

Welcome to Yale Cancer Center Answers with your hosts doctors Anees Chagpar, Susan Higgins and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert on Myelodysplastic Syndromes. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. It is breast cancer awareness month and tonight you will hear a conversation with Dr. Donald Lannin. Dr. Lannin is Professor of Surgical Oncology at Yale School of Medicine. Here is Dr. Anees Chagpar.

Chagpar Don, you are one of the more senior surgeons, you have been around for a while. Tell us a little bit about how breast cancer screening and management has changed over your professional career.

Lannin It has changed tremendously. I finished my residency in 1982, so I have been doing this for 33 years and for at least 30 of those 33 years, I have participated in some kind of breast cancer awareness during the month of October, but I feel that in the past, especially the first 15 years, our message was primarily about awareness. We had the feeling at that time that people were not really aware of the risk of breast cancer and as a result, they presented rather late in the course of the disease and we were very optimistic that by increasing awareness, we could promote earlier detection and hopefully prevent some late-stage disease and the deaths from breast cancer.

Chagpar And did that work, it seems these days a lot of women know about breast cancer, in October everywhere you go, everything is pink?

Lannin Yes and I think it is time to change the idea of Breast Cancer Awareness Month a little bit. As you mentioned, most all women now are aware of it and if anything there is a myth about people overvaluing the merits of early detection, so early detection is still of some benefit; I am not saying screening and early detection are not of any benefit, but we realize now the benefit is pretty small and I think in breast cancer awareness we should now focus more on education, people should develop more of a realistic expectation for what early awareness and early detection can accomplish and realize that we really need to focus on understanding the biology and the treatment for the disease.

Chagpar You are opening a whole can of worms that I think a lot of our listeners have heard about in the past and actually causes quite a lot of public outcry.

3:07 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%201011%20YCC%20Answers%20-%20Dr%20Lannin_234872_5.mp3Lannin Yes.

Chagpar Let's talk first of all about screening. What are the standard recommendations for getting a mammogram? We have heard everything from every

women over the age of 40 should get a mammogram on an annual basis, and hearing things from the US Preventive Services Task Force that maybe women over the age of 75 might want to consider, and maybe women under the age of 40 or even 50 might not want to have a mammogram every year. Some countries say that you should get a mammogram once every two years. Tell us a little bit about what you tell patients and what the merits are or things that we need to consider when we are thinking about getting a mammogram.

Lannin I still think that getting a mammogram yearly is probably reasonable. The public has become accustomed to that and it is well accepted. I do not see a big reason to change it, although I do think getting it every two years is probably almost as good as getting it every year and I think it is an individual decision and certainly, women under 50 or over 75, the data is just not there that it is terribly beneficial and so I think people may or may not decide to get it.

Chagpar When we look at the randomized control trials, because there are randomized control trials that show that mammograms actually do have a benefit, the vast majority as you say, of the benefit, is in that 50-to 70-year-old group and many of the trials actually showed that the benefit was with every 2-year screening, so for those listeners who are wondering, where did all this controversy come from, that is where some of it came from, and I agree with you Don, we still recommend annual screening mammography over the age of 40, and I agree with you too that needs to be tailored a bit, especially when you are creeping up in age. I have patients who wonder whether if you are going to do something on the basis of that mammogram, then the mammogram is worth getting.

Lannin That is correct and I think we are becoming aware of the fact that over diagnosis of breast cancer is a real issue. It has been estimated that about 30% of all the breast cancers we treat probably would do fine if we never found them and treated them and that is a pretty big number, and that is a direct consequence of not only screening, but also generalized awareness and the fact that women now get biopsies for very limited indications and sometimes I think we almost are fishing for it, throwing out these needles looking for something and if we do that we are going to find some things that probably are not terribly significant.

Chagpar This whole concept of over diagnosis is a term that a lot of people, especially in our listening audience, may not understand. For a lot of people, a diagnosis is a diagnosis, what the heck is over diagnosis? Can you define that for us?

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Lannin It is important to realize the difference between over diagnosis and just false positive from screening. If a woman gets screened with mammography or physical exam or anything else, one of the risks has been known for many years

that they may have an abnormality and then you biopsy it and it is not a cancer. That is a false positive and women are pretty willing to accept a rate of false positive unnecessary biopsies, but over diagnosis is when you biopsy something that turns out to be a cancer, but it is actually cancer that would never progress and never bother the woman the rest of her life, but of course the difficult thing is, we do not know with certainty which of those are over diagnosed cancers, so almost all patients with breast cancer end up having surgery, radiation and some kind of drug therapy and in many cases, they would probably do just as well as if we had never found the cancer to begin with.

