

Welcome to Yale Cancer Center Answers with your hosts Drs. Francine Foss, Anees Chagpar, and Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at Yale Cancer Center, Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. 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. This week you will hear a conversation about sarcomas with Dr. Dieter Lindskog. Dr. Lindskog is an Associate Professor of Orthopedics and Rehabilitation at Yale School of Medicine and Clinical Research Program Director for the Sarcoma Program at Yale Cancer Center. Here is Steven Gore.

Gore That is one of the longest titles I have ever seen of anyone that has been on the show. Wow! So, orthopedics, that means you are a surgeon?

Lindskog Yes.

Gore I think that a lot of people will know what breast cancer, lung cancer, and maybe even leukemia are, but I think sarcoma is a word that most of us are not familiar with. What is a sarcoma?

Lindskog A sarcoma is a cancer that arises from connective tissue. It is actually a rather broad group of tumors which can arise from any number of different tissues; bone, fat, muscle, and are very different from what you think of in a breast cancer where there are only a couple of different types and most of those are treated in a relatively similar fashion. In terms of sarcomas, depending on what type of tumor tissue it is, will help guide how we deal with them.

Gore So there are many kinds of sarcomas.

Lindskog Many kinds.

Gore How do people get diagnosed with a sarcoma?

Lindskog Most of the time, they present with a mass that they can palpate. Oftentimes, it is just pain that is the presenting symptom.

Gore So they might feel a mass in a limb. Would it usually be in a limb?

Lindskog Most commonly in the limbs. The thigh and the femur are the most common places to develop sarcoma.

Gore Do they have trouble walking?

2:38 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Lindskog They could, certainly.

Gore And then they will tend to present to their primary care doctor? Where do the referrals come from? L

indskog From the primary care doctors, from other orthopedic surgeons. It is not often that people will show up in my office on their own.

Gore I would not think so. You said that sometimes they are not in the limbs. Can it be in the abdomen then?

Lindskog They can be in the abdominal wall and the chest wall at times as well. But they arise from connective tissue, so that the places you have more muscle, fat, and other things are where you tend to find them.

Gore What do you need to do to evaluate somebody with a tumor in the limb?

Lindskog The most common thing that we will do is some imaging as simple as an x-ray to an MRI scan. Ultimately, these will usually go on to be biopsies to obtain some tissue and prove a diagnosis as well as to determine the individual kind of sarcomas to help us figure out how to treat them.

Gore So you will do a limited biopsy first before you plan a definitive treatment?

Lindskog Yes. Oftentimes we will do what we call image guided biopsy. We rely on our friends in the radiology department either with CT scans or ultrasound to use that imaging to biopsy particular parts of the tumor, which will give us the best idea and the best chance of making a diagnosis.

Gore Do you do that in the radiology department or in an operating room?

Lindskog They do them in the radiology department.

Gore Like a needle biopsy or a core biopsy?

Lindskog Yes, a core needle biopsy.

Gore I see. So, it is really not a surgical procedure, per se.

Lindskog No, the number of surgical biopsies we do has really decreased. We really only do that these days if the needle biopsy is nondiagnostic, and the needle biopsies are usually good 9 times out of 10.

4:55 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Gore That is interesting because what I remember about sarcomas, which of course is not terribly much, is that many of them kind of look alike and I just would have guessed you need more tissue for the pathologist to tell you what to do. Lindskog With the stains and some of the molecular testing that they can do even on a needle biopsy, which again, 9 times out of 10, we get an answer and it is the right one.

Gore That is great. It is good to see. The good thing about this job is to see the progress since I have been in medical school and even since my oncology training, which was a while ago. So, the pathologist tells you that this is a blank kind of sarcoma and then what happens?

Lindskog Then they get treated according to how we fill in that blank. And the good thing is I do not have to remember how to treat every single individual flavor or variety, but they get categorized into groups, with a few variations. Most of the soft tissue sarcomas or the cancers that are arising in connective tissue outside of the bone, are essentially treated similarly. Bone tumors depending on which variety can be treated according to a different protocol and that is sort of how it is.

Gore And is the therapy primarily surgical for most of these diseases?

Lindskog Surgery plays an integral role in most of the diagnoses. In certain instances, there are soft tissue sarcomas such as a rhabdomyosarcoma in a child.

Gore That is a mouthful.

Lindskog I do not have to spell it often, fortunately.

Gore What does it mean?

Lindskog It is a malignant tumor of skeletal muscle. So, it is the pathologic derivative from skeletal muscle. It is very responsive to just chemotherapy and radiation alone, so most of the time that does not require a surgery for treatment. In certain instances, there are tumors like a Ewing sarcoma, we will treat just with chemotherapy and radiation as well if it is in a location where surgery is not going to be able to remove all of the tumor without sacrificing something too important.

