A Team Approach For Treating Sarcoma in Children and Adults
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Webcast
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Introduction

Andrew Schorr:
Sarcoma is a rare cancer, in children, usually found as cancer in the bones, in adults, more typically in the soft tissue. In either case it's serious, and you need to go to a specialized team. There is such a seam at the Seattle Cancer Care Alliance. We'll hear from the head of that team coming up next on Patient Power.

Andrew Schorr:
Hello and welcome to Patient Power sponsored by the Seattle Cancer Care Alliance. I'm Andrew Schorr. Several times we have talked with a true leader in the fight against sarcoma, and that is Dr. Earnest "Chappie" Conrad, who is the chairman of orthopedics at Seattle Children's Hospital. He's also director of the sarcoma service for the Seattle Cancer Care Alliance, and he's co-vice chairman of orthopedics at the University of Washington. Dr. Conrad has established over many years a very unique and internationally renowned center at Seattle Children's in helping children fight sarcoma and the research that can really move things along. We want to get an update from Dr. Conrad on, first of all, where are we now in the fight against sarcoma, different types in children, helping them grow, live and thrive. And also the overlap, if you will, with understanding and research of sarcoma in adults and how all of that works together and what's available for adults, teenagers, children affected by sarcoma who come for treatment here in Seattle.

Dr. Conrad, thank you so much for being with us once again.

Dr. Conrad:
It's my pleasure.

Andrew Schorr:
Well, let's talk about one area which you really helped pioneer here, and that is limb sparing in children. So it used to be years ago where a child had bone cancer or sarcoma, and the limb was amputated. Where are we now in our efforts? How far have we come in helping not only the limb be saved but also in trying to help the child grow?
Sparing Limbs of Children with Sarcoma

Dr. Conrad:
In the last 25 years limb-sparing procedures rather than amputations have been the most popular and effective treatment for adults and children with sarcomas. And it's what we do about 90 percent of the time, especially for kids with bone cancer.

Andrew Schorr:
Tell us what that means though. I know it's kind of difficult, isn't it, because a child would naturally grow, but you have a tumor that you're trying to cut out. How do you calculate what you need to do or what materials you may use to fill in to not only have the child be able to grow but also to try to limit the number of other surgeries you may need to do down the road?

Dr. Conrad:
For the typical child, the typical child is a middle-age teenager, they're 14 or 15, and they don't have a huge amount of growth left remaining in the most common location, which would be around the knee joint or in the lower femur. So that child is an easier child to do the surgery on because they don't grow more than an inch or so after they have their tumor out.

It's the younger child that's the big challenge, and we actually seem to see more commonly the younger children. The biggest challenges obviously would be a child under the age of ten because they're growing. If they're really young they can grow 10 centimeters, 10 or 12 centimeters, and emulating or trying to reproduce their growth is very challenging. We try to do it still somewhat mechanically. We have some fancy implants that will grow sort of magnetically, nonsurgically, but they still have a high complication rate and multiple surgeries.

Andrew Schorr:
Where are we now with helping these children? So, first of all, we're talking about a bone cancer--or it could be in some cases soft tissue, I know in adults more commonly in soft tissue--where are we now with our knowledge of sarcomas, different types, and our ability to help people live through it?

Dr. Conrad:
That's a great question. Unfortunately I think we're at about at half time of the game. We've made--these children started with a survival in the 70s of 20 or 30 percent. Their survival now at five years, their chance of living is about 75 percent, so we've helped a lot of children. The success rate with saving their leg is somewhere between 50/50 and 75 percent at five years, and we've made some pretty significant improvements in the mechanical total knees that we use for those children that lower the complication rates. But the more success you get the more they want to do, and that makes it a little more challenging. But now we have better techniques for making these fancy bionic knees work, and they really do work better. The mechanical knees in the teenagers work well. Again, still, growth
is a challenge for us, but it is a pretty reliable procedure. It does sentence the child to consuming almost a lifetime of orthopedic care, and I think that's the issue we're trying to focus on now.