Chagpar As you point out, the real issue is that you do not know which is which, which are the cancers that you find early and, thank goodness, you did because that would progress and potentially have some really negative side effects and which are the ones that, if you left alone, they would do just fine. For a lot of patients who may be listening and their families, they all think, thank goodness, we caught that cancer early because we do not know if we would have been in the bucket where leaving a cancer there would have been just fine and many people may not like the idea of finding a cancer and saying, that is likely nothing.

Lannin I think one of the areas where we need a lot more research is understanding the molecular nature and factors that will give us that information about the true risk of cancer progressing and at this point, it is very difficult to tell a patient, well this is probably a cancer that will never bother you, we'll just leave it alone, patients would not be happy with that and I am not quite ready to tell patients that, but I think we still do not want to bury our heads to the problem, the problem still exists that we need to develop ways to identify which cancers will not progress and then hopefully not treat them and I think there is quite a bit of controversy about which cancers are in this group of over diagnosed cancers. Some people think that they are just TCIS, that is a noninvasive in-situ cancer, but my feeling is that actually they are most of the time small low-grade invasive cancers and certainly the grade I DCIS is over diagnosed. I think the real value in mammography is detecting the grade III DCIS before it becomes invasive and the main reason I would still not want women to give up mammography is because I think that it is a very important thing to remove the grade III DCIS before it become invasive.

Chagpar But maybe looking more closely at other kinds of cancers, especially the low-grade DCIS and maybe even some of the low-grade invasive cancers, to start understanding whether in fact they have any long-term implications if left in situ, is that what you are thinking?

9:53 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%201011%20YCC%20Answers%20-%20Dr%20Lannin_234872_5.mp3Lannin That is exactly what I am thinking. I think there are many of these low-grade cancers that we find just by accident with the screening that would not ever bother the patient in the next 20-30 years and somehow I think we have to be able to identify those and treat them much less aggressively.

Chagpar So kind of like prostate cancer when we talk about people who may not be happy to keep a cancer in situ, there are a lot of men out there who have prostate cancer who are following this wait and watch approach because a lot of their prostate cancers are pretty indolent.

Lannin That is exactly right, and I think breast cancer and prostate cancer have a lot of similarities and that certainly is one of them. I think we probably need to develop categories of women where we can do watchful waiting and from what I understand the results in prostate cancer are actually quite satisfactory with that approach.

Chagpar Do you know of any studies or any tests that are either in research or in development that are looking at that? Maybe genomic markers that can give us a clue, is this something that we are going to see come to clinical trials in the next few years or is this kind of just an idea that is percolating around in academicians minds?

Lannin Both, there are starting to be trials for grade I DCIS and that is certainly a place to start, but as I mentioned, I think the problem goes beyond that, I think it is the low grade invasive cancers as well and I am not aware of any trials at this point testing the watch and wait philosophy for those, but I think they will need to be developed over the next several years.

Chagpar Let's shift gears a little bit as we talk about over diagnosis to other screening modalities. When we talk about MRI, a lot of women, especially historically, were really interested in pursuing MRI as a sensitive test to find cancers early. How do you feel about that? It seems to me that some MRIs may find results like you were saying, with fine needles out there and catching fish that you may not want to catch?

Lannin That is exactly right. We went through a phase 10 years ago where we thought the key was to have more sensitive detection, so that we could catch cancers earlier and MRI was certainly a very promising modality for that, so about 5-7 years ago, we used MRI quite extensively and what we found is it really did not seem to make that much difference, and so now we actually use a lot less MRI than we did just a few years ago for that reason.

Chagpar When should patients get an MRI? Should anybody get an MRI or are these tests just too sensitive?

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Lannin That has to be an individual choice and there are some women whose breasts are so dense on mammogram and they have a cancer that you can evaluate the extent of better with an MRI, but I think that is a pretty small percent. Then there are women who have BRCA mutations that we know are at real high risk to get a cancer and so it has become pretty well established that if they are not going to undergo prophylactic mastectomy, that MRI is a reasonable way to monitor and screen these woman; however, I would caution

that there is no data that that is effective and it is probably at best similar to mammography where we might reduce the mortality from breast cancer about 20%, so I think it is a difficult question for a woman to weigh that compared to prophylactic mastectomy that reduces it to about 95%.

Chagpar Lots of controversy with regards to over diagnosis and are we screening too much, too little or just right. We are going to talk a lot more about this after we take a short break for a medical minute. Please stay tuned to learn more information about breast cancer with my guest, Dr. Donald Lannin.

