



*Hosts*

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Vice Chairman and Professor  
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## Breast Cancer Care in the United Kingdom

### Guest Experts:

**Anees Chagpar, MD**

*Director of the Breast Center at Smilow  
Cancer Hospital at Yale-New Haven*

**Mike Dixon, MD**

*Professor of Surgery and Clinical Director  
for the Breakthrough Research Unit at  
Western General Hospital in the UK*

**Yale Cancer Center Answers**

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. 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](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This week, Francine and Lynn welcome doctors Mike Dixon and Anees Chagpar. Dr. Dixon is Professor of Surgery and Clinical Director for the Breakthrough Research Unit at Western General Hospital in the UK, and Dr. Chagpar is Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. Here is Francine Foss.

Foss Dr. Dixon, let's start off by having you tell us a little bit about yourself and what your role is in your center.

Dixon I am a breast surgeon. I got interested in breast disease because I did some work in pathology, which is the investigation of how disease is developed. I became very interested in breast cancer and how breast cancer develops. I then trained as a general surgeon and then did breast surgery. I have been at Edinburgh for about 20 years. I head up the research unit in Edinburgh and I am a little bit unusual compared to the United States in that I do not only breast cancer surgery and removing the cancer, but I also do some plastic surgery and rebuilding surgeries in women who have to have slightly bigger operations and then I am able to rebuild the breasts. The system is a little bit different from the United States, although as in the United States, we work very closely with other teams of doctors including plastic surgeons.

Foss Can you tell us a little bit about your center? How many patients do you see? How many physicians work in the breast cancer unit?

Dixon The size of the center is remarkably similar to Smilow. We treat about 750 patients a year in our main center, but we have a little bit of a different arrangement in the whole of South East Scotland, and some smaller hospitals are covered by surgeons in our unit. We have about nine surgeons. All but a couple of those surgeons work in the main hospital and out in the smaller hospitals as well. We look after about 1,200 breast cancer patients in our region. The reason we have this set up is this way we make sure that wherever patients live, they get the same access to breast cancer care. All the surgery is delivered by specialty breast surgeons, which actually is very similar to the set up in Smilow.

Foss Anees, you are the head of the breast cancer unit here at Smilow Cancer Hospital. Can you talk a little bit about how many patients we see here and what our model is compared to Dr. Dixon's?

Anees They are actually very similar, as Mike said. As you know, Smilow has been growing by leaps and bounds, particularly over the last several years. We see anywhere between 600 to 700 patients

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a year and that is steadily increasing. We also, like Dr. Dixon's team, have a multidisciplinary approach. So we have breast imagers, we have surgeons who take out cancer, we work with the plastic surgeons for reconstruction, we have medical oncologists and radiation oncologists, psychologists, psychiatrists, social workers, nurses, and geneticists, and that multidisciplinary approach is very similar to the system in Edinburgh, I imagine.

Foss Can we talk a little bit about how a woman actually gets referred to your center? How does that happen here at Smilow and how does that happen in Edinburgh?

Dixon In Edinburgh, we have a little bit of a different set up. There are two main ways that patients get to us. One is that they have breast screening and are found on a routine mammogram to have an abnormality. They are then called back to the screening center where they have a biopsy, which then shows that they have a cancer or a precancerous change in their breast, and that would constitute about 40% of all the patients we see. The rest of the patients are referred by their primary care doctor because they go to their primary care doctor with a symptom. That symptom is most commonly a lump, but it can sometimes be pain, changes in the outline of the breast, discharge from the nipple, and occasionally a lump under their arm. So, there are a variety of symptoms which would make the primary care doctor concerned that this woman could have an abnormality in her breast and that she needs further assessment.

Foss So, there are patients that do not actually have cancer when they come to see you and they do not know they have cancer?

Dixon We have roughly about 9,000 patients a year who will come through with symptomatic problems, and very few of those women will actually have breast cancer. Patients come because they have breast pain, because they have breast infection. So, the important thing to realize for women out in the community who have a breast symptom is the majority of patients with breast symptoms do not have cancer, and that also includes the majority of women, particularly younger woman, who have a breast lump. There are many other causes of breast lumps other than cancer. What we do is investigate that breast lump. As Dr. Chagpar says, we will do mammography, ultrasound, breast x-rays and ultrasound, and if an abnormality is present, then we will do a needle test, send that needle test to the laboratory, and the laboratory will then tell us whether that is a benign lump, which is a straightforward lump that does not require any treatment, or if it's a breast cancer. The really important thing for people out there who have a breast symptom to realize is the majority of women who have a breast symptom or breast lump will not have cancer.

