HIFU for Prostate Cancer Finally Gets the FDA Nod. What to expect.

After more than 10 years of clinical trials, the Food and Drug Administration on October 9 approved the first high-intensity focused ultrasound (HIFU) device for ablation of prostate tissue. HIFU has already been approved for use in prostate tissue outside the US, and more than 50,000 men globally have been treated with focused ultrasound for prostate cancer. The option of a non-invasive procedure that can selectively target and treat diseased tissue is very appealing for prostate cancer patients. We are talking to Dr.Stephen Scionti of Sarasota Prostate Cancer Center on HIFU, its implementation here in America and how HIFU can help prostate cancer patients.

Full Transcript:

Priya Menon – Good afternoon and welcome to CureTalks. I am Priya Menon, Scientific Media Editor of CureTalks, joining you from India. This is CureTalks' 96th episode, and we are talking about role of HIFU in prostate cancer treatment and the recent FDA approval of the same. Our prostate cancer talks are conducted in association with Prostate Cancer International and the Prostate Cancer Foundation. After more than 10 years of clinical trials, the Food and Drug Administration on October the 9th approved the first high-intensity focused ultrasound device for ablation of prostate tissue. HIFU has already been approved for use in prostate tissue outside the US, and more than 50,000 men globally have been treated with focused ultrasound for prostate cancer. The option of a minimally invasive procedure that can selectively target and treat diseased tissue is very appealing for prostate cancer patients. We are talking to Dr. Stephen Scionti of Sarasota Prostate Cancer Center on HIFU, its implementation here in America, and how HIFU can help prostate cancer patients. Dr. Scionti is a board-certified urologist and is globally recognized for the advanced prostate cancer diagnostic methods. He has pioneered advances in HIFU treatment and is the Founder and Director of the Scionti Prostate Center in Sarasota, Florida. Welcome to CureTalks, Dr. Scionti. It's a pleasure to have you here.

Priya Menon – My co-host for the show is Mike Scott. Mike is Co-founder and President of Prostate Cancer International, a prostate cancer-specific, a non-for-profit educational and informational organization based in Virginia. Mike works for Calcium and is also a member of the Board of Directors of the National Organization for Rare Diseases and the International Myeloma Foundation. Hi, Mike! Hope you are doing great.

Mike Scott – Hi there, Priya!

Priya Menon – Supporting Mike on the panel are prostate cancer advocates and survivors, Allen Edel, Tony Crispino, and Jim Wickstrom. Welcome and a great…., and it's great to have you all guys here. Before I hand over to Mike, I would like to thank our audience for sending in such great questions, which we will be addressing towards the end of the discussion. If you would like to ask a question live, you can please press 1 on your keypads to let us know and we will bring you on air to ask them. Mike, it's over to you.

Mike Scott – Thank you, Priya. Good evening, Dr. Scionti. How are you?

Dr. Stephen Scionti – Mike, nice to speak with you. I am doing fine here in Sarasota.

Mike Scott – Good. So, obviously, a number of people are very excited to have a new option for the treatment of prostate cancer; and I am sure some of the manufacturers of the equipment are even more excited. I…, I would appreciate it if you could take a little time to sort of talk us through where you think we are today in the potential use of this new technique in America and…, and there are…, I think there are…, there are

number of things that would be nice if you could address. Some of us are a little concerned by the lack of any published stature on outcomes over time and I don't mean that in a…, in a…, in a nasty way. I…, I am just saying that. I…, I think also given the nature of the approval by the FDA, there may be some confusion about the…, sort of breadth of use of…, of HIFU in the…, in the management of prostate cancer because the actual indication is, to say the least, a little vague and so any…, any light you think you can shed on how you expect to be using HIFU and other people like you who do have experience, I think it would be interesting for us to hear about. So, over to you.

Dr. Stephen Scionti – Okay. Oh, thanks, Mike. First of all, I am a…, I am a prostate cancer clinician, and so my practice is really focused on minimally invasive ablative treatment for prostate cancer, ablation and…, and I am sure I don't want to be redundant and I am sure the audience probably knows what ablