

Yale CANCER
CENTER

answers

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Innovations in Breast Cancer Treatment: What's New in 2010?

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Welcome to Yale Cancer Center Answers with Dr. Francine Foss and Dr. Lynn Wilson. I am Bruce Barber. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous lymphomas. If you would like to join the conversation you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening Francine and Lynn are joined by Dr. Anees Chagpar. Dr. Chagpar is the Director of the Yale Breast Center at Smilow Cancer Hospital.

Foss Let us start off by talking a little bit about your interest in breast cancer and how you came into the field of breast cancer?

Chagpar I always wanted to be a doctor and very rapidly became interested in surgery, and within the field of surgery, breast cancer is unique. It is a fascinating area that involves a myriad of disciplines all working together, and for me that was something that was very compelling. I loved everything about breast cancer. I loved the patients, I loved the fact that we could really make a difference for these women, I loved the fact that we worked as a team, and I loved the fact that breast cancer research was moving at such a wild pace that every time you turned around something new was around the corner.

Wilson Anees, we were talking a little bit before the show about your background and some of the things that you have done in terms of your education and developing a specialized expertise, can you review some of that with us?

Chagpar I am Canadian. I was born and raised in Toronto. I did my undergraduate degree in biochemistry at the University of Alberta followed by my MD there and then I went to the University of Saskatchewan and did my general surgery residency and took some time to do my masters of surgery where I looked at microsatellite instability in breast cancer, so looking at molecular biology and how that effects prognosis for breast cancer patients. Then I was fortunate to go to MD Anderson and be their inaugural breast fellow and learned about multidisciplinary breast cancer care and that was fabulous, then I went to the University of Louisville where I have been for the last seven years. I also did a stint at Harvard doing a Masters in Public Health in clinical effectiveness there, then came back to Louisville, did Masters of Arts in bioethics and medical humanities. I really had a very broad educational background, but it has been a lot of fun and I think has really complimented my clinical background.

Foss You have a very unusual background for a breast cancer surgeon. It sounds to me like your research is probably multidisciplinary across all of these different areas.

Chagpar Yes that is true, I really enjoy, as we talked about in the beginning, collaborating across disciplines

3:13 into mp3 file <http://yalecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

and doing things that bring together multiple disciplines of diverse expertise. I think that really allows you to gain innovative insights into complex questions.

Foss Tell us about the problem of breast cancer in the United States today. We have all heard this number, 1 in 9 women. We have also seen that there has been a lot of progress in breast cancer. Tell us about the magnitude of the problem.

Chagpar Every year approximately 200,000 women in the United States are diagnosed with breast cancer. It is the number one malignancy affecting woman in this country and in fact, it is a global problem, but the nice thing about breast cancer is that we really have made strides. If you look at the incidences of breast cancer over the last five years it actually has decreased, to some extent because we have gained an understanding about the relationship between hormone replacement therapy and the incidence of breast cancer, which has affected women's behavior, but unfortunately part of that reduction in incidence was due to a reduction in mammography rates and we elucidated some of that by looking at national databases that found that this was a trend. Breast cancer continues to be an issue but we are making huge strides in terms of early detection, better treatments, and better prognosis for patients.

Wilson Could you share with us what types of women are at higher risk for breast cancer, is it younger women, older women, different types of race, what are some of the factors that might be concerning for increased risk?

Chagpar The two main risks of developing breast cancer are being a woman and getting older. While we often talk about breast cancer as a women's only disease, you have to remember that 1% of all breast cancers do occur in men. So, being a woman is big factor, also getting older is a big factor. The median age, or the average age for women to develop breast cancer, in this country is 67. It is not to say that young woman do not develop breast cancer, they do, and that is important to realize because when young women develop breast cancer, it is often very aggressive and is something that we really need to pay close attention to. We talked a little bit about hormone replacement therapy and we know that there is a huge relationship between both endogenous hormones, the hormones that your body makes, and exogenous hormones, hormones that you take, that increases your risk of breast cancer. There are certain genetic populations that have an increased risk of breast cancer, so we often think about BRCA1 and 2 gene mutation carriers, but there are a variety of genetic syndromes, P53 mutations, P10 mutations, and they can all increase your risk of developing breast cancer. Then there are benign breast disease problems that can also increase your risk. Things like atypia and lobular carcinoma in situ, increase your risk of developing breast cancer. So there are a myriad of risk factors that we're cognizant of.