Foss Anees, can you talk about our center, I know that I have sent a number of patients to you, some on very short notice when we have noticed something that we were concerned about. Can you talk about the approach for such a patient in your clinic?

Chagpar Very similar to Mike's system, patients come to see us from a whole variety of venues. Some

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come from imaging where they have had a mammogram or an ultrasound or even an MRI that has found an abnormality and needs to be worked up with a biopsy or people who have had a biopsy that has been proven to be cancer; some people come with benign symptoms as well. We also have referrals from other cancer specialists, like yourself, and one of the things that I am very proud about at Smilow is that we can offer a lot of that therapy in a one-stop kind of system. So, as you know, some of the patients that we have shared come, see me, we will do an ultrasound right in the office. We will do a biopsy right in the office and help that patient get all of the care that they need under one roof, and I know that Mike's system works very much the same way.

Foss Mike, do you think that having a pathology background has helped you at all?

Dixon Yes, I think it has, and the reason why it has is that when you look under the microscope at breast cancers, you realize that there is a whole range of different patterns, and we talk about breast cancers as one disease. It is clearly not one disease, it is not two diseases; it may even be more than 100 diseases, but what it does make you aware of is that not all breast cancers are the same. I think that is something that we have learned over the years, that treatment needs to be individualized based on the patient's fitness and the type of cancer they have, and I think that is one of the biggest advances over the past 5 to 10 years, and even before that. I think that is based on our understanding of the fact that there are these different types of cancers, and they look different under the microscope, and if they look different, they behave differently, and if they behave differently, they need a different approach to treatment.

Foss Anees, just to touch on that point here, even though you are clinically a surgeon, you certainly have seen a lot of breast tumors under the microscope because of the combined modality approach. Could you talk a little bit about that and how that helps you as a clinician?

Chagpar One thing that all of our tumor boards here have in all of our disease sites at Smilow, and breast is no different, is a multidisciplinary tumor board. We review all of these breast cancer pathologies as a group. We get together all of the different disciplines to talk about each individual patient case, review their images, and review their pathology, and as Mike says, you get a sense of what's going on with that patient's tumor by looking at it that way, but also in that multidisciplinary context, you get a sense of each person as an individual, what is their social context, what is their imaging, what are their comorbidities, are there other medical problems that could influence their treatment? Getting back to what Mike was saying about personalizing therapy, as you know, Francine, that has been one of the pillars of Smilow, and it has really been about personalizing therapy and targeting management. Part of that is to understand that breast cancer is a spectrum and that there are multiple different diseases encompassed in that, and we are doing a lot of work in terms of really understanding the genomic basis of cancers, how those cancers look and act and behave at a molecular level, at a gene level. And as we continue to do research in the laboratory to understand these cancers, we are developing targeted therapies that can pinpoint agents that may

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in fact, help to inhibit pathways of particular tumors or inhibit particular genes that will make a difference to individual patients. So, bringing that into clinical trials and the networking between the clinicians who treat patients and the basic scientists in laboratory is something that is really important, and I think something we do really well here at Yale.

Foss Anees, all of that individualized profiling of the tumors must cost a lot of money, and I am wondering from the point of view of Dr. Dixon in the UK, what is your approach to looking molecularly at these tumors? Do you do it in all of your patients? Do you have the same approach that we have here at Smilow?

Dixon I think there is a common misconception that a socialized medicine system somehow offers a lesser quality of care.

Foss That is what we are here to dispel!

Dixon And I am here to dispel that. Smilow is amazingly impressive at how quickly they see patients because they see them all within a few days, but we have targets that are a few days longer, but we see the majority of outpatients within a few days of their primary care doctors, there are no delays for surgery. One of the things that we are probably better at I think than the US is that we are more interested in getting good value for money in our healthcare system. The reality is there are a lot of molecular tests you can do on breast cancers, but how many of them are a value and change your treatment. We are more selective on what tests we do, and we do the tests in patients where we think it will make a difference on what treatment they can get, but can our patients get the tests that are available? Generally, yes.

Foss Let's talk a little bit more about what the most important tests are after we come back from our break for a medical minute. Please stay tuned to learn more about breast cancer, both in the United States and the United Kingdom from doctors Chagpar and Dixon.

*Medical  
Minute*

*There are over 11 million cancer survivors in the US, and the number keeps growing. Completing treatment for cancer is a very exciting milestone but cancer and its treatment can be a life-changing experience. Following treatment, the return to normal activities and relationships may be difficult and cancer survivors may face other long-term side effects of cancer including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. Resources for cancer survivors are available at federally designated comprehensive cancer centers such as the one at Yale Cancer Center to keep cancer survivors well and focused on healthy living. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available at [yalecancercenter.org](http://yalecancercenter.org). You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.*

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Foss This is Dr. Francine Foss, and I am joined today by my guests Dr. Mike Dixon and Dr. Anees Chagpar, and we are discussing breast cancer on both sides of the Atlantic, at Smilow Cancer Hospital and at Edinburgh. We talked a little bit before the break about some of the important molecular tests that can be done on these breast cancer samples. Dr. Dixon, you mentioned that while there are a panoply of tests out there, there are only a few that are really important in terms of dictating your medical decisions. Could you talk a little bit about what those are?

Dixon The main tests help us predict whether patients will benefit from certain treatments. So, one common treatment used in breast cancer is hormone therapy, and breast cancers have on their surface receptors for the female hormone estrogen. So, we measure estrogen receptors as a routine, and if a cancer has estrogen receptors, then we know that that patient will benefit from hormone therapy. Another test is to measure something called HER2. HER2 is a growth factor. Growth factor means that if you stimulate that growth factor, it will cause the cancer to grow. There is a drug called Herceptin, which is directly targeted at that growth factor. If you give Herceptin to a cancer that has a lot of HER2 on the surface, then that cancer will die and the patient will respond to that treatment. So, HER2 testing is important. It is important to know how fast the cancer is growing because chemotherapy essentially is a drug, which works against growing cancers. What we do is we measure these, but we measure them with what is called immunohistochemistry. All that means is that we stain slides of the cancer for these tests. We tend not to do the molecular profile test that is widely used in United States called Oncotype DX. What Oncotype DX actually does is it very accurately measures estrogen receptor. Another hormone receptor is a progesterone receptor. The HER2 that I have talked about is the target for Herceptin, and how quickly the cancer is growing. It measures it very accurately, but that is probably all it really does, and if you are very good at measuring each of these individually, you can combine the individual tests to get something that is almost as good as Oncotype DX. The difference is that Oncotype DX is a few thousand dollars, and these other tests are relatively cheap.

Foss Anees, in the United States, do we use the Onco test and does insurance pay for that?

Chagpar Yes to both questions, but it is important as Mike says to really tailor your therapy, and to order tests that are going to change your management. Very much like the system in the UK, we will, as a matter of routine, stain tumors for estrogen receptor, progesterone receptor, and HER2, because those really can tell us how particular tumors will respond to individualized therapies. We will use Oncotype DX in a situation where patients may respond to chemotherapy, but they may respond equally well to hormonal therapy, and we are wondering whether we should offer chemotherapy or hormonal therapy alone. Sometimes that Oncotype DX test can help us to make those decisions. In addition, there is a clinical trial that is currently ongoing and is available here at Smilow, looking at patients whose cancers have spread to the lymph nodes. Oncotype DX had not previously been tested in this population and is now in clinical trials here at Smilow, and in a number of centers around the country looking at the value of Oncotype DX in that population, but I think the other thing to remember is that there is a lot that goes on outside of clinical practice

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routinely. The idea of potentially looking at newer genomic targets is something that is certainly of interest in terms of research and will help guide targeted therapies down the line. I know that that is an area of interest on both sides of the Atlantic, to really try and push the field forward figuring out what particular genomic targets might exist. They can help us to understand what therapies will help individual patients.

Foss On that issue of identifying those novel genomic targets, Mike, you had mentioned to me earlier that you have a large tissue bank that you have been very successful in collecting these tissues. Could you elaborate a little bit on that and on the importance of having a tissue bank?

Dixon The advantage of a tissue bank is that it allows you a series of samples, which you can then analyze and learn more about the disease. One of the specific aspects of the samples that we have collected is that we have samples from patients before they start a drug, during treatment with the drug, after a few weeks of the drug, and then after a few months of the drug. What that does is you then start to get an insight into how drugs like hormone therapy work, how the cancer shrinks, but more importantly, why cancers do not shrink, what happens in that cancer? What is it that actually makes the cancer grow? What changes occur in that cancer that are stopping it responding to the hormone drug? We start to get not only an ability to predict which patients are going to respond, but you start to be able to understand what you would need to do to that cancer to make it more responsive to that drug. These samples are absolutely important and essential to improve our understanding of how cancers respond to drugs and why sometimes they do not respond.

Foss One of the key aspects of your collection is the fact that you do have pre and post samples. My understanding in the United States is that for many of our clinical trials, we collect samples previous to starting therapy, but do not have a lot of samples on therapy. Anees, could you comment on that?

