Dr. Erinjeri on Cryoablation - DTRF 2022 Patient Meeting Webinar #2

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Jeanne Whiting: So we'll move to our last presentation and this is from Dr. Joseph Erinjeri, who is interventional radiologist and physician scientist at Memorial Sloan Kettering Cancer Center. He's going to give us a presentation on cryoablation as a treatment for desmoid tumors. Thank you Dr. Erinjeri, we always appreciate your participation.

Dr. Joseph Erinjeri: No problem. It's can you hear me okay?

Jeanne Whiting: Yeah. It looks like you have a workday today anyway in your

Dr. Joseph Erinjeri: Yeah, we're in the OR and actually after this, I'll be back to the OR today. But it's always a pleasure to be here with the Desmoid Tumor Research Foundation. I think I think the real stars of the show at the Desmoid Tumor Research Foundation are the patients who are always coming up with great ideas to help push this research along.

And I can, you know, I know many of you are my patients and really have pushed me to develop new techniques in cryoablation. So, let me kind share with you, Let me get my screen. Oops. Let me get my screen shared and then we will kind of share where we're at right now with cryoablation for the treatment of desmoid tumors.

Make sure you're seeing the screen okay. Are you guys seeing the screen? Perfect. Okay, great.

Jeanne Whiting: Yes, we're good to go.

Dr. Joseph Erinjeri: Okay, perfect. So, as you know, desmoid tumors frequently recur after surgery, and we've seen many papers on this. And this is no secret. And this is what has influenced all of us in the community, to look for other treatments other than surgery.

And in fact in some studies, up to 30% of patients undergoing desmoid tumor resection will recur. And so, despite the high recurrence rate of surgeries it's still often the first treatment. And normally the way this goes is you've got a symptomatic desmoid patient and they frequently go on active surveillance for a while to see what the growth rate is and when they have progression, that's where we have this decision point between surgical resection or systemic therapy.

And then if there's disease progression after that it's usually systemic therapy. We call the group kind of before this line, the first line therapies, and we call the group after this line, the salvage therapies. So we often asked, what are the other therapies that could be used for primary or salvage therapy of desmoid tumors?

And there are several that have been tried. RFA, cryoablation, Hifu and now more more increasingly Deb-TACE, which I'm sure in some part of this Foundation seminar you've heard about. Today we're gonna talk mostly about cryoablation. We're all the concept of cryoablation is not so complicated.

We know what happens when you use an aerosol bottle and it gets cold when a gas expands rapidly. There is a physics effect called the Joule-Thompson effect, which basically causes gases like nitrogen, argon, or CO2 to cool when they rapidly expand. And so here is actually a prototype of the first cryoablation needle that was created.

And this is from the actual patent application. And what you, and by the way, it's not mine, it's somebody else's pictures. But here you inject argon through the center of a small needle. The gas expands near the tip that causes rapid cooling of the tip. And then the gas is vented out. The temperatures that can be achieved with this type of system are in the order of negative 150 degrees centigrade.

And interestingly enough you know, different types of tumors have different thresholds for dying. And you'll notice that in the second to last line here, you know, sarcomas in mouse have a very low temperature of about negative 60 degrees, and that's probably similar to desmoids. It's one of the reasons why aggressive cryotherapy is necessary to kill desmoids.

And if you just kind of lightly cool a desmoid tumor maybe to negative 10 or even negative 20, you may not get a really good effect. I won't bore you with some of the work we've done looking at the basic science of cryoablation, but I will tell you that what we know is there are factors that are involved with optimizing cell death and cryoablation, and one is the target temperature.

Colder temperatures are better, some are the time to target temperature- cooling faster is better. Some are the time at target temperature- longer is better. And then repeating the freeze thought cycles is also better. So we know of how to optimize cryoablation to make it more effective. I just wanted to show you one picture of what it actually looks like under a microscope when you freeze a cell.

This is actually a Chinese hamster ovary cell, and this is it's put on a special microscope where you can look at the stage actually cools to low temperatures. And you can see at negative three degrees, you can see these black ice crystals. They're black under this type of microscopy just starting to touch this cell.

You can see that once it reaches negative 20 degrees, you get you know, the ice crystals traversing the cells. And then at negative 40 degrees you can see the cell itself is completely frozen. And notice how it's no longer this nice spherical cell, but it's all irregular. That's cuz those ice crystals have actually broken the cell membrane and the cellular components have leaked out.