6:27 into mp3 file <http://valecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

- Foss Now that we are aware of many of these new risk factors, have we changed our recommendations about screening? At what age should a woman start to get mammograms?
- Chagpar That is an interesting point, and as you know, over the last year or so the United States Preventive Services Task Force came out with new recommendations and that led to a flurry of media and recommendations. Truth be told, across academic institutions and across professional societies, the vast majority of us still recommend, for average risk women, starting having mammography at age 40 and having annual mammograms. The USPSTF did look at a number of epidemiologic studies and did have a number of models to try to tease out the benefit of mammography starting at age 40 versus at age 50, and to tease out whether we should be doing this annually or every two years, and when we should stop, but across the board currently the recommendations stand at annually starting at age 40.
- Wilson Speaking technically about mammography, that is a screening test that has been around for a pretty long time. Tell our listeners how that technology has changed, evolved, hopefully improved over the years.
- Chagpar One thing to remember is, although it is an old technology and it has been around for a long-long time, it still is one of the very best technologies we have for detecting breast cancer. So, while you often hear buzz about thermography and infrared imaging, which sounds very hot and cool and sexy, mammography still does a better job of picking up early breast cancers than many of these other techniques. Mammography itself has come a long way, in years past, we had what was called analog mammography, or conventional screen-film mammography, which has now transitioned more to the digital age and what this does is, it does not pick up more breast cancers necessarily, but it reduces the call back. It is a lot like taking a picture with a regular camera versus with a digital camera, you know how with a digital camera you can put it on your computer screen, you can adjust the brightness, you can adjust the contrast, and sometimes you can see things that you did not see otherwise. Whereas with a screen-film mammogram, just like with a film picture, you get what you get and so it really has helped to reduce the call back rate. There has also been implementation of new technology in the form of computer-aided detection, which helps us to find things that we might not have otherwise seen as well, but the best thing that goes with a good quality digital mammogram is a high quality radiologist, you just cannot beat that.
- Foss In terms of access for women, some of these new technologies that you just talked about, are they commonly available at most medical centers?
- Chagpar No, and you know what, I think that is probably a good thing because a lot of these have not had the evidence yet that we need to really embrace them. There are newer technologies, however, that are available at most medical centers, that do serve as a nice adjunct to mammography, such as

9:59 into mp3 file <http://valecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

ultrasound, MRI, these are things that your radiologist may recommend as complimentary to a standard mammogram.

- Wilson Once it's worked out at what age someone should begin screening with mammography, which I think is pretty well worked out, share with us some of your thoughts about self examination? Is that something that women should be thinking about or doing, or not doing, how regularly if you thinks it is a good idea?
- Chagpar That is another area that has a lot of controversy, as you know. There are some who say we should be doing monthly self-breast exams, others who say, well, that is really difficult because many women have lumpy bumpy breast tissue, fibrocystic change, and some worry about increasing anxiety in women, they are feeling their breasts every month and they feel a lump and O my gosh, could this be cancer? They wonder if we are doing these women a favor by advocating monthly self breast exam. The recommendations have gone back and forth on this and I think the standard is that we recommend monthly self-breast exams if you are comfortable with that, and if you feel anything abnormal you should talk to your doctor, but the purpose of self breast exam is to get comfortable with understanding your own body and what your breasts feel like.
- Foss Can you talk a little bit about some of these genetic syndromes that you mentioned that I think a lot of people are now familiar with and how that is really predictive of outcome and predictive of other cancers that patients are going to develop in a family syndrome, etc.? I think there are a lot of people out there that are scared off by genetics. Can you talk a little bit about the role of genetics and breast cancer and in screening?
- Chagpar The first thing that I will say right off the bat is that this really is a conversation, it is not a test. In recent years there has been a lot of direct-to-consumer marketing of genetic testing, which I think is a really bad idea because as we talked about, there is more than just one syndrome, there is more than just one test, and how you interpret those results can be all over the map. It is not a black and white answer, it is a complex thing, and so the first thing that I will say is that if you are concerned about your genetics, you are concerned about your family history, and you want to know more you should seek out a genetic counselor because that is a service that you should avail yourself of in terms of learning about genetics. In terms of genetic syndromes, as I said, they are all over the map. We think about BRCA1 and 2 as the only breast and ovarian cancer syndromes, but there are many. There are syndromes that are associated with P10 mutations and P53 mutations and these have different characteristics in terms of the family pedigree and what cancers can run in families, and so what I would say is that this is a conversation you need to have with your physician and get a referral to a genetic counselor to delve more into that.

13:19 into mp3 file <http://valecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

Wilson We are going to take a short break for a medial minute, please stay tuned to learn more information about the treatment of breast cancer with Dr. Anees Chagpar.

*Medical
Minute*

It is estimated that nearly 200,000 men in the US will be diagnosed with prostate cancer this year and over 2000 new cases will be diagnosed in Connecticut alone. One in six American men will develop prostate cancer in the course of his lifetime. Major advances in the detection and treatment of prostate cancer have dramatically decreased the number of men who die from this disease. Screening for prostate cancer can be performed quickly and easily in a physician's office using two simple tests, a physical exam and a blood test. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for prostate cancer. The da Vinci Robotic Surgical System is an option available for patients at Yale that uses three dimensional imaging to enable the surgeon to perform a prostatectomy without the needs for a large incision. This has been a medical minute and more information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Radio Network.

Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host Dr. Francine Foss. Today we are joined by Dr. Anees Chagpar and we are discussing treatment for breast cancer. Dr. Chagpar, give us your thoughts on how the treatment for breast cancer has changed over the last even five years, especially in surgery since you are a surgeon.

Chagpar The wonderful thing about breast cancer treatment in general, and surgery in particular, is that it is such a rapidly evolving field and we have made tremendous advances. I am going to take us back 30 years ago when women did not have many choices. You would go to your doctor often with locally advanced breast cancer and there was only one choice, it was called a radical mastectomy; the breast, the muscles, the lymph nodes, everything was removed. It was a very disfiguring procedure, but it did control the disease, and since that time, we have had huge clinical trials that have demonstrated that you do not need to do such radical surgery, that in fact, a radical mastectomy has equal survival to a simple mastectomy where you can leave the muscles, you can leave the lymph nodes, and survival is exactly the same. Then we discovered that we did not even need to do a mastectomy, you could simply remove the cancer, and the survival was exactly the same. Now, local regional recurrence with the chance of getting cancer back in the breast was higher if you remove just the cancer, but if you added radiation, then the local recurrence rates were also the same. So, survival was the same, local recurrence rates were the same, and now women have choices of do I want a mastectomy, do I want a lumpectomy, or partial mastectomy where just the cancer will be removed and radiation, and then even within those categories there are more choices. For example, with patients who have a mastectomy you do not have to go flat any more. Now we have options of skin sparing mastectomy, sometimes nipple sparing

16:46 into mp3 file <http://yalecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

mastectomy, and immediate reconstruction. That reconstruction can be done in many different ways. You can have autologous tissue, where you take tissue from your own body often from places where you have too much tissue to places where you would like to have a little less. So moving tissue from your belly, giving you a tummy tuck type procedure, or from the back, or using implants of any size that you want to have, to reconstruct the breast and give you a cosmetic outcome that you are happy with while also removing the cancer. For people who want to have a partial mastectomy or a lumpectomy, we now have ways of doing that that improves cosmetic outcomes. This whole concept of oncoplastic surgery, where we combine plastic surgery type techniques with oncologic procedures, we can remove a cancer and provide an optimal cosmetic outcome at the same time, this is really moving the field forward.

