Breast Cancer Decisions and Choices

Guest Expert: Michael DiGiovanna, MD, PhD
Associate Professor of Medical Oncology

Yale Cancer Center Answers is a weekly broadcast on WNPR Connecticut Public Radio Sunday Evenings at 6:00 PM

Listen live online at www.wnpr.org
OR
Listen to archived podcasts at www.yalecancercenter.org
Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Foss is a Professor of Medical Oncology and Dermatology and she is an expert in the treatment of lymphomas. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening we welcome Dr. Michael DiGiovanna. He is an Associate Professor of Medical Oncology and an expert in the treatment of breast cancer.

Chu Mike, many people often think of breast cancer as a familial genetic disease, but in fact, when you look at the numbers, that makes up a relatively small percentage of the patients that you typically see in the clinic. Can you explain that a little bit more?

DiGiovanna People often think of cancer as potentially being hereditary, and running in families. Among cancers, breast cancer usually comes to peoples mind foremost as a possible hereditary and genetic cancer. However, only about 5% to 10% of breast cancers are hereditary and run in families, and the other 90% to 95% are just sporadic cases.

Chu Of those 5% to 10% of genetic cases, what are the key genes that people should think about, or have heard about?

DiGiovanna There are two genes that have been discovered that can have a mutation that runs in the family. These two genes account for about half of these cases of genetically inherited breast cancer and those genes are called BRCA1 and BRCA2 for breast cancer 1 and breast cancer 2.

Foss Can you talk a little bit about other kinds of cancer? We have heard about BRCA1 and BRCA2 with ovarian cancer for instance, and we just heard a little about pancreatic cancer as well. Can you talk about other cancers associated with these genes?

DiGiovanna Francine, you have just touched upon the two most important ones, and the most important is ovarian cancer. In fact, these shouldn’t be called breast cancer genes; they should really be called breast and ovarian cancer genes because there is very high rate of ovarian cancer as well. For someone who is a carrier of BRCA1 or BRCA2, the risk of developing breast cancer sometime in their life is about 50% to 85%, but the risk of developing ovarian cancer is about 30% to 50%. That’s an even more important thing potentially, because we have very effective screening for breast cancer to catch it at an early stage when it’s more curable, but there is not a proven effective screening for ovarian cancer to catch that at an early stage, and therefore, it’s perhaps even more important for a carrier of one of these genes to be aware that they are at a high risk of ovarian cancer. And so, if such a woman is finished with child bearing and older in her reproductive age,
we often recommend considering having the ovaries removed prophylactically, as the only sure way to lower the risk of developing ovarian cancer.

Chu When would one typically think about getting these genetic tests, BRCA1 and BRCA2?

DiGiovanna We consider it based on what we think the odds are that a person, or their family, might have one of these genes involved. I will talk about the factors that make it more likely that one of these genes might run in the family. The more cases of breast or ovarian cancer within a family, especially with first-degree relatives meaning a woman's mother, sister or daughter, the more likely that someone might be a carrier. The younger the age of onset of the cancer makes it more likely that there may be a mutation in one of these genes, for example, for breast cancer, the average age of diagnosis is about 60, but for many of these carriers of these genes, the average age might be in the 40s or even younger. For a woman, even without a family history, if she is diagnosed with breast cancer up to the age of 45, we would recommend considering testing for one of these genes. Some other factors that raise a likelihood of these genes being positive are if the patient is Jewish, because about 1 out of 43 Jewish people carry a mutation in one of these two genes. Another thing to consider is that these genes can be passed on to men in the family and the men can pass the genes on to their children, and these genes can cause breast cancer in men as well as prostate cancer in men. So, any family that has a male breast cancer patient should also consider being testing for one of these genes.

Foss Is there a difference in terms of race; you mentioned that Jewish people have a higher frequency of these genes, but what about African Americans and Asian American patients?

DiGiovanna It’s a little bit lower in Asian American patients. However, among other races there is quite a lot of this gene as well.

Chu Can you comment on some of the other main risk factors for developing breast cancer?

