary dissection. So that's something that we're doing quite a bit as well.

Ruth Adewuya, MD (host):

Thank you for sharing that. It's exciting to see that even in that staging piece, that there's also been that evolution in the space. I want to make sure that before we end our conversation, that I talk also about another part that is important to you, your research interest around fertility issues in young women with breast cancer. Can you share a little bit of what you're doing in that space?

Jean Bao, MD (guest speaker):

Fertility counseling, I think, in my opinion, is underutilized for a variety of reasons, such as needing to start cancer treatment as soon as possible, so we don't want to delay that. Socioeconomic barriers, lack of awareness or education on the part of the patient and the provider, and maybe lack of timely access to fertility specialists. So the cancers that we see in young women are more likely to be high risk and more locally advanced in older women, so they're frequently treated with chemotherapy, which can impair fertility. And in many of these women also need to take tamoxifen for at least five to 10 years, which then delays childbearing. So a study I did at my previous institution showed that many young women have fertility concerns, but less than a third met with a fertility specialist, and even fewer actually underwent fertility preservation. So it's really important for us to discuss fertility risks and options and refer them to fertility specialists as early as possible to discuss fertility preservation strategies like freezing eggs or freezing embryos.

Traditional ovarian stimulation for egg harvesting can take a few weeks, and that sometimes could delay treatment initiation, but now we can do random start ovarian stimulation, so that can be done anytime during the menstrual cycle to avoid delaying chemotherapy initiation. We also have very exciting data on the safety of pausing tamoxifen temporarily to attempt pregnancy in young women via the POSITIVE trial. The follow-up in the study is still relatively short, but the data so far really further support the safety of pregnancy after breast cancer. And I think it's also unfortunate that many insurances do not cover fertility preservation for cancer patients, and the out-of-pocket cost is tens of thousands of dollars, and that's a big reason that many patients do not pursue this. So we definitely need better legislation in this regard, and I think we as cancer providers need to recognize the importance of fertility counseling and family planning.

Ruth Adewuya, MD (host):

What are some key takeaways that you have for clinicians who are in this space as they continue to care for patients and potentially for those who aspire to specialize in breast cancer care?

Jean Bao, MD (guest speaker):

Yeah. Well, to those who aspire to join us in breast cancer care, please come and join us. We need more passionate people and more inquisitive minds to advance breast cancer care. I think breast surgery is such a unique combination of surgery and long-term patient interaction mixed with research and education and patient advocacy. I find what I do is so, so rewarding. In terms of take-home messages, I think if we feel a lump or if the patient reports feeling a lump, get breast imaging, if they have a strong family history or any abnormal biopsy history, feel free to send them to a breast specialist like myself, or further risk assessment and counseling regarding future imaging. And I think double mastectomy in some ways is perhaps overutilized, but I think with appropriate counseling, I don't necessarily think it's a wrong procedure to do.

Ruth Adewuya, MD (host):

Such an excellent way to end the conversation. I think it's full circle to where we started. Dr. Bao, thank you so much for chatting with me today. It's been an excellent conversation.

Jean Bao, MD (guest speaker):

Thank you so much, Dr. Adewuya, for having me. It's a pleasure.

Ruth Adewuya, MD (host):

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