Wilson How do we evaluate the lymph node if we do the smaller operation with the lumpectomy? Talk to our listeners about how we evaluate the lymph node, do we need to do a big operation? Can we do a smaller one to evaluate that part of the situation?

Chagpar This whole mastectomy lumpectomy thing is just about how do we take care of the cancer that is in the breast? The lymph nodes are an entirely separate issue, and we can actually address the lymph nodes in a minimally invasive way whether we do a mastectomy or we do lumpectomy. It was around 1994 to 1996 that Armando Giuliano came up with this idea that we could use sentinel lymph node biopsy to evaluate the lymph nodes, and this is a technique where we can inject a radioactive tracer and/or a blue dye into the breast. That dye will follow a pathway much the same as cancer cells would take in the breast to the lymph nodes, so we can accurately identify which lymph nodes are most likely to harbor cancer because the dye took the same path that the cancer would have taken to those first lymph nodes. We can then take out those first lymph nodes, give that to our pathologist right in the operating room and find out if those lymph nodes have cancer or not. If the lymph nodes do not have cancer, we do not need to take out all of the lymph nodes under the arm giving us all kind of complications like lymphedema and so on because we know that does not improve survival, but if the cancer is in those lymph nodes, then we go and take out the remaining lymph nodes because we know that there is a chance that there may be other lymph nodes that are involved.

Foss Is the use of this sentinel node technology commonplace now in breast cancer surgery and management?

Chagpar Absolutely.

Foss As I understand, you have done a lot of national database work looking at the use of sentinel node biopsies, looking at the incidence of chest wall recurrences in women, could you talk a little bit

19:56 into mp3 file <http://valecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

about that whole concept of research and looking at these national databases and how that really helped us to move forward in the treatment of breast cancer?

Chagpar With regards to sentinel node biopsy, I came from Louisville, Kentucky which houses the world's largest database of sentinel node biopsy in women with breast cancer and we have done a national, in fact, international study, looking at women early on in the genesis of sentinel lymph node biopsy for breast cancer to evaluate this technique. That laid the foundation for a lot of us to make sentinel biopsy common place. But a lot of my work now has been looking at women who have a positive sentinel node. Lynn, you and I were talking a little bit about if a woman has a sentinel node that has cancer, we take out all of the remaining lymph nodes, but only a proportion of those women will have non-sentinel node metastases. In other words, will we have cancer in those remaining lymph nodes, well if they did not have any cancer in the remaining lymph nodes and we could know who had cancer in the remaining lymph nodes and who did not, then we could potentially spare those who did not, the dissection, and so how do you evaluate that and how do you predict that, because that is really how we can start to tailor therapy for individual women. I have done a lot of work trying to find clinical prediction models that can accurately tell us who will need that completion dissection and who won't, and I am currently working on building in molecular models into that concept to try to refine those models a little bit better.

Foss When you talk about molecular markers, could you tell our listeners exactly what that is?

Chagpar We have looked at this in a variety of different ways, molecular markers are essentially anything that you can look at that is in the tissue, that is a small molecule or a biomarker that can give you some information. One of the things that I was doing and have an NIH grant to do, is to look at mammaglobin and CK19. These are markers that are on epithelial breast cancer cells that we can find in lymph nodes, so when we take out that sentinel lymph node we can look for these markers, and we actually have an assay that will give us quantitative data, so it will tell us how many breast cancer cells with these markers are in this lymph node. So you can imagine that if you have lots of cells that have these markers, so lots of breast cancer cells in these sentinel lymph nodes, that there is a higher likelihood that the non-sentinel lymph nodes will be involved, whereas if you have few, then there is less of a likelihood, so building in that kind of modeling. Just a couple of days ago, I was talking to some of the researchers here at Yale about building in circulating tumor cell markers into that whole concept, and so it's trying to gather as much information as we can from the primary tumor and as much information as we can from the sentinel lymph node at the time of that decision point of whether or not we need to complete that axillary dissection. This is going to help us to tailor that therapy.