**Andrew Schorr:**
So helping a child, then, not just survive the cancer but have a high quality of life orthopedically.

**Dr. Conrad:**
That's clearly better than having an amputation the vast majority of the time, but it is--it does assume some risk, and it does assume some need for multiple procedures. That's not really escapable. We'd like to lower that risk, and I think we're just beginning to do that now.

**Andrew Schorr:**
Dr. Conrad, now, at Seattle Children's you've worked hard to have a multidisciplinary team because for you as a surgeon but also as a leader of the team there are a lot of people who have to work together. Tell us how fine tuned you feel that is now and how important that is.

**Multi-disciplinary Team for Sarcoma Patients**

**Dr. Conrad:**
Well, it's taken 20 years, but I'm really pretty proud of the team. We have a great team at Children's and we have a great team at the University and SCCA. That team really involves an oncologist working with a surgeon, working with a pathologist and a radiation therapist and other surgical partners. It really involves being in clinic together and being in conference together at a weekly basis and really sort of hashing out some of these challenging issues. It's a humbling business. There are lots of outliers that are constantly giving us sort of challenges week by week, and it's really critical to have that chemistry and those communications to be able to really provide the kind of care people deserve for these problems.

**Andrew Schorr:**
You mentioned about outliers, and I alluded to earlier different types of sarcoma. So whether you're talking about adults or children tell us about the diversity, if you will, of sarcoma and the challenges that presents.

**Dr. Conrad:**
So sarcoma is a malignancy of connective tissues. We like to say the tissues that hold you together, bone and muscle and tendon and nerves and arteries. And in kids it's mostly a tumor--most of the tumors are benign tumors. They are in the skeleton, and then there's osteosarcoma and Ewing's sarcoma, which is the most common bony sarcomas, and they get a smaller number of soft tissue sarcomas. In adults, people in their 20s, 30s, 40s, 50s and 60s, they mostly get soft tissue sarcomas with a smaller number of bone cancers that actually start in bone. So we
focus on soft tissue sarcomas in adults with a small number of bone tumors, and a larger number of bone cancers in children with a smaller number of soft tissue tumors.

If you take the subtypes for bone cancers there's only a few subtypes, osteosarcoma and Ewing's. If you take the subtypes in soft tissue sarcomas, there's 10 or 20 subtypes, at least 10 common subtypes, and each of those subtypes behave a little differently than the next and respond to a different drug. So in the adult world one of the challenges we have is in finding a particular drug that's going to be effective for high-grade tumor and control that tumor and keep it from metastasizing vis-a-vis the subtype, the molecular subtype of the tumor. We spent many years defining those subtypes under the microscope, and now we're trying to do it with a DNA fingerprint and with imaging, and finding drugs that are going to really be effective for the different subtypes is going to be the second half of the game.

Accurate Diagnosis in Sarcoma

Andrew Schorr:
Now, when people get to you they probably have a confirmed diagnosis of sarcoma, but around the country, maybe around the world, there are probably a lot of people where, A, it is not seen as sarcoma, or it's not understood which type it is. How can we help people who are listening to this get an accurate diagnosis?

Dr. Conrad:
Your first treatment and your first diagnosis is critical. It's not like starting school as a child and making up for a bad first grade with a good second grade and third grade. Once you get a bad start with a malignancy, especially a sarcoma, it's hard to make up for the losses. So your first treatment is critical. Your first diagnosis is critical, and it's really important that people get--even if they don't travel to a center, a sarcoma center, it's really important that they get some kind of opinions and confirmation from some sarcoma experts, and they're all over the regions, about confirming their diagnosis its accuracy and what the treatment plan is. It's really critical for people with high-grade tumors.

Biology of Sarcoma Tumors for Adults and Children

Andrew Schorr:
Now, let's talk about biology for a minute. I've heard from you before that the biology of tumors, sarcoma, in teenagers, let's say, seems to be different sometimes than it is in adults. What's going on there?

Dr. Conrad:
We'd like to know exactly what's going on. It's actually becoming one of our major focuses is why an osteosarcoma in a 15-year-old is so different in a 30- or 40-year-old and so much more difficult to treat. Some of that has to do with the age of the patient, and some of it doesn't. The age of the patient we can sort of deal with. You can't give the same chemotherapy to a 40-year-old that you can to
a 15-year-old because they just don't bounce back as vigorously as a 15-year-old. But there are some biologic difference, and it's all at the molecular level, and it's fairly complicated biology, and we're just beginning to understand some of those mechanisms and explain what the biologic predictions would be for what drug would work for which tumor. That's going to be critical to us really solving some of the challenges for patients with tumors that are resistant to first-line treatment.

Andrew Schorr:
Now, I mentioned at the outset here in Seattle and through the Seattle Cancer Care Alliance we have a lot of sarcoma resources brought together both for adults and children, and there's sort of an overlapping and a sharing of knowledge and resources. Tell us about that, and I was, for instance, thinking about PET scanning. You and I have talked about that before and trying to see whether certain therapies are working, and how do resources, for instance, imaging resources like that, get shared so that people can get the best care no matter what age they are.

Dr. Conrad:
So PET scans have revolutionized the diagnostic and early evaluation for sarcoma patients and many other cancer subtypes because a PET scan can help us decide whether you have a tumor that is at risk to metastasize, whether you really have what we call a high-grade tumor, because we struggle with sarcomas under the microscope. They are very challenging even for the experts, and to have a confirmatory test on top of the microscopic pathology is really important for sarcomas. So that's the first goal.

The second goal is if we do a PET scan when you have your biopsy and we decide you need chemotherapy we can repeat it after your first two months of chemotherapy, and we've actually shown that in those first two months you really get your first obvious change in your tumor from your chemotherapy if it's going to get better. So within two months we can tell you pretty reliably with a PET scan whether your chemotherapy is being effective enough to continue or whether we need to change to other drugs or just not give more drugs. And that early sort of efficacy if your tumor is in place has been really a critical improvement in making decisions quickly for people with high-grade tumors.

Andrew Schorr:
I understand this sort of imaging is really renowned here in Seattle.

Dr. Conrad:
It was pioneered in a very impressive imaging program run by Ken Krohn and his colleagues and Dr. Janet Eary and several other of our radiology colleagues at the University of Washington. It started with sarcomas and lymphomas and brain tumors. It's now extended out into the more common tumors, and it is critical imaging for all patients with high-grade tumors.

Andrew Schorr:
All right. Well, let's apply this to sort of individual situations. So a parent finds out somewhere in the country that their child has--it's suspected that they have a very
rare cancer or sarcoma, maybe something that their pediatrician has never seen, so from what you said earlier it's very important that they get connected with a specialty center such as yours. When they do, what happens next? So walk us through understanding what's going on with that child, if surgery is needed, how you determine how aggressive and when. Just walk us through what might be a case, if you will.

Dr. Conrad:
So we like to see everybody within the week. We see the child. If they've not had a biopsy they need to have an MRI. For soft tissue sarcoma and also for many of the bone tumors they get an MRI, and we also check to make sure there's nothing going on in the places where the tumor goes, such as the lung. And then they have the biopsy. If they've already had the biopsy and we're seeing them as a new patient then we need to see the actually tissue slides, the pathology slides from that biopsy so that we can review it and the x-rays. When we have the patient and their family and the initial x-rays, usually the MRI, and the pathology slides, we review all that together, and we get the team together, and we discuss it at conference, and we give them a recommendation for treatment about whether they have a high-grade tumor, and if they do what kind of chemotherapy they need to have, what kind of surgery, what kind of radiation therapy. And we will describe a plan based on the patient's diagnosis, the grade of the tumor and whether they have any disease that's gone anywhere else.