DiGiovanna We would have to say, without trying to be funny, that the number one risk factor is simply being female, being a woman, because in our country almost one out of eight to one out of nine women will be affected with breast cancer sometime in their life. So, just being a woman is the number one risk factor, and that’s why breast cancer screening is recommended for all women, not just women who have a family history of the disease. We recommend that all women begin screening for breast cancer with a yearly mammogram starting at age 40, and in addition to mammograms, part of the screening is teaching women to do breast self exams and having them have annual breast exams by their doctors as well. For families that have a young age of diagnosis of cancers, we may even recommend starting screening earlier than age 40.

6:26 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Apr-12-09.mp3
Chu: Who would typically teach a woman how to do self-examination?

DiGiovanna: Their primary care physician or their gynecologist should really be teaching them the proper techniques of doing self-breast examination.

Chu: And how frequently should the self-exams be done?

DiGiovanna: We recommend that they be done once a month, and for women who are premenopausal we recommend that they be done after the menstrual period has finished, because in the period leading up to the menstrual period the breasts may actually get enlarged and tender and lumpy naturally. So, after the menstrual period would be the best time to do a breast exam.

Foss: Now that we are using mammography more often, we are picking up more cancers early, and many women say that they don’t even feel these lumps. How often is it that a woman can actually detect the lump herself but it does not show up on the mammography, and how often is it that there is a lump on mammography that a patient doesn’t feel?

DiGiovanna: So, there are several aspects to your question. One aspect is how perfect mammography is, and it’s not perfect. It’s estimated that about 15% of cancers can be missed on a mammogram just because they are not dense enough to show up on an x-ray; which is basically what a mammogram is. So 15% of cancers, even if one can feel a lump, might not show up on a mammogram, might be entirely invisible to the mammogram. Therefore, it is fairly frequent that women, even those who do get regular annual mammograms, get diagnosed with breast cancer not because of the mammogram, but because they find a lump or their doctor finds a lump. So, it's critically important that both the breast exam and the mammogram be conducted in the screening of all women.

Chu: There has been a lot of discussion about the use of MRI and other more sophisticated imaging techniques for breast cancer screening. What are your thoughts on that?

DiGiovanna: We can now perform MRI of the breasts, and they come in very useful sometimes when there is an equivocal finding on a mammogram, or an equivocal finding on an exam, and you want to confirm whether it looks like it could be a cancer or not. Very often we use MRI now for those reasons. A trickier question is whether we should use MRI for screening, the way we do with mammograms, and there is some controversy in this area because it does in fact seem that MRI is more sensitive than mammograms. It does seem that MRI can pick up some cancers that the mammogram missed. The downside of the argument, however, is that MRI is overly sensitive. They pick up many-many things in the breast that aren’t cancer that are just benign things in a women's breast, and that would lead to the necessity for a biopsy to know for sure if that something is benign or not.
not. It is estimated that if we told all women to begin having screening MRI of the breast every year, about one out of four, or one out of five, women would need a biopsy every time because of something that turned up on the MRI, and of course, most of those would be benign and not anything to worry about and an unnecessary biopsy. For that reason, we are currently not recommending that all women have screening MRI exams. However, we are recommending it for certain women. For example, for very young women perhaps, who have a family history of early onset breast cancer, because in very young women mammograms are even more difficult to use because the women's breasts are so dense that it’s hard to find the tumor on a mammogram and the mammogram is therefore less sensitive. We also recommend MRI screening for carriers of the BRCA1 and BRCA2 gene because they have such a high chance of developing breast cancer that its considered worth the possibility of finding other things, and so, BRCA1 and BRCA2 carriers are the most definitive group of people who should get screening MRI. The other recommendation is for anyone who is considered to have at least a 20% lifetime chance of developing breast cancer, could consider screening with MRI scans, but not the average woman.

Foss Are the screening MRI scans available in all hospitals and treatment centers, or does one have to go to a specialized center for that?

DiGiovanna A good question. They are not available in all centers, because even hospitals that have MRI might not have the equipment to adapt the MRI to be able to look at the breasts.

Foss Mike, can you reassure women about the annual screening mammogram in terms of the radiation exposure. A lot of people are concerned about the medical use of radiation year after year.