And so slow cooling is bad because it only causes cellular dehydration. Whereas rapid cooling causes this intracellular ice formation, which is the harbinger of cell death with cryoablation. I show this one slide and it isn't for self-promotion, but it's mostly to say that, and I've probably spoken at this meeting five times and it's taken a long time for me to publish a paper where I was able to I, I feel like strongly say that we think cryoablation provides disease control for extra abdominal desmoid fibromatosis comparable to surgical resection.

And and I would say this isn't published in some radiology journal where we have all our friends reading our papers. This paper was published in Annals of Surgical Oncology. It did take several years to get it published, even after we wrote the paper kind of convincing the editors of this journal that we thought this was an important piece of the literature that the, that surgeons should know about.

I wanted to show some of the data from this study, which came out in 2022. And this is non-randomized data where we took 22 patients who had cryoablation and 33 matched surgical patients that were matched using

propensity score matching. And when you look at patients that had one treatment with cryoablation versus one surgery, what you see is the curves are fairly overlapping and maybe as time goes on, surgery is a little bit better than cryoablation, but after multiple treatments and so where we can go back and touch up areas where the first cryotherapy didn't, maybe didn't work as well as we would've liked, you can see that cryoablation is actually you know, at least comparable and perhaps even superior if we had bigger numbers.

Now, I can't really say that you see the p values are both less than less or greater than 0.05, but we can at least say that the disease control is comparable both after one treatment and after multiple treatments. We looked at risk factors that would predict recurrence after cryoablation, and we found three strong ones.

One was the size of the tumor that is bigger tumors tended to recur more, that younger patients tended to recur more, especially those who were less than 25, as well as patients who were treated in the salvage setting or the recurrent setting did worse than those were treated in the primary setting.

And so another reason why we really in our multidisciplinary group here at Sloan Kettering, we kind worked together to try to move people away from surgery as a primary therapy towards other therapies like cryoablation. And when we produce this nomogram where we ask the question, depending on how many risk factors do you have, what is your risk?

You can see that for patients that have zero or one risk factor, these patients actually in our in our study actually had, we had no local recurrence. Whereas if you had two or more risk factors, you actually had, you know, a much higher local recurrence. So of course, we're always looking in our multidisciplinary group to find the patients that have the right risk profile to put forward as for cryoablation as their primary therapy.

The most common side effects that we tended to see post cryoablation were some degree of pain. Most pain resolved within hours. 50% of patients will go home the same day. 50% will go home the next day. In general, for the patients who do have pain, that pain can peak usually, frankly, around two weeks, not two weeks, seven to 10 days.

And that's because the inflammation continues to grow as the body is reacting to the dead desmoid tissue inside the body. Here's a case. This was a patient with a 30 year old 32 year old patient with a patient painful rectus desmoid. Here we are showing a picture where you can see the tumor here.

Now, under CT guidance, you can see that we've put some contrast to push the liver away from the abdominal wall, and we've got the cryo needle in place. And you see this low attenuation or dark gray ovoid structure. That's the actual ice ball. That's the ice ball forming underneath the skin. You can see that we've put some fluid in the skin as well to puff the skin up.

Then when we pull the needle out, because of this, it makes it much more clear. You can see the tumor, and then there's this lighter gray area, which is the ice ball surrounding the tumor. When we look at this patient 48 months post procedure, you can see there is almost you can almost not see where the desmoid tumor is, what happens to the tumor.

The body has a set of garbage collector cells called macrophages. They come in and eat up the dead collagen and take it away. Here's another patient who's a 20 year old in this case, with a painful right intrathoracic desmoid tumor. And you can see in a couple projections, it's quite large. It's trying to get in between the ribs here.

This is what a kind of a very large cryo case would look like. The patient is under anesthesia and we're putting, in this case it was like, you know, greater than 10 cryo needles into the patient. And then we're, you could see actually the frost that's forming over the needles as we're freezing.

Here's again, a couple of pictures with the cryo needles in place. You can see the low attenuation ice ball in both the right and left images. One with the needles in place and one with the needles removed. This was the pre picture. You can see 12 months post. We've got a small area of recurrence and as I mentioned, this is okay because with cryoablation, since it's minimally evasive, we can go back in and touch that area up and that's exactly what we did.

We put another needle into that area and after three years you can see this area continues to not have enhancement anymore, and the area continues to shrink. Here's another patient. Just an example of doing cryoablation in a difficult location. Here is a patient with a desmoid tumor that is deep to a implant.