Andrew Schorr:
All right. We're going to continue a discussion of what might be a journey which could be a life-long journey, as we've talked about earlier, when we continue our discussion with Dr. Chappie Conrad, a renowned expert in sarcoma in children and in adults, right after this.

Andrew Schorr:
Welcome back to Patient Power as we continue our discussion on sarcoma in children and also the understanding of how the knowledge that's gained in sarcoma in adults, how all that works together and hopefully as we make more progress in these rare cancers both in the bone and in soft tissue. And we're visiting with Dr. Chappie Conrad who is the chair of orthopedics at Seattle Children's, and he's director of the sarcoma service at the Seattle Cancer Care Alliance.

Dr. Conrad, following our journey, if you will, related to parents and a child who come to you maybe from afar related to sarcoma, you make a recommendation. So, let's say, would surgery, let's say, in cancer in the bone typically be first? Might there be any drug therapy, and then how that might rule out--and you can define the example because I know everybody's case is different, what that might mean over weeks, months or even years.

Dr. Conrad:
So the first decision is whether the tumor has a risk of metastasizing and whether it is what we refer to as high grade. If that's the case then chemotherapy comes
first. It comes first because their biggest challenge is to keep tumor out of metastatic areas, spreading elsewhere. And early treatment is better, and we can evaluate whether the treatment is effective if the tumor is still in place. So the normal reaction to just take the darn thing out and get it out of me is not the best reaction and method of treatment for these patients. The best method of treatment is to give them two cycles of chemotherapy and see if that's going to be effective on their tumor, and that's the model we've promoted in Seattle for the last 20 years. It's a very effective model, and PET scanning has made it a very, very quick assessment.

After they've had their first two cycles they may or may not get more chemotherapy depending on the location of their tumor and its subtype. And then they'll have surgery, and surgery will happen after chemotherapy. They may or may not get some radiation therapy just before surgery or just after surgery, but radiation therapy is another important adjuvant or additional treatment in addition to the chemotherapy. So it's basically a chemotherapy sandwich with surgery in the middle. They get chemotherapy early on for high-grade tumors before their surgery, they have their definitive surgical procedure, and then they have chemotherapy and radiation therapy afterwards, and that's the basic model for high-grade tumor. It's the basic model for osteosarcoma in children.

**Long-Term Survival**

**Andrew Schorr:**
All right. In that situation, now, where are we with the hope of curing it and long-term survival?

**Dr. Conrad:**
The cure rate is higher for children under the age of 20 than it is for adults. The average survival for a child with a high-grade sarcoma whether it's in bone or soft tissue is about a 75 percent survival rate over the first five years, and very few of them fail after that, but there are some failures after five years.

In the adult world it's much closer to a 50/50 game with high-grade tumors. About 50 percent of the patients will survive five years, and 50 percent will not. It's very dependent on the tumor subtype, the age of the patient and the size of the tumor.

**Andrew Schorr:**
That's right. It's certainly not a one-size-fits-all prediction at all. And I would say even when the statistics may be not in someone's favor or in someone's favor you need to have that personalized discussion with your clinical team. Dr. Conrad, so therefore what follow-up might somebody have. And in the case of a teenager, for instance, who had that one surgery, might they need others?

**Dr. Conrad:**
If they have a bone tumor and they get a fancy mechanical knee, they have a pretty significant risk of having multiple procedures. It's somewhere between 25 and 50 percent, depending on the age of the child. So they have multiple...
procedures for sure when they have bone cancer as a young child. But most of them have good function, and most of them have an effective knee that they can use. They can't play high school football, they can't do vigorous sports, but they do have a very functional knee that gives them good daily function, and they can do sedentary things in sports, like swimming and golf and cycling, and their function is pretty good. It's better function than an amputee would have.