DiGiovanna And that's a legitimate concern, and in fact, it is a legitimate concern with breast cancer because it is known that exposure to large amounts of radiation can be one of the risk factors for breast cancer. However, the amount of radiation in a mammogram is so low that it’s estimated that you save far more lives from detecting breast cancer early than you might cause damage by doing the MRI. In fact, when we talk about the possibility of radiation causing breast cancer, that’s usually radiation that’s given in high doses, for example to treat other types of cancers like lymphomas in the chest, and that usually only causes breast cancer if the radiation exposure to the breast is during puberty or very early adulthood when the breasts are still developing. When an older woman gets radiation to the breast, the breast seems resistant to having that cause any breast cancer.

DiGiovanna Typically, if there is an abnormality on the mammogram, a woman would have a biopsy and the initial biopsy can be done either by the mammography doctor themselves, or the patient can be

12:35 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Apr-12-09.mp3
referred to a breast surgeon. Very commonly the first biopsy that we do is just a needle biopsy so that we can make the diagnosis, and then if its cancer, we plan the surgery to best accommodate the particular cancer that’s found. On the other hand, some places might do a surgery biopsy first and then if its cancer, very commonly, you might need a second surgery in addition. By doing a needle biopsy first, it allows the diagnosis to be made, allows the potential for just having one surgery instead of multiple surgeries, and it also sometimes allows us to give the option of giving systemic treatments like medical treatments such as chemotherapy before the surgery instead of after the surgery.

Foss That leads to another question, which is, what is the importance of a multidisciplinary team approach to this kind of a problem, where patient's maybe don’t even know that they have a cancer going into this procedure? At what point does a medical oncologist get involved and are there multidisciplinary teams that are involved from the very beginning?

DiGiovanna Yes, and this is becoming all the more important as our treatments evolve. Typically somebody who has breast cancer needs a number of different types of specialists; a breast surgeon, a breast medical oncologist, and often a breast radiation doctor as well. In addition are the many doctors behind the scenes, such as the mammographers, radiologists, and the pathologists who interpret the biopsies and so on and so forth. What's becoming more important in getting all of the doctors involved early on in a multidisciplinary team is that many patient's might require medical treatment in addition to surgery, radiation in addition to surgery, and sometimes the medical treatment is chemotherapy, sometimes its anti-estrogen therapy, which we will probably talk about later, and we now sometimes do those treatments before the surgery versus doing the treatments after the surgery. It really requires the team approach to decide for any particular patient what the best order to do things is for that patient.

Foss Let’s talk a little bit more about the treatment for breast cancer when we come back from the break. You are listening to Yale Cancer Center Answers, and we are here discussing the treatment of breast cancer with Dr. Michael DiGiovanna.

Medical Minute

Over 170,000 American's will be diagnosed with lung cancer this year and more than 85% of these diagnoses are related to smoking. The important thing to understand is that quitting even after decades of use can significantly reduce the risk of developing lung cancer. Now everyday, patients with lung cancer are surviving, thanks to increased access to advanced therapies and specialized care and new treatment options are giving lung cancer survivors new hope. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for lung cancer and patients enrolled in these trails are given access to medicines not yet approved by the Food and Drug Administration. This has been a 15:45 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Apr-12-09.mp3
Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu and we are pleased to have Dr. Michael DiGiovanna here to discuss breast cancer. Dr. DiGiovanna is a medical oncologist at Yale Cancer Center. Mike, we talked a little bit about the diagnosis of breast cancer and about the multidisciplinary approach. Can you tell us what the approach is for a patient, say who has a lump removed and doesn’t have metastasis, and a patient who has a lump removed and does have evidence of other disease. How do we approach these patients?

