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00:00.000 --> 00:10.300 Support for Yale Cancer Answers comes from AstraZeneca, a biopharmaceutical business that is pushing the boundaries of science to deliver new cancer medicines. More information at astrazeneca-us.com.

00:10.300 --> 00:44.900 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about interventional radiology and liver cancer with Dr. David Madoff. Dr. Madoff is Professor of Radiology and Vice Chair for Clinical Research at Yale School of Medicine, where Dr. Chagpar is a Professor of Surgery.

00:44.900 --> 00:51.800 <vChagpar>David, maybe you can start by telling me a little bit about what interventional radiology is and what exactly it is that you do?

00:51.800 --> 02:02.500 <vMadoff>That is actually a great question because when I tried to tell my parents, they still do not even know, but what I will say is that interventional radiology is a subspecialty of radiology, it is approved by the American Board of Radiology, and basically what we do is we perform minimally invasive procedures that utilize advanced imaging technology to guide treatments of various medical conditions that in many cases once required surgery. So, I can actually give you an example if you would like? One example, and this is not oncology necessarily, but if you have a patient who is a pediatric patient and presents with appendicitis and has a large abscess and it is very difficult to treat by a pediatric surgeon, an interventional radiologist will go in and place a small drain such that the patient does not need to have a very large scar and can resume activities and be discharged from the hospital in a very short period of time. Otherwise, the patient will have major surgery and a small child for example may be in the hospital for up to a month.

02:02.500 --> 02:20.400 <vChagpar> So, interventional radiology is really x-ray doctors who do interventions, things like putting in tubes, putting in drains, maybe ablating cancers, those kinds of things?

02:20.400 --> 02:20.5000 <vMadoff>Exactly.

02:20.5000 --> 02:46.800 <vChagpar> And that brings us to the whole world of cancer. Historically when we talk about cancer on this show, we think about primarily 3 main modalities. We think about surgery, we think about chemotherapy, and we think about radiation. Tell us where interventional radiology can potentially have an impact in terms of supplementing those 3 big buckets?

02:46.800 --> 03:45.300 <vMadoff>Yeah, great question. Over the years, I must say that in my experience with various organizations such as the Society of Interventional Radiology, we have been making a push towards becoming what you call the fourth pillar of oncologic care, one being surgery, the other being

medical oncology and the third being radiation oncology. Now, radiation oncology actually developed in a very similar way to what we consider interventional oncology; however, they do not use needles, catheters, wires, etc., they more use external radiation. So, based on years of experience and the opportunity for, or I should say lack of opportunity for other modalities to really effectively treat the cancer, interventional radiology or what I would again say interventional oncology has had an ever increasing role.

03:45.300 --> 04:12.500 <vChagpar> But just to push back on that, and maybe seek some clarification, we have had on this show some radiation oncologists who for example have done things like accelerated partial breast irradiation with catheters or have done seed radiation for prostate, are those radiation oncologists or are those interventional radiologists or are the lines there blurring?

04:12.500 --> 05:12.400 <vMadoff>Well, in actuality, the lines are blurring a bit. I mean we do have a lot of collaborations with radiation oncologists, and in fact, there are a number of opportunities where a radiation oncologist would refer a patient to interventional radiology or vice versa. And a lot of it would depend on the stage of the disease, for example, we are talking about liver cancer today - in the setting of a patient that has maybe a solitary or maybe a few lesions or tumors in the liver, a radiation oncologist could possibly take care of it; however, if the lesions become too voluminous or the tumor burden is too great, they really need more of a regional approach, in which an interventional oncologist would place a catheter into an area of the liver and you would be able to infuse or administer the treatment intraarterially as opposed to through external means.

05:12.400 --> 05:39.600 <vChagpar>Usually on this show when we talk about people putting things into arteries or blood vessels that kill off cancer cells, usually we are talking about chemotherapy, which falls into the realm of medical oncology. So, are you talking about interventional radiology doing what was done by the medical oncologists?