**Andrew Schorr:**
In either case, whether it's a child or an adult though, they will be followed closely over many years.

**Dr. Conrad:**
Yes. All of them are followed five years. When they have a high-grade tumor they're followed every three months for two or three years and then every year for an additional couple of years. And then they go into long-term follow-up programs where there are people that will assist them with the overall general health after treatment, which are critical programs at least to be connected to every couple of years.

**Andrew Schorr:**
Right. That's my vote for the survivorship program. Certainly there's one at the Seattle Cancer Care Alliance now and how critical it is for a cancer survivor so have that sort of specialized assessment. And that brings me to a question. Either because of the drugs or the sarcoma itself, is there a higher likelihood that someone might have another cancer that could follow later on?

**Dr. Conrad:**
They do have a slightly higher risk. After going through chemotherapy and radiation therapy, they have a one percent sometimes a two percent risk of having a secondary leukemia, and they're followed carefully for that. And that's more common in some of the harsher sarcoma subtypes. We know how do identify those risks by the subtype of the sarcoma, so it doesn't apply to all the patients but it does apply to some of the patients.

**Andrew Schorr:**
All right. We've gotten a few questions in. One relates to diagnosis. We talked about this a little bit earlier. Sandra wrote in from San Francisco and she says, "My daughter is waiting on biopsy reports. They have been sent to several places, and the diagnosis has been, quote, favorable, for melanoma two times, but one melanoma oncologist believes it is a sarcoma in the cartilage. Are there similarities with these two cancers? How do we know which treatment to do?"

**Dr. Conrad:**
There are similarities between melanoma and sarcoma. It makes the diagnostic separation occasionally extremely difficult. It's a little bit unusual in a child. It's more of an adult scenario, and you don't usually confuse a cartilage tumor with a melanoma, but there are exceptions to that too. If you had that scenario my advice would be to go to some of the bigger centers with established pathology
Andrew Schorr: Dr. Conrad, you mentioned that at Seattle Children's, for example, you try to see people within a week when they're referred to you, and that sounds like there's a speed involved. Yet here we have people from maybe anywhere in the country or even outside the country trying to get an accurate diagnosis before they pull the trigger on any treatment plan. So help us understand the speed at which treatment would be required, the right treatment to really knock back, hopefully cure one of these sarcomas.

Dr. Conrad: Whether it's a child or adult my advice is not to have a delay more than six to eight weeks in terms of initiating treatment. And the extreme limit would be two or three months. But as a general rule we like to not have delays in therapy at about six weeks. Six weeks is a long time when you're initiating a plan. Usually you can, you know, you can only generate so many slides from any one piece of tissue, so the slides have to sort of be shared around. So if you're getting two different opinions it's hard to orchestrate that, but you need to get those opinions and make a decision and proceed with therapy, and I think the six-week rule is a pretty good basic rule.

Andrew Schorr: Dr. Conrad, over many years you've met a lot of parents and you've met a lot of kids and you've dealt with adults as well and families. I've read that you have a high level of respect for them, and I can just imagine a parent, now, trying to navigate what's right for their child, and then, as you mentioned, some treatments can be pretty aggressive. These people have a lot of courage, don't they?

Dr. Conrad: It's incredible. The courage of the average man and woman is, they're not average people, and I'm astounded. It's a source of strength in a sometimes frustrating, humbling profession to see the courage of people when they're staring at the sarcoma tiger and all the challenges, even when they're failing their therapies. But people are predictable, and they want to have what's best for their family, what best for themselves, and are especially passionate about what's best for their children. You don't stay in this business very long if you can't tolerate high expectations, and it has a lot to do with communications and how you respond to new patients and to failures. We try to be very, very responsive to our patients and their families.