DiGiovanna There are two scenarios that you raised. One is the patient who has had the tumor removed and has no evidence of disease anywhere else in the body. That’s a patient who is potentially cured or potentially curable, and the other scenario is the patient who has already had spread of the tumor to other parts of the body. That’s what we call metastasis, or advanced breast cancer and is the definition of stage IV breast cancer, the highest stage. Metastasis are cancerous tumors growing in other parts of the body that came from the breast, because part of the cancer spread through the body is usually through the blood stream, through the arteries and veins, and lands in another place in the body and is growing in that part of the body. That’s the most difficult stage of cancer to treat, and even though it's treatable, it's almost always not curable. That is the stage of disease where patients will often ultimately die because the medicines that we have aren’t perfect enough today to eradicate all of the cancer. All of the other patients, which is more than 90% of patients who at the time of diagnosis don’t have evidence of metastasis, they have their surgery removed, but we always know that there is some possibility that they have very tiny amounts of cancer that has spread, but at the current time of diagnosis it’s too small an amount to be detected. We can’t find it even with our most sophisticated scans and it’s not causing any symptoms or any abnormalities on the patient’s physical exam, but there is a chance that cancer could be hiding in other parts of the body. The first thing we do is try to estimate what the odds are that somebody could have what we call microscopic amounts of cancer hiding in other parts of the body. The way we try to guess those odds are by things such as what the size of their tumor is and whether it has spread to lymph nodes in the armpit, and if it has, how many lymph nodes in the armpit has its spread to? These are things that help us guess what the odds are that some cancer might be hiding in other parts of the body. And these are the exact reasons why cancer is more curable when it’s detected early, because the earlier it’s detected and removed, the less likely it is that any cancer has had the opportunity to spread to other parts of the body. After we estimate what the odds are that someone might have microscopic amounts of cancer in other parts of the body, we decide if it’s worth using what's called adjuvant therapy, which means some kind of medicine given to the patient to try to eradicate any microscopic amounts of cancer that could be hiding in other parts of the body. There are two things that have
improved the cure rate of breast cancer, mammograms for early detection and better and better treatments with adjuvant therapy; improvement in our adjuvant therapy. Therefore, adjuvant therapy is a critically important question, because this is how we save more lives and increase the cure rate for breast cancer. Typically, there are two types of adjuvant therapy. One type is chemotherapy, conventional chemotherapy like many people have been treated with in the past. For the many types of breast cancer that contain what's called estrogen receptors, those are the cancers that are dependent on estrogen, the female hormone, another option for adjuvant therapy is using pills that are anti-estrogens to block a woman's estrogen pathway. If we think that the risk is high enough that there is cancer hiding, we might choose to use both chemotherapy and anti-estrogen therapy.

Chu

In 2009, when we talk about breast cancer and other cancers, there is this focus on individualized personalized medicine, but in many ways breast cancer really is the model, the poster child for individualized personalized medicine, because there are a number of markers that are available that can help us, help you folks, figure out what type of treatments could be offered to a patient with breast cancer.

DiGiovanna

Yes, and breast cancer as you suggest has led the way in that. The first one that I mentioned is the estrogen receptor. A little more than half of all breast tumors have estrogen receptors and that’s a sign that the cancer requires estrogen to grow. One very effective way to treat it is to deprive it of its estrogen with these anti-estrogen pills, like I have discussed. We have been using that type of therapy for decades now. In just the last ten years, we have had an additional type of treatment. About 20% of cancers make another type of receptor called HER2, and we now have a drug and medication that can attack the cancers that overproduce HER2, and that drug is called Herceptin. We discovered that when we add Herceptin to chemotherapy for the HER2 positive type of breast cancer, we get a huge additional benefit in curing more patients. So breast cancer has lead the way with being able to identify which patients will benefit from anti-estrogens, which patients will benefit from treatments that target HER2, and its also leading the way in trying to predict which patients need these treatments or not, by more sophisticated methods. I mentioned that traditionally the way we made that decision was with very crude estimates, such as how big the tumor is, and how many lymph nodes it spread to. We now have additional, more technologically advanced methods. For example, there is a test that can be performed on the tumor called the Genomic Health Oncotype DX test, and what this test does is it takes a chunk of the tumor and measures the level of 21 different genes that are involved in the tumor behavior and aggressiveness. Based on the results of these tests, we can very precisely estimate how much additional benefit a woman would have if she takes chemotherapy in addition to anti-estrogen pills compared to taking just estrogen pills alone. This is a very sophisticated way to try to personalize the decision for every individual patient whether they need chemotherapy or not.

23:09 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Apr-12-09.mp3
Foss  Can any woman get this test?

DiGiovanna  Any woman who has had breast cancer can get the test.  There is one laboratory in the country that performs it at this time, but what we do is we have the pathology department at the local hospital send a piece of the cancer in the mail to this laboratory in California, and within ten days we have the answer back.