Chagpar Yeah, I think that has changed a lot as we have begun to understand how important it is to really look at response to therapy not only from a clinical vantage point but also from a biologic one looking at samples. Many of the patients who are on neoadjuvant trials -- so trials where patients get therapy prior to their surgery-- will have biopsies taken before they start treatment, during treatment, say after a few weeks, and then their surgical specimen after therapy to really give us that wealth of information.

Foss Mike, when you get your samples, at different time points are those actual biopsies or are they needle biopsies? What does the patient have to go through for you to get those samples?

Dixon They are needle biopsies done under local anesthesia, and the patients have to be happy that these samples are taken. I think the essential component of a study like this is to make sure that you cause the patient no discomfort or distress. And actually those patients that are most likely to volunteer for studies like this, are those whose initial biopsy was pretty painless. It is important

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that right from the start you make sure that whatever you do to a patient is as painless as possible because that will actually make them more likely to give you a second sample.

Foss On the whole topic of clinical trials, can we compare and contrast the type of clinical trials that are ongoing in breast cancer in the two countries, the kind of national clinical trial effort that is under way. Anees, maybe you could start by telling our listeners what is the national effort in breast cancer in the United States.

Chagpar It is huge. I think one thing that is important for our listeners to understand about clinical trials is that many people have a misperception about clinical trials, and they think that this is experimental therapy and they are a human guinea pig. One of the things that I think is so critical is that people really understand a few things. The first is, clinical trials are our way of advancing science and improving therapy, but the second, perhaps more important fact to understand, is that people who participate in clinical trials tend to do better than people who do not, and the reason for that is, is that we are always comparing what we think is standard therapy to something we think is even better. We appreciate the efforts of our patients in helping us to advance the standard of care. There are many clinical trials that go on all over the country, many that go on all over the world. I am sure that there may have been clinical trials that Mike would have been able to participate in that we would have also been able to participate in regardless because it is more than a national effort, although certainly it is a huge national effort. It is a global effort as well.

Dixon I would absolutely reiterate that. Many trials now are international because the important thing is to try and get patients into the trials relatively quickly so that we can get an answer relatively quickly. The fact is that the reason we know how to treat breast cancer is because the previous generation went into clinical trials. So much of our practice is based on the results from trials, and the impressive thing about breast cancer is that generation on generation, outcomes are just improving all the time, and although some people say to me, Mike, we are putting a lot of money into breast cancer. I say, well, look at our results. The fact is that within a generation we have dramatically improved the outcomes of women with breast cancer. Most women with breast cancer will not die of breast cancer; they will die of something else. Unfortunately, we all have to succumb to something, but it is great for us as surgeons and people treating patients with breast cancer that we are proving increasingly successful in giving those people a normal life, and more importantly, a fantastic quality of life.

Foss And Anees, I am sure that you would agree with that.

Chagpar Absolutely!

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- Foss Can you talk about some of the reasons why you think we have made tremendous strides in breast cancer in the last 10 years?
- Chagpar I think it is multifactorial. One, I think that we have certainly done a tremendous amount of research, and that has been due to the efforts of our patients, as I say. I think women with breast cancer are incredibly generous in terms of trying to help other people and advance our standard of care by participating in clinical trials. Second, is that there has been outstanding collaboration across boundaries, and those boundaries are geographic and those boundaries are also by specialty. When you have collaborations from the bench to the bedside, from this side of the Atlantic to the other, you can really make significant strides. I think that we have begun to understand perhaps more than any other disease the fundamental biology of breast cancer. I think that combination has helped us to make tremendous strides.
- Foss Mike, any comments on that?
- Dixon I think what Anees says is right. We are enormously grateful for the women who have previously gone into trials, have helped us work out what the best approach is for the next generation and we are enormously grateful to the current generation of women who are going into trials because they will make us better in the future. The other thing to say is that women as a whole have been enormously positive in relation to breast cancer. They have collected funds. They have supported research projects. And it is for the people by the people of the people. It is true democracy, I think, in breast cancer research because the reason we have done so well is that women themselves have said, you know, we need better!
- Foss Most women in the United States are very proactive, I would imagine.
- Chagpar Yeah, absolutely! We have fantastic supporters. Everything from advocacy groups who lobby the government for additional funds for the NIH, to people rallying around early detection and screening, to people raising funds for clinical trials. I would agree, it is the women and men and families and people who make what we do possible.

*Dr. Anees Chagpar is Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. Dr. Mike Dixon is Professor of Surgery and Clinical Director for the Breakthrough Research Unit at Western General Hospital in the UK. If you have questions or would like to add your comments, visit [yalecancercenter.org](http://yalecancercenter.org) where you can also get the podcasts and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.*