05:39.600 --> 06:15.500 <vMadoff>Well, years ago, back in the 1950s I would say and even in the 60s, a lot of surgical oncologists would place catheters externally or pumps into the artery supplying the liver or they would ligate the artery going to the tumors, but over the course of the last few decades, it has been shown that that has not really been effective and that you really need a more direct approach that targets to the cellular level by using a lot of the techniques that we can use today.

06:15.500 --> 06:26.900 <vChagpar> And so, you are still using chemotherapy as you deliver these drugs with these catheters that you place, is that right?

06:26.900 --> 06:44.500 <vMadoff>Correct. So, as an interventional oncologist, I administer my own chemotherapy in terms of the procedures that I am doing. Now, I do not administer systemic chemotherapy that is really the realm of the oncologist, but that is what we have been doing probably since the 1980s.

06:44.500 --> 08:08.300 <vChagpar>Just to clarify it for our listeners, it is kind of like a fourth pillar in a sense that you have surgeons who take out tumors and historically they would place catheters because they were the only ones who knew how to get the catheter to the right blood vessel if they were going to give chemotherapy to a very localized area. You have the radiation doctors who give radiation, usually from the outside, external beam, but sometimes they can do that through catheters too on the inside and then you have the medical oncologists who give chemotherapy or other systemic therapy through the blood stream, but usually that is to get it to the bloodstream all over the body, but what you are talking about is really putting in catheter nonsurgically through what we call a percutaneous kind of route. Through the skin you are able to under x-ray guidance put your catheters into a position where they can get right up to the tumor and deliver the chemotherapy right to that tumor without them having a big surgery and really being able to get chemotherapy to a localized area, is that right?

08:08.300--> 08:38.900 <vMadoff>I do not think I could say it any better myself, but I do think that what you are saying is totally true in the sense also, even though they are minimally invasive procedures, actually they do have some side effects. However, in past years, due to cautionary reasons, patients had been admitted to the hospital, but now a lot of these therapies even if they are very significant therapies, can be done entirely as an outpatient.

08:38.900 --> 09:04.700 <vChagpar>Let's talk a little about that because when we talk about chemotherapy, people usually get all kinds of ideas about what chemotherapy is like, I am going to lose my hair, I am going to be sick, I am going to feel nauseous, but the kind of chemotherapy that you give although it is chemotherapy, does it have all of those side effects or are there other side effects/complications that you are more worried about?

09:04.700 --> 10:57.600 <vMadoff>That is a great question. Typically, there are some side effects from these procedures. Now, the rationale for administering intraarterial therapy to the tumor is a number of reasons: One is, it is based on the vascular supply of the tumor. Typically, the artery is nearly 100% of the tumor's vascular supply. So, if you are giving a chemotherapy intravenously, a very large dose of it may not end up in the tumor itself and therefore, you may have, I would not say an unsuccessful treatment but you may not have an optimized treatment. Nowadays due to a lot of advanced technology from many of the vendors that we use in interventional radiology, they have a lot of software that allows the interventional radiologist to simply guide the catheters almost to the level of the tumor. So, therefore, you may get very little what is called non-target embolization or non-target therapy which means that some of the therapy may be going somewhere you do not necessarily want it. That being said, your question really had to do with systemic effects and the goal here, at least in interventional radiology, is that you can administer a much higher dose to the tumor yet you do not really get the same side effects as you would from a systemic therapy, like if you look at the systemic indices on how much

chemotherapy is in the bloodstream, it is much lower with the transarterial therapy.

10:57.600 --> 11:46.600 <vChagpar>Essentially because you are putting a catheter right up to the tumor, getting it right into the artery which is its main food supply and pretty much killing off all of the cancer cells and delivering your chemotherapy directly to that tumor so that it does not go everywhere else, so it does not go to your scalp and kill off all of your hair follicles, you do not lose your hair and it does not go to your GI system necessarily, so you do not necessarily get sick, but it kills off the cancer cells right where you want it, that is what you are saying? So, then the question is, how come that is not offered to everybody, I mean it sounds like it is a really cool thing to do. For example, there are a lot of people who have breast cancer, how come we cannot do that in breast cancer?