Gore I am assuming that Ewing is not a location in the body like a rhabdo, whatever rhabdo is.

Lindskog Ewing is named after the person who discovered and named it. We do not know what the normal tissue type is, so it is a little bit of an oddball.

Gore Where does it show up?

7:55 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Lindskog Interestingly that one can be either a bone sarcoma and occur in the bone, or in the soft tissue.

Gore And it is primarily in kids right?

Lindskog Primarily in kids, yes.

Gore So, you take care of kids and adults?

Lindskog Yeah, correct.

Gore Interesting. I know pediatric surgery is often a different field from adult surgery, so you must have had to do a little of both.

Lindskog Well in orthopedics, we take care of kids and adults.

Gore Like football players who break their bones and everything.

Lindskog Yeah, we have exposure to that from all of our training, so we really take care of the gamut of ages.

Gore I think that when people think of bone tumors we remember one of the Kennedy kids who lost his leg, one of Teddy Kennedy's kid, I think, right?

Lindskog Yeah.

Gore He had to have a limb resected and we always remember the brave pictures of him skiing and all that stuff which is really fabulous. Is that still the case for the bony tumors, does it usually mean a loss of a limb?

Lindskog It does not nowadays. There still are instances where it is the right answer, but what we call limb salvage or limb sparing surgery where we can remove the tumor completely and reconstruct the leg is the vast majority of cases nowadays, 95% of the time we will go with the limb salvage.

Gore That sounds a lot more appealing, but obviously if you have to have your limb resected you do, but I would think there is probably still some rehab involved. Is there not?

Lindskog Absolutely. A good way to think about an amputation or any of these operations, is it is just a different way of reconstructing your limb. One you reconstruct it on the inside and one on the outside.

Gore Good point. What do you do when the kids are still growing? Like an adolescent whose bony plates haven't fused and everything.

10:08 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Lindskog That is actually the most challenging problem that we deal with. We have lots of solutions which means there is no good or perfect one. We have prosthesis that you can lengthen. You can actually mechanically make them grow so to speak and get longer, but that is fraught with surgical complications and there are lots of risks.

Gore These are prosthesis which are implanted? Is that what you do for that?

Lindskog Yes. Mechanical prosthesis, metal prosthesis that you will actually make it expand to try and grow the bone.

Gore Inside. Wow! But you are saying that is not totally primetime yet?

Lindskog Well, it is in use, but there are lots of issues with it currently. It is either more operations to lengthen it, they have a noninvasive mechanically lengthening prosthesis at this point, but it certainly does not work perfectly and there are lots of issues.

Gore So part of your title includes rehabilitation. How do you interface with that phase of a patient's treatment, after you have done your primary surgery?

Lindskog Our department includes orthopedics and rehabilitation. We rely on our partners in physical therapy and really guide that phase of their rehabilitation.

Gore I see.

Lindskog And their recovery. I am not integrally involved in that absolutely.

Gore Gotcha. Do you ever need to go back and do something differently if their rehabilitation is not going well or that is really not part of a surgical approach?

Lindskog Certainly, the surgeries that we do are relatively high risk in terms of further operations down the road. Sometimes patients won't be gaining all of the motion in their joint and we have to take them back to the operating room and sometimes mechanically stretch them out and those sorts of things. The rehabilitation and recovery phase of this is involved, but the No. 1 goal is always to cure them of the disease.

Gore Do medical oncology and chemotherapy play any role? You mentioned the rhabdomyosarcoma which is treated with chemotherapy, but in some of these other diseases is primarily your job or?

Lindskog Absolutely, there is a team that we work with on a day-to-day basis, there is the surgical side, there is the chemotherapy that is managed by our medical oncology team and radiation therapy. Some of the sarcomas need all of us. Surgery, chemotherapy, and radiation, some need 1 or 2 and as I

13:31 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

said, sometimes it is just radiation and chemotherapy, but for instance, primary bone sarcoma is responsive to chemotherapy and requires surgery to remove it, but are not very sensitive to radiation, so that would be managed with 2 modalities. The general soft tissue sarcoma tends to be managed with surgery and radiation treatments. The radiation in those instances will decrease the risk of it coming back. From most soft tissue sarcomas, we do not have a wonderfully effective chemotherapy, so that is not added to everybody's care, but in certain instances, patients who are at especially high risk, certainly, that will be part of it.

Gore This is a fascinating topic and one that I do not know that much about, so I am really enjoying this discussion, but right now we are going to take a short break for a medical minute. Please stay tuned to learn more information about sarcomas with Dr. Dieter Lindskog.