We weren't sure how this would affect the implants. The plastic surgeon was willing to take the implants out for us to do this procedure. We said let's give it a shot and see if we can do this without injuring the implant. And you can see we've actually got the ice ball surrounding portions of the implant and three months post cryo, we've got a good effect on about 70% of the tumor. You see there's still a little residual tumor in the bottom right corner of the implant area. So what do we do? We go back in a second time, place a second needle from a

slightly different approach, and at nine months post the second cryo, we've got a good treatment response.

And this person has not recurred. Got a couple more cases to show. Here's a 31 year old with a a very small desmoid tumor, but it's sitting in a tough spot right above the bladder. And so again, we can use our same techniques where we put some fluid inside of the pelvis to push the bladder away. We also put a foley catheter in the bladder to decompress the bladder.

We had to see the tumor with the ice ball surrounding it. And at, I don't remember when the follow up was for this one, but you can see we no longer have the enhancing mass in that area. Now I'd think prior to this year, this was a patient with an eight centimeter abdominal wall desmoid. This is probably a size that in the past we would not have cryoablated.

You can see here's the outline of the tumor and especially because you see it's in basically close proximity to the bowel with the tumor, this large typically we cannot put fluid in to separate the bowel and the tumor. And we've been working on you know, a technique akin to laparoscopy, which is CO2 insufflation.

So in this case, we actually access the peritoneal space and we put CO2 inside the peritoneal space to push the abdominal wall away from the bowel. And that actually can sometimes also compress the bowel a bit. So now you can see that we've got good separation between the tumor and the bowel here.

And now you can see a post picture where we have, you know, the ice needles that have just been taken out and we have this low attenuation ice vault around this person. This is a, from a very recent case, so I don't have the follow up, but we're very excited about this technique because we think that CO2 insufflation of the abdomen will be a powerful tool to allow treatment of larger abdominal wall desmoids.

We always have to worry about the complications. We are close to the skin often, and frostbite injuries can be a problem if, as long as the area of freezing is smaller than about the size of a dime, it will heal on its own. I've never had to do a skin graft, but, you know, skin grafts are something that sometimes have to happen to cover up an area where there has been a frostbite injury.

And then of course, nerve injuries. These are the most challenging things. The ice is very effective at killing the tumors, but it can kill the nerves that are adjacent, particularly in the extremities. There are new MRI guided cryo

systems that are coming out. The equipment typically right now is not that great and we're hoping those new systems will be more effective.

So in conclusion cryoablation of desmoid tumors can achieve long-term disease control, both in the first line and salvage settings. And I think this is probably our great accomplishment as a team here in the Desmoid Tumor Research Foundation. Patients and scientists together cryoablation is an appropriate treatment consideration for select treatment-naive patients with extra abdominal desmoid tumors.

Thank you very much. Now I will take some questions.

Jeanne Whiting: Yeah. We have so many questions. Can you please share what the training entails for an interventional radiologist learning how to cryoablate desmoid tumors? How many of these procedures per year does Sloan Kettering perform, and about how many locations would there be interventional radiologists who really you could go to, to get a good procedure?

Dr. Joseph Erinjeri: I think I think it's not so much, I'm sure there are interventional radiologists across this country who are technically experienced and, you know, routinely do cryoablation for renal tumors and lung tumors. But I think what really sets any desmoid center apart is the multidisciplinary care.

I think that's really the difference. So, you know, if, when you go to a center, and I don't think it's just the technical aspects, I really think it's the team approach that, that makes a big difference. You know, we do on the order for, just for desmoids, we probably do 30 a year. Which, you know, I think is probably a high number and a lot of places, I think, you know, they might only see this like, you know, like once a year or less. So we, I think we have a center of excellence, which is great. But I think as we publish more about this, we'll be able to see more people engaging it throughout the interventional community.

Jeanne Whiting: Okay. Somebody from Canada said, are there any clinics in Canada that perform cryoablation?

Dr. Joseph Erinjeri: I don't, I just don't know the answer to that question. I don't know those people that well. I'm sure they do cryoablation for other things. I just don't know if they do them for desmoids.

Jeanne Whiting: So how does somebody decide that they could go to a center? How does a patient make that decision to seek a center travel to the center?

Dr. Joseph Erinjeri: Yeah, I think I think the first thing is you've gotta first, you know, have a, you know, therapeutic relationship with the doctor. You gotta meet the doctor, you should see you in the clinic. They should be reviewing your scans, should be following you for a certain amount of time.