11:46.600 --> 12:42.500 <vMadoff>Well, first of all, a lot of what was done in interventional oncology was started in the liver and a lot of the reasons for that is literally that it was the disease that had really no other treatment, there were really no good surgeries back then and it was, I would not say experimental, but there were a lot of people that believed that these therapies in fact worked. Today, I believe that there is now a lot of other therapies that other oncologists or radiation oncologists or surgical oncologists can offer that can directly compete with what we do and that being said, I do think that some of the interventional oncologic interventions are under-utilized.

12:42.500 --> 12:46.100 <vChagpar> And maybe some of it has to do with anatomy too do you think?

12:46.100 --> 12:48.900 <vMadoff>Absolutely.

12:48.900 --> 13:26.800 <vChagpar>The liver is a great organ to think about interventional radiology or interventional oncology because it has got lots of blood vessels going to it, and when we look at the anatomy of the liver, the liver for our listeners is broken up into these lobes and each lobe is supplied by particular arteries and has particular veins that drain it, and so, you are able to especially when you have got a bunch of disease in a particular lobe, go and kind of kill off all the cancer cells in that lobe by putting your catheter right into the artery that goes to that lobe, is that right?

13:26.800 --> 13:57.600 <vMadoff>Well, I wish it would be so easy. I mean I do agree with you that is the plan, but there are a lot of tumor cells that are resistant to the therapy because the liver is probably one of the largest organs in the body. The amount of material you can give is finite, so you may not really be able to get every single cell. There are other ramifications which include underlying liver function, you really need to see how patients are able to tolerate the therapy.

13:57.600 --> 14:16.900 <vChagpar>It sounds like this is a good therapy for a lot of patients but may not be completely the silver bullet, we are going to find

out more about right after we take a short break for a medical minute. Please stay tuned to learn more about interventional radiology and liver cancer with my guest, Dr. David Madoff.

14:16.900 --> 14:31.900 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, a biopharmaceutical business with a deep-rooted heritage in oncology and a commitment to developing cancer medicines for patients. Learn more at astrazeneca-us.com.

14:31.900 --> 15:14.300 This is a medical minute about survivorship. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life-changing experience. For cancer survivors, the return to normal activities and relationships can be difficult, and some survivors face long-term side effects resulting from their treatment, including heart problems, osteoporosis, fertility issues and an increased risk of second cancers. Resources are available to help keep cancer survivors well and focused on healthy living. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

15:14.300 --> 16:00.900 <vChagpar>Welcome back to Yale Cancer Answers. This is Dr. Anees Chagpar, and I am joined tonight by my guest, Dr. David Madoff. We are talking about interventional radiology and liver cancer, and right before the break, David, we were talking about the fact that this whole area, using x-rays to kind of guide catheters so that you can deliver chemotherapy directly to a particular tumor or particular lobe of the liver, particular region to kill off cancer cells in that area sparing a lot of the side effects that go on in the rest of the body, but right before the break, you said there are other ramifications, and this is not the silver bullet, there are other things to consider, it is not quite so simple. Tell us more about that.

16:00.900 --> 16:48.700 <vMadoff>There are a lot of areas that we need to consider as I had stated it seems that patients need to have a much more healthy liver in order to get a lot of these therapies. Patients that are jaundiced, for example, their skin is yellow, their eyes are yellow or they have really poor liver function, may not be really amenable at all to this. There is also a lot of, as you alluded to earlier, anatomical variations which may not allow a catheter to be placed to the tumor, and sometimes the tumors are so large that you may not really be able to make an effective therapy.

16:48.700 --> 17:30.200 <vChagpar>But it sounds like all of those things might be things that would also obstruct us from doing other therapies. For example, if somebody has got a large burden of tumor, well surgery might not be an option if you do not have enough residual liver function, radiation might not work because there is too much disease and systemic chemotherapy may or may not work simply because of burden of disease and would have all kinds of toxicity, so it sounds like this would still be a good option even in those cases compared to the other options that are out there.