Medical Minute There are over 13 million cancer survivors in the United States and over 100,000 here in Connecticut. Completing treatment for cancer is an exciting milestone, but cancer and its treatment can be a life changing experience. Following treatment, cancer survivors can face several longterm side effects 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 to keep cancer survivors well and focused on healthy living. The survivorship clinic at Yale Cancer Center focuses on providing guidance and direction to empower survivors to take steps to maximize their health, quality of life and longevity. 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 yalecancer-center.org. You are listening to the WNPR, Connecticut's public media source for news and ideas.

Gore Dieter, before the break, you were telling me about the various ways that treatment modalities are mixed and matched for different kinds of sarcomas that you treat, always involving some surgery it sounds like, but sometimes with radiation, sometimes with chemotherapy.

Lindskog Most of the time involving surgery.

Gore Most of the time right? We want to give you credit, you trained a long time to be able to do the stuff that you do. I know in some other cancers that we deal with, we use chemotherapy to shrink the tumor before people get surgery to make it more amenable to surgery. Is that something that is done in your field or not really?

Lindskog Yes, for bone sarcomas, the general treatment protocol is they will receive some chemotherapy preoperatively. They will have their resection and then receive another several rounds or cycles of chemotherapy afterwards; it is a fairly well established protocol.

16:40 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Gore Are treatment approaches very different from children and adults with these diseases, or are the diseases distinct?

Lindskog There is significant overlap, but there are groupings of the types of disease by age. So most osteosarcomas, most Ewing sarcomas, occur in kids and teenagers.

Gore Osteosarcoma is bone right?

Lindskog Correct. Osteosarcoma is bone. Whereas in adults, you see more of the soft tissue sarcomas and a different type of bone sarcoma called a chondrosarcoma.

Gore Chondro, if I recall has something to do with cartilage.

Lindskog Correct.

Gore Interesting. Does that grow out of the cartilage?

Lindskog Well, it grows within the bone, not necessarily out of the cartilage at the joint. But the cell that goes awry forms cartilage.

Gore Interesting. And does the tumor actually have cartilage as part of it?

Lindskog Yes, as it is growing, it will differentiate into cartilage and can look like either fairly normal appearing cartilage if it is a low grade, what we consider a low-grade tumor or sometimes it does not even look like cartilage at all and it is hard to identify as cartilage if it is a high-grade tumor.

Gore When you went into orthopedics, did you know you were going to end up doing this end of orthopedics.

Lindskog No, not at all. When I was training, I was exposed to oncology fortunately early on, and was fascinated by it and could not convince myself not to do it. It is very different from the rest of orthopedic surgery. A lot of orthopedic surgery deals with relatively healthy people who are injured.

Gore Lots of sports medicine.

Lindskog Lots of sports medicine, fractures, joint replacements, and we deal with aspects of disease and illness that a lot of orthopedics does not.

Gore I certainly remember in medical school, it seemed that people who were attracted to orthopedics tended to be athletic, if not athletes themselves, and maybe that was a myth, or maybe that has changed over time, I do not know.

19:13 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Lindskog It probably has not changed that much.

Gore Just to be totally ignorantly generalizing here, you would not expect that population of people necessarily to gravitate to oncology.

Lindskog They say it is about 2% of orthopedic surgery that is oncology. So, it certainly is not the majority of it and there are not an orthopedic oncologists on every street corner.

Gore It sounds like you were drawn to it.

Lindskog Yeah.

Gore What was it that pulled you in?

Lindskog I think I really enjoyed the idea of saving lives. I liked the intellectual aspect of trying to figure out the diagnoses. When you look at an x-ray and you see a broken bone, it is not that hard to figure it out, but there are a lot more diagnostic aspects to orthopedic oncology than certain other aspects of orthopedics.

Gore Does one have to do special training for orthopedic oncology? I imagine you must.

Lindskog It is an extra year beyond regular orthopedic training specializing just in treating orthopedic oncology patients.

Gore And do most major surgical centers have orthopedic oncology?

Lindskog Certainly most of the major cancer centers, not every orthopedic, what you would think of as an orthopedic hospital would have one necessarily.

Gore I remember when I was training at the University of Chicago back in the 80s, and the whole limb sparing surgery thing was pretty new. And I do not remember the guy's name there, but it was one of the places to go to get limb sparing surgery and to be trained in that and that seemed like a very particular thing and I was just wondering how generalized that is.

Lindskog It is still fairly particular.

Gore That is fascinating and it seems like you need to have a grasp not only of the surgical procedures, but lateral emotional pieces.

Lindskog We deal with a lot more emotional aspects than a lot of orthopedics.

21:32 into mp3 file <http://medicine.yale.edu/cancer/podcasts/2015%200222%20YCC%20Answers%20-%20Dr%20Lindskog.mp3>

Gore Although I guess anything where you might be dealing with amputation, which other orthopedists have to deal with, is always fraught with a lot of emotional content as well, I suppose.

Lindskog Yeah, I think so.

Gore Do you train fellows as well?

Lindskog We do not have a fellowship program here. Our department really focuses on training residents. We have 20 residents in the program, and only a couple of specialties with fellowships. So, we are a training center that really focuses on the resident training.

Gore So if a resident really takes to this and worked with you as a mentee and so on, you get them prepped and send them elsewhere?

Lindskog Yeah. They will have to go and do their fellowship at a place that has a specialized fellowship program.

Gore Are there many of those?

Lindskog No, there are probably only about a dozen in the country. G

ore I understand that Yale is building a newer, I am not sure building is the right word, but putting together a new rheumatology orthopedic muscle something.

Lindskog The musculoskeletal institute, I think is still the current name.

Gore Yeah, thank you. And they have just hired somebody new for that.

Lindskog Yes, to run it. Mary O'Conner, who trained at the Mayo Clinic was actually running the Mayo Clinic in Jacksonville.

Gore I hear Mayo and I think Minnesota.

Lindskog She got the advantage of Florida and the Mayo Clinic.

Gore Well there are more people breaking their legs there from springtime sports, but I guess they do not really ski. Will you be a part of that, or your field? Or do you really more speak to the cancer side.

Lindskog More to the cancer side. As they transition to the musculoskeletal institute itself, I will be still doing a majority of my stuff through the Smilow entity.

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Gore Are a lot of those activities actually going to be moving physically? It was my understanding that it was going to be at the St. Raphael's campus.

Lindskog The plan is that they will focus those activities at the St. Raphael's campus. There won't be solely there, but that will be the location where most of the joint replacement and spine surgery orthopedics certainly is done and there is a lot of it happening right now and those decisions are being made right now.

Gore I see. But you will be focusing on the cancer piece, which of course makes sense in Smilow.

Lindskog Yes.

Gore And do have offices in different places as well?

Lindskog That is the plan.

Gore So it will be an interesting challenge to see nowadays with video monitors everywhere, it is like our whole life is on Skype it seems.

Lindskog Yes, that should make being in multiple places easier.

Gore I know what you mean. My office here at Yale is a couple blocks from the hospital and I had to telecon this morning. I had a meeting this morning that was just not going to work out for me to walk back and forth two blocks which seems kind of silly, but it was much easier to do a teleconference, but I think with the St. Raphael's thing, it is more so. What is the future as you see it, future direction of your field? What can we look forward to in sarcoma treatment?

Lindskog I think in terms of sarcoma treatment, there are really 2 avenues which hopefully won't be in the too far future. One is, as the molecular and genetic testing of these tumors gets more advanced, I think we really have a better idea of the similarities in the vast majority of these tumors which should help us be able to come up with better chemotherapies and biologic treatments for what actually has gone wrong. That is on the one hand. I think the other hand is we are really poised to I think perhaps a little further down the road, change from metallic reconstructions to be able to develop biologic reconstructions. Where

we are able to grow a new bone and put it back into somebody rather than having to replace it with a large piece of metal.

Gore And what are you going to grow it from? You are going to mix up some calcium and baking soda? Is it stem cell research that you are talking about basically?

Lindskog You know, stem cells in scaffolds that will essentially be able to regenerate large bulk segments.

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Gore Is that something we can look forward to in real time or is it still sort of 22nd century?

Lindskog It is probably optimistic to see it in regular practice in my career, but certainly steps are being propelled down that road.

Gore I have to say that I have been in this business since about 1990 and I trained a little before that and we were talking about molecular medicine back then and we were learning sort of oncogene by oncogene and tumor suppressor gene by tumor suppressor gene, and it did not feel like there was any real progress happening. There was a lot of stuff, a lot of interesting scientific stuff, but I look back now, 20 something years ago, and I feel like what we were doing is light year's different than what it was. It would be very cool if the same is true in your field.

Lindskog Yeah, absolutely.

Gore Do you think that with this molecular testing and understanding the driving gene mutations and so on, will there ever be a time when we have drugs that reduce the tumors and we do not need surgery or there is probably always going to be a place for surgery?

Lindskog I think in orthopedic oncology and what I do, I think that it is unlikely that we are going to be able to get to the point where the damage that these tumors do before they are found is reversible. So, I am pretty comfortable in my job security.

Dr. Dieter Lindskog is Associate Professor of Orthopedics and Rehabilitation at Yale School of Medicine and Clinical Research Program Director for the Sarcoma Program at Yale Cancer Center. We invite you to share your questions and comments, you can send them tocanceranswers@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 format atyacancercenter.org. I am Bruce Barber and 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.