Wilson We have a variety of treatments for breast cancer, some of them you have already mentioned, surgery, radiation, hormonal therapy, and chemotherapy. Talk to us about the importance of

23:43 into mp3 file <http://yalecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

multidisciplinary management of a breast cancer patient and what that means and how you coordinate all of these various treatments for any given patient? It sounds very complicated.

Chagpar It is very complicated, but that is what makes it fun. One of the things that really enticed me into the whole field of breast cancer was this multidisciplinary approach. The fact is that you need that team, you need a breast cancer surgeon and a radiation oncologist, and a medical oncologist and an imager, and a pathologist, a plastic surgeon, a geneticist, and the psychologist and the social worker and a team of nurses, all working together as one concerted team for the patient because the truth of the matter is that every decision that is made has an influence on every other discipline. For example, if you are a patient who is having surgery, you may want to have reconstruction, so you need a plastic surgeon. Well the decision of whether or not you are going to need radiation may influence the plastic surgery treatment, and when the radiation occurs, will be influenced by whether or not you need chemotherapy, and that is going to be influenced by what the pathology looks like. The pathology has to be coordinated with the imaging to make sure it makes sense and then we have to treat the patient as a whole patient because this does not occur in a vacuum. So there is a whole psychosocial part that also plays in, and it really is a coordinated multidisciplinary team that gets together. Here at Yale, like in other centers, we are really focused on the patient. How do we organize this care? How do we put it all together? We all sit down every week at a conference and discuss every patient. How can we do the best for this patient? We have nurse coordinators that take patients through every step of the process so that everything is a well-oiled machine and it really is spectacular when a patient comes out and says, my gosh, this was very complicated but boy do I feel well taken care of by this team of experts, all of whom took care of me.

Foss It sounds to me like there is obviously a lot of work that goes into the initial treatment decisions, and as you mentioned, there are a lot of interdisciplinary approaches that are involved in that initial step. What happens to women as they move through their treatment, so after a year, the second year, the fifth year, ongoing hormonal therapy, ongoing monitoring, how does the multimodality approach impact the long-term management of breast cancer?

Chagpar There is a lot of activity in that initial period and as time goes on you do move into this more chronic survivorship mode, which is great because a lot of people are now beginning to see breast cancer as a chronic disease because we do have long-term survivors, which is fabulous for a cancer. One of the things that we have at Yale, which I think is really unique, is the survivorship program where patients are seen by a whole team of people who are dedicated to that whole aspect. What is the nutrition like? What about physical therapy? What about psychosocial needs? And then the medical aspect carries on as well, so that is an important aspect as you transition your care, but it should be a very seamless transition.

27:30 into mp3 file <http://yalecancercenter.org/podcast/oct0310-cancer-answers-chagpar.mp3>

Foss That moves into something that I would like to spend some time on, which is one of your interests recently, has been to get involved with this whole concept of mindfulness and impact of the mood on the immune system and the whole person on outcomes in breast cancer. Can you talk to us a little bit about that?

Chagpar When I came from Louisville, as we talked about before the show, I enjoyed having cross-disciplinary research interests and one of those was to team up with psychologists and immunologists to look at stress and its influence on breast cancer patients both from a global perspective, but also from a biochemical perspective, how does this affect your immune system standpoint. We have transitioned that into the whole mindfulness concept and so it is interesting, I just came back from a meeting with Judson Brewer who is a mindfulness expert here at Yale, who is going to help us look at mindfulness and outcomes in breast cancer patients and how that really does affect stress, how that affects the immune system, and how that affects clinical outcomes. It is incredibly exciting work that I think has real clinical impact.

Dr. Anees Chagpar is Director of the Yale Breast Center at Smilow Cancer Hospital. If you have questions or would like to share your comments, visit yalecancercenter.org where you can also subscribe to our pod cast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.