17:30.200 --> 17:58.400 <vMadoff>Well, in those scenarios, I would agree that

interventional radiology probably does offer an opportunity for therapy that others may not be able to do or the goal in all of this is really to alter survival, and if we are not altering survival, we are not improving patient outcome in a given patient, we may not have the answer either.

17:58.400 --> 18:47.200 <vChagpar>And when you talk about that, I think that is one of the underlying themes of a lot of cancer management, which is each modality may not in its own right have the answer, which is why so often on this show we talk about multi-disciplinary team management. Are there cases that you can tell us about where interventional radiology actually might make it easier for the other modalities to be helpful or where you can use a combination, maybe interventional radiology to shrink the cancer and then surgery to take out the cancer and then systemic chemotherapy to make sure that they do not metastasize other places and radiation therapy for local control, does that work?

18:47.200 --> 21:14.700 <vMadoff>There are a couple of ideas that this brings up. One, is that in the setting of liver cancer, really what is considered curative is surgical resection and/or transplantation. So, one of the things that an interventional radiologist can do is at least decrease the tumor burden to the extent that patients can actually get their surgery in patients that are on the transplant list, sometimes they will have tumor burden, or want to be on the transplant list I should say, they may have tumor burden that is just outside the criteria that will allow them to have this, so an interventional radiologist can go in there and shrink the tumor such that the patients can be maintained on the transplant list, and the reason why this is so important is because the transplant waiting time is very, very long, having been in New York for the past 8 years before coming to Yale, I can tell you that the wait time is probably about 18 months to 2 years, so if you could either A - bridge the patient to transplant which again is just maintaining them within the criteria or B - shrinking the tumor which is called downstaging because you have bridge transplant and downstaging. The other procedure that we can do and this is something that I have been involved in actually for the last 20 years is a procedure called portal vein embolization and this is a procedure which goes on the ability that the liver is one of the organs that actually can regenerate. So, in patients that have what looks like surgically resectable disease; however, they may have insufficient liver volume or liver function after the major surgery, we can go in and plug up portal veins which are, if you look at the anatomy, 80% of the liver's blood supply is portal vein and 20% is hepatic artery; if you can plug up with material a lot of these portal veins and divert flow away from the liver that is going to be resected and towards the liver that is going to remain, the liver actually can grow before surgery making the surgery much easier for the surgeon and the patients could have a much better postoperative course.

21:14.700 --> 21:38.900 <vChagpar>I think that is one of the things that is really critical to understand and one of the things that many medical students find fascinating, at least I did, was that the liver is one of those organs that can actually regenerate itself to a large degree even in adulthood, so you take off

somebody's arm, their arm does not regenerate, but you can cut out part of the liver and the liver can magically grow back some of that liver function.

21:38.900 --> 22:13.900 <vMadoff>Exactly. So, what I would have to say is that we can treat a lot of patients that have very large disease burden, provided that they do not have disease outside the liver and you could, like I said earlier, the liver is a very large organ, you could stop blood flow to approximately 80% of the patient's liver, portal veins and yet they can still go home the same day as an outpatient because it is only a tiny little incision that you make to do all this work.

22:13.900--> 23:24.700 <vChagpar> And it sounds like this interventional radiology really is helping in that multi-disciplinary approach to taking care of patients who have liver cancers. Now, something that a lot of our listeners may be curious about is, when we have talked in the past on this show about liver cancer, there is always this kind of fine line between primary liver cancers, the cancers that start in the liver and hepatic metastases, cancers that start somewhere else and go to the liver because as you say, a lot of the blood supply ends up going through the liver, and so, the liver tends to get metastases or cancer deposits from cancers that have started somewhere else - in the colon and other places, so when you are talking about all of these interventions with interventional radiology that can deliver chemotherapy to a particular area or help with the surgical resection of these cancers in the liver, are you talking primarily about primary liver cancers, about metastases or does it really matter?