Medical Minute This year over 200,000 Americans will be diagnosed with lung cancer. More than 85% of lung cancer diagnoses are related to smoking and quitting, even after decades of use, can significantly reduce your risk of developing lung cancer. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven to test innovative new treatments for lung cancer. Advances are being made by utilizing targeted therapies and immunotherapies. The BATTLE-2 Trial at Yale aims to learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Donald Lannin. Right before the break, we were talking about breast cancer and more specifically, we were talking about screening, this concept of over diagnosis that has been heard about in the media and whether we are doing too much, too little or just right and whether in fact some breast cancers may actually do just fine even if not treated. Don, I think one of the questions is going to be for women who may be particularly scared about a diagnosis of breast cancer and are thinking, jeez, I just do not want to get this treated, maybe, just maybe, this is something that is not going to hurt me, how do you feel about that? How would you advise women, do you think that they can wait and watch and not get treated thinking that there may be an over diagnosed case or do you think that we are too early to make that kind of call?

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Lannin I think that women need to see a very experienced treatment team to help with those sort of decisions. I would hate to belittle the effectiveness of treatment and talking on a radio show I certainly would not want to give the message to the vast majority of breast cancer patients not to worry about treatment because that would be the wrong message, but I think more and more, a sophisticated treatment team can come up with a better idea in which cases they are likely to be over diagnosed and which cases may do quite well without

at least aggressive treatment.

Chagpar I agree, I think that at this point for women who are diagnosed with breast cancer you really do want to get that treated with an experienced team to figure out what treatment therapies might be right for you and a lot of therapies actually are not very toxic and as we pointed out before the break, there may be really interesting clinical trials that are seeking to minimize therapy for those cancers that may be over diagnosed and always talking to your doctor about participation in clinical trials might be something worth thinking about. Let's move into therapies. What are the therapies that are available for women with breast cancers, especially early breast cancers today? Do you think there have been changes over the course of your professional career in terms of how we treat patients, are we doing more, are we doing less, should we be doing more, should we be doing less, or have we reached the sweet spot right now?

Lannin There has been tremendous change over the 33 years I have been doing breast surgery. When I trained, almost every patient was treated with a modified radical mastectomy and in the 80s and 90s a big movement was to go back to doing lumpectomy and more minimally invasive surgeries. Even then, however, axillary dissection was the standard way of removing the lymph nodes on every patient and then in the late 90s and early 2000s, sentinel node biopsy came along and we became much less aggressive in terms of removing nodes in the axillae and that is a trend that continues today and I think it is a good trend because that does reduce quite a bit of morbidity and the treatment seems to be just as effective without the axillary dissection in most cases.

Chagpar So we are doing less surgery, but what about other modes of therapy, are we doing less radiation, less chemotherapy, less hormonal therapy or are we compensating for the less surgery with more of other things?

Lannin To some extent I think we probably are, especially with radiation and in some cases I am not sure that is actually a good trend, I would not want to replace good surgery with bad surgery and radiation, so I do not think we want to depend on those other modalities instead of good surgery but the truth is we do have very effective drug therapy now for breast cancer and more and more we are getting very good targeted therapy that is biological in nature and many times much less toxic than we used to think of this as chemotherapy.19:32 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%201011%20YCC%20Answers%20-%20Dr%20Lannin_234872_5.mp3Chagpar Do you think that more patients are getting chemotherapy these days than in the past?

Lannin I think so, yes, and especially neoadjuvant chemotherapy. We give a lot of chemotherapy now before surgery and that is a trend that has gone up dramatically in the last 7 or 8 years and I think it has several advantages.

Chagpar Like what?

Lannin Well, one is you get an idea whether the chemotherapy is working, so that you can maybe avoid chemotherapy that is not as likely to work, but then

if it works, it gives you a lot of information about the prognosis of the patient and may allow other subsequent treatments and there are certainly trials of that going on.

Chagpar Yeah, we have seen a lot more patients being treated with systemic chemotherapy or targeted therapies, but in large part it is because we have a lot more effective therapies when we think about new biologic treatments that we have, patients do incredibly well with this and so you hate to deny patients really effective systemic therapy where you can offer it. What do you think about radiation therapy? Do you think we are doing more of that or less?

Lannin I think we are doing more and there are some categories of patients that I think probably would do well without radiation, but they are getting radiation just because no one wants to take a chance on not giving it, and I think there are some new biological tests coming along that may help us tailor radiation a little more specifically and that is going to be very important in the future.

Chagpar There is a clinical trial ongoing at Yale where we are looking at that and genomic signatures, particularly in patients with DCIS to determine whether those patients would benefit from radiation or not. I think it is interesting, the trend in radiation went from standard radiation to accelerated partial breast irradiation to hypofractionated irradiation to extended fields. Talk a little bit about that progression and how you see that trend which if you mapped it out kind of looks like the Rocky Mountains a bit.