And, you know, I would encourage patients that, you know, ask the right questions, which would probably be do you treat desmoid tumors? Are you part of a multidisciplinary team that treats desmoid tumors? Do you perform cryoablation? If you do, do you do it only for desmoid tumors or do you do it for other tumors as well? How many of these procedures do you, do, you know, a year? I don't think these are insulting questions. You know, there are things that I don't do a lot of and I just tell people, Hey, I could happily refer you to somebody who might do you know more than this, than I do. But those are the kinds of questions I'd be asking.

Jeanne Whiting: That's so helpful to have those questions. Thank you. What percentage of cryo treatments lead to nerve injury in your experience?

Dr. Joseph Erinjeri: So I think in our practice, you know, I, if I quote people, I think the risk of nerve injury is on the order of you know, one to 2%. I think though, that when you're in extremity, it's just so hard and you've gotta be so, so careful.

The main risk would be in cases where the tumor is abutting nerves. I think it's really, as I mentioned, you have to get a really fairly aggressive freeze in order to not have a recurrence. And this is always the trade off is how much is the recurrence gonna be versus how much is the you know, risk for injury to adjacent structures like nerves.

Jeanne Whiting: Okay. Again, who would be clearly excluded from this kind of procedure? One question is, so this can definitely not be done with a desmoid near a mesenteric artery?

Dr. Joseph Erinjeri: Yeah. Notice we talked about extra abdominal desmoids, intra abdominal desmoids, you know, pretty much cryoablation is not an option for

Jeanne Whiting: For intra abdominal.

Dr. Joseph Erinjeri: Correct.

Jeanne Whiting: All right. Dr. Erinjeri, this patient says, I've been watching your presentations at the DTRF meetings for years, and I just wanna say thank you. Thank you for continuing to pay attention to this community and to advance and innovate this treatment to be an option for more desmoid patients.

Dr. Joseph Erinjeri: Wow. I'm so, that's such a nice thing. Makes me feel wonderful. And I do feel, I do feel a kinship with these patients and I think that, you know, it's nice to I'm sure after going around to see a lot of doctors, you know, you know, it's like maybe the first time they heard of it or maybe heard of it some at some point, you know, in a book. And you know, when you meet somebody who, Oh yeah we see this all the time. Like, that must actually feel good.

Jeanne Whiting: Couple other questions. Comparing the cryo to the effect of sorafenib, for example, and how often do you see regrowth after a procedure?

Dr. Joseph Erinjeri: Both good questions. I think that, you know, as I think the number is, you know, 60% of patients get, you know, a treatment effect, you know, with sorafenib and I'm sure as time goes on the newer agents will have even higher response rates.

For us, we have, if we look at that cohort of patients, about two thirds of patients will get complete disease control with one treatment. 95% of patients will get disease control with three or less treatments. 5% of patients will not get disease control with three treatments, and they will often go on to either a targeted therapy or cytotoxic chemotherapy like Doxil.

Jeanne Whiting: Okay. Very helpful. Dr. Ratan, you came on. What would you like to say?

Dr. Ravin Ratan: You know, I think, Dr. Erinjeri has it right. I think it also depends a lot on, I mean, I think we tailor the therapy to the patient as I know that they do a Memorial Sloan Kettering, right? So an intrabdominal desmoid is not gonna get cryoablation.

Someone who's got a superficial desmoid and the abdominal wall, it might be a great fit. And I think, as he said, and an answer to a previous question, I think the secret sauce is really just making sure that the right people are involved. That the cases are discussed carefully and that therapies match properly to the patient.

Dr. Joseph Erinjeri: Yeah, there are people that get operated on that it's the right therapy for them. There are patients who want cryo and I say, Listen, you gotta try sorafenib, you gotta try this other, you gotta try these therapies. You gotta think about a trial. And I think when you hear the same reinforcement from, you know, different multi parts of the multidisciplinary team, I think that helps to really strengthen the confidence that we have in the treatment. So, yes, I'm I completely agree with Dr. Ratan.

Jeanne Whiting: Excellent point. Bringing it back to the multidisciplinary team and how important that is. Wish I could go on and on. Lynne's telling me I have to close. Thank you, Dr. Erinjeri.

Dr. Joseph Erinjeri: No problem. I gotta run too. See you later guys.

Jeanne Whiting: Good luck.

Dr. Joseph Erinjeri: Keep up the good fight!

Jeanne Whiting: We will! We will.