23:24.700 --> 23:44.600 <vMadoff>Well, in terms of the overall prognosis and in terms of the overall therapeutic plan by the oncologic team, I think that it does matter; however, a lot of these procedures that we do offer can be used in both circumstances.

23:44.600 --> 23:58.900 <vChagpar>So, with regards to, if you have a primary liver cancer, interventional radiology may play a role, but if you have a colon cancer for example that has got metastases to the liver, interventional radiology still may play a role.

23:58.900 --> 24:59.200 <vMadoff>Yes, now typically in the setting of colorectal cancer, systemic therapy is usually the first-line therapy. And when it fails or when the patients run out of options, we often get involved. Now, that being said, there is data coming out to show that if you can do for example, we did not really discuss this yet but administering radioactive beads into the liver by doing this earlier and by doing this in combination with systemic chemotherapy, patients may actually have better outcomes. So, it does portend having a collaborative approach with all of these disease types; however, again, I would really stress that we can offer opportunities for treatment, but it really depends on the disease type, the oncologic plan, the underlying liver function, etc.

24:59.200 --> 26:00.600 <vChagpar>So you kind of need a team approach here, which is a mantra that we keep singing on this show where all of these professionals really get together, put their heads together, figure out the optimal

plan for an individualized patient and tailor that accordingly. You mentioned placing radioactive beads and I wanted to get to this whole concept because there has been both in the late literature and a lot of talking about ablating cancers either with radiation like radioactive beads or with laser or with microwave or with RFA, which is radiofrequency ablation, and one would think that all of these really require a directed approach, which presumably could use radiology, like x-rays or ultrasounds or MRIs and that kind of thing, so tell us how interventional radiology plays a role in doing all of that.

26:00.600 --> 27:12.400 <vMadoff>In terms of all those different modalities that you mentioned, they have very different roles. Now, what we do is called local regional therapy. That means, local therapy is really targeted therapy to a very select cancer or a subset of low-volume disease, whereas regional therapy is if you have disease really scattered throughout either one lobe of the liver or the entire liver. So, when you are talking about typically a radiation approach, you usually consider that to be a regional delivery. There is a new idea called radiation segmentectomy that can act like an ablation. Ablation is simply like doing a biopsy and instead of just taking tissue, which we may do at the same time, you can either heat the tumor or you can freeze the tumor and that may have some dramatic effect in overall managing that particular tumor type, but again, those are typically reserved for patients with very small volume or low-volume disease.

27:12.400 --> 27:26.600 <vChagpar>And another place where interventional radiology of course comes into play and we talk about this all the time too is, you people are often the people who help us to get the biopsies when they are in places that we cannot reach in other ways, is that right?

27:26.600 --> 28:16.000 <vMadoff>That is exactly right. Because of the excellent technology that we have at this time, there is almost no place that we cannot get to. Of course, you have to be smart about it and you have to be able to understand the imaging, but by and large, biopsies are one of the procedures that we do that I would say may even have the most impact of any type of procedure that an interventional radiologist does. I mean, without understanding what the disease is, without looking at the genomic profile, which can change over time and as I am sure all discussed, we are now in the age of procedure medicine, we can really tailor therapy just based on a biopsy.

28:16.000 --> 28:38.800 <vChagpar>The other thing that I always find fascinating about interventional radiology is, as you kind of alluded to, you are in the world of high-tech, there is a lot of technology, there is a lot of imaging and a lot of cool gadgets giong on, which often means a lot of space for clinical trials. So, tell us what is new and hot and interesting in your world.

28:38.800 --> 29:17.900 <vMadoff>Well, I think right now, there are multiple clinical trials that are interesting. For one, doing embolization therapy in the liver with immunotherapy, so the idea is that you would treat a tumor, release antigens, give an immunomodulator and actually have your own body fend off

the tumor cells itself. There is also a lot of interest in pancreatic cancer where you can do a lot of really high-tech procedures in a disease type that has a very, very, very, very poor prognosis.

29:17.900 --> 29:43.200 Dr. David Madoff is Professor of Radiology and Vice Chair for Clinical Research at Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.