Lannin It does, and my perspective after 33 years may be a little different because these things come around in circles, and we almost never used to give radiation after mastectomy and now that is very common actually and these things go around in circles.

Chagpar Coming back to surgery, you talked about doing less and less surgery going from modified radical mastectomies to lumpectomies and sentinel node biopsies, but the other trend that we have seen that it 22:53 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%201011%20YCC%20Answers%20-%20Dr%20Lannin_234872_5.mp3

is a bit like going around in circles again is more and more patients are opting for mastectomy and prophylactic mastectomy nationally, have you seen that trend?

Lannin Yes.

Chagpar What do you think about that?

Lannin That is absolutely a trend, we went in the 80s and 90s from less mastectomy and more lumpectomy to now in the 2000s, there seems to be a definite trend going back more to mastectomy, especially bilateral prophylactic mastectomy. There is probably a number of drivers for that, one is our imaging modalities are so sensitive, things like MRI pick up a lot of little abnormalities that make patients nervous.

Chagpar Is this one of those sequela of the over diagnosis that you were talking about?

Lannin That is part of it certainly. Another part of it is we are much better at genetic testing and finding women that are at high risk to get a second breast cancer and to the extent we can do that, I think the prophylactic mastectomy is very appropriate, but it is definitely a trend that women nowadays, especially young women, do not want to worry about breast cancer the rest of their life and rightly or wrongly they have the opinion that if they remove both breasts they do not have to worry.

Chagpar That is true, and I think the other thing that has happened is not only do they not need to worry, they generally do not need to have another mammogram or MRI which they may have been having every year or every six months, especially if they had a BRCA mutation and we actually have really good plastic surgery now and reconstructive techniques, which I think makes a difference for a lot of women.

Lannin That is completely true. I think one of the drivers is that reconstructions now are so good that it is not the mutilating procedure it was thought of 20 years ago.

Chagpar So are there particular populations of patients that you think are particularly at risk that in those patients, you really want to be very vigilant about screening, when we talk about disparities in terms of different racial groups or different ethnic groups, you talk a little bit about that.

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Lannin Yes, it is sort of two questions, one is the risk factors, high risk women, and there is this assumption that they would do better with screening, yet there is really no data that screening works better on high-risk women. It is more of a hope than anything else, but then there are other groups, in particularly African-American women, who have a triple whammy. They have everything against them in terms of breast cancer. If you look at African-American women, they have a much higher incidence of triple-negative cancers and of high grade.

Chagpar What is that? What is triple-negative, just for our listeners?

Lannin Triple-negative cancer is a cancer that lacks the estrogen receptor, progesterone receptor and HER-2 receptor and that simple signature correlates with a lot of other gene changes that make that cancer particularly fast growing and particularly aggressive. Now, African-American women, biologically, for reasons we do not understand, are at much higher risk for triple-negative cancers than most other racial ethnic groups, so that is the first whammy, then the second whammy is they tend to present with more advanced stage cancer and part of that is biologically it is more aggressive, so of course it is going to present later, but there are still some socioeconomic disadvantages that may inhibit at least some African-American women from getting access to care as quickly, so they

have bad cancers to begin with, they present with later-stage disease and then the third whammy that we are just learning and we actually have an article coming out in the next month or so that I cannot give the specifics on until it is published, but it looks like African-American women do not respond as well to chemotherapy and that is something that we really do not know why that is, but it seems true that they do not respond as well. I am hopeful that that is going to lead to a lot of new stimulus and a lot of new work to look at why that is and perhaps we need trials of specific drugs just in African-American women because they may respond to some other drugs better, we just do not know, but the drugs that are currently in use, they do not seem to respond to well.

Chagpar Don, that makes me think about African-American women in clinical trials, we know that there has been a sad history of African-Americans and clinical trials which I think has largely dissipated now that we have significant regulation with regards to the ethics of clinical trials but when African-Americans do not participate in clinical trials, by definition the drugs that get approved get approved on the basis of data of the patients who participate in those trials, who may be largely Caucasian, and so what you are telling me makes me think that maybe there are drugs that would be better suited to African-Americans that we just simply do not know about because we may be lacking African-American participation in clinical trials.

Lannin I think that is absolutely right and that is the big problem and we may need trials specifically for African-American women because you know having 12-15% African-American women in a trial may not be enough to tease out the different racial effects.

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Dr. Donald Lannin is Professor of Surgical Oncology at Yale School of Medicine. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written form at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.