Foss  Should a woman do this when they are first diagnosed with breast cancer, or is this something that’s only useful for patients with metastatic disease?

DiGiovanna  No actually, this is used not for patients with metastatic disease, but for the patients who are diagnosed with early stage when we are trying to decide whether chemotherapy is needed as a part of their adjuvant therapy or not. It’s really the doctors decision as to whether to order this test, because in some cases it’s fairly clear-cut that a woman should have chemotherapy and in other cases, for example, a woman with a very tiny unaggressive type of tumor, it might be very obvious that she doesn’t need chemotherapy. It is the cases where we are on the fence and we would like to refine our guess as to how much benefit the chemotherapy might have, when the doctor will decide if the tests should be ordered.

Chu  A quick question, so a woman listening right now might say, I have had my breast cancer removed by surgery, and the surgeon says that they got it all, so why is there a need to get what you are calling adjuvant chemotherapy, say for up to four to six additional months after surgery was performed?

DiGiovanna  The reason is similar to what I stated earlier, that there is always some possibility that very tiny amounts of the cancer have gotten into the blood stream and traveled throughout the body even before the tumor was removed, even when we catch the tumor early.  So, breast cancer can do that even at an early stage with a very small tumor and that’s why with every single case we ask ourselves, should we consider using this adjuvant therapy or not?

Foss  Can you talk a little bit about how comfortable a woman can feel that their therapy has been effective, and how many years after completing adjuvant therapy is a woman really safe from the recurrence of breast cancer?

DiGiovanna  That’s a very difficult question.  Traditionally a lot of people know that if you have made it five years that’s a very good sign, and many cancer patients, breast cancer patients, like to throw a party when they reach the five year mark, because we have always thought that most of the recurrences, if they are going to happen, likely happen in the first five years, especially in the first two or three years.  However, we are learning that cancer can relapse quite commonly after five

25:55 into mp3 file  http://www.yalecancercenter.org/podcast/Answers_Apr-12-09.mp3
years, particularly the type of cancers that are positive for the estrogen receptor, the estrogen dependent type. We are learning more and more that perhaps half of those relapses are going to happen after five years, between years five and ten, and because of that, our treatments are catching up and now we very commonly give anti-estrogen treatments for ten years as opposed to in the past when we gave it for five years. We actually have clinical trials that are going on now that are comparing whether we should give it for 15 years compared to 10 years. We are realizing that again, when we talk about individualizing treatment, women who have estrogen receptor positive cancers may still have some small risk of relapsing many years later, so we are considering extending their treatment with anti-estrogens for a long time as opposed to women who have the type of cancer that’s negative for estrogen receptors. Those are the ones that clearly have the highest risk of relapsing in the first few years, and when they get out to five years, they have a much lower risk of relapsing after that.

Foss What is the role of the antibody Herceptin in those patients? Is it possible to administer this antibody for years and years? Is there any proof that it will also prevent the progression of breast cancer?

DiGiovanna As we talked about, Herceptin is the drug that specifically attacks the HER2 positive type of breast cancer, and relatively recently we have been using it as part of the adjuvant therapy. In fact, the first results just became available in 2005 and initially clinical trials used Herceptin for one year and gave excellent results. The Herceptin reduced the chance of relapsing by 50% above and beyond the results that we already had with chemotherapy. There is one trial that hasn't finished yet that is comparing two years to one year. When we have those results, we will have the first clue as to whether going longer than one year might be helpful or not.

Chu Mike, as the therapies are extending for longer periods of time, is there concern that maybe there will be increased side effects that develop?

DiGiovanna Yes, one of the potential side effects we worry about with some of the newer types of anti-estrogen therapy is the potential for osteoporosis. Very interestingly, some recent data has suggested that some of the osteoporosis medications themselves might help prevent breast cancer from relapsing, so it’s a very interesting story that’s coming full circle now.

Chu Clearly we have a lot more to discuss and we will have to have you back on a future show. You were listening to Yale Cancer Center Answers and I would like to thank our guest Dr. Michael DiGiovanna for a very fascinating session. Until next time, I am Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions or would like to share your comments, go to yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum from Connecticut Public Radio.