Andrew Schorr: Now, when a diagnosis comes to sarcoma typically the family has never heard of it, really, or isn't clear about it, and then there are all these subtypes. We got an e-mail in just a couple minutes ago from a gentleman named Remy, and he said he
was just recently diagnosed with synovial sarcoma on his left knee, and it's been seen that there are metastases to his lungs. So he's trying to get a handle on this. How does he find out what treatments are available for that?

**Dr. Conrad:**
He can call around his regional center. He can go to the national guidelines. Most people are doing lots of computer searches. The NCCN guidelines are a great basic information source for patients who want to know what the basic steps are for treatment. In terms of the details of what you should have as a metastatic synovial patient, then I think you need to sort of talk to one or two experts on what they think. The best treatment for metastatic disease is some kind of chemotherapy and evaluation of the responses, but there's a lot of good basic information on the internet. I think the NCC guidelines are the guest beginning source for treatment protocols for sarcomas. It has all the different cancer types in that system, and sarcomas is pretty well developed, and the experts have worked on that together from around the country.

**Progress in Treating Sarcomas**

**Andrew Schorr:**
Dr. Conrad, you mentioned when you're talking about sarcoma in terms of the patient's perspective that they're faced with the sarcoma tiger, and you as a leader in the field, you've been faced with it, too. What's your dream for taming the tiger? How much progress have we made? You talked about sort of being at the 50-yard line or halftime, and what are the next challenges? How are we doing? How far do we have to go? And do you have hope?

**Dr. Conrad:**
I have a lot of hope. I think in the next five to ten years, in the next five years we'll have some new drugs. We already have a couple of potential candidates to supplement sort of the first team. We have a good first team set of drugs and a pretty good second team. You need three or four teams or five or six to fight these tumors because many of these tumors are resistant to the first-line therapy or the second-line therapy. What we desperately need are some new drugs or some new methods for managing these high-grade tumors. We can assess response very quickly. We're getting better at surgical treatment and local control, but we desperately need new biologic therapies that will help save the people that are not responding to first-line therapy. And that's about half of the high-grade patients, so it's a large number of patients.

**Andrew Schorr:**
Now, that leads to clinical trials. Now, I know most children now are in clinical trials, and I know it would be helpful for many adults to hopefully maybe get tomorrow's medicine today and answer questions for everyone by being in a trial. Do you want to speak about trials and where we are with that now?
Dr. Conrad:
Trials are absolutely critical. The children that we treat, about two-thirds to three-fourths of the children that we treat are on clinical trials, and it's because we all consider, there are smaller number of tumors so it's easier to focus on them. We all want our children to have the best treatment so they're more intensely evaluated than the average adult, despite our best efforts.

But some adults have a negative reaction to clinical trials, and I would like to argue against being negative about trials because the trials allow us to evaluate the effectiveness of therapy, and they're absolutely critical for an unusual sarcoma type and for high-grade sarcomas. Our oncologists in my world are not doing their jobs unless they are doing a good job of getting people on clinical trials so that the patients can be evaluated after the fact. Otherwise you just cannot evaluate what happened and what went wrong with therapy unless they're on a trial. Clinical trials are really essential.

Andrew Schorr:
It's a relatively small number of people who are affected by sarcoma, but certainly scary diagnosis, and I think this really speaks to people working together as a community. It's a community no family wants to be part of but they find themselves, and then with researchers, clinicians such as you and your team, hopefully you can continue to make progress. I want to congratulate you on your achievements over decades now and wish you all the best, Dr. Conrad, with continued moving the ball forward in fighting the sarcoma tiger.

Dr. Conrad:
Thanks, Andrew. I appreciate your support for our patients.

Andrew Schorr:
Well, this is what we do on Patient Power. Thanks to the Seattle Cancer Care Alliance for helping us educate people around the world, and in this case about sarcoma, the great work that's done at the Seattle Children's led by Dr. Conrad and the work he and his team carry forward to adults through the University of Washington and other branches of the Seattle Cancer Care Alliance.

Thank you so much for joining us. Remember, knowledge can be the best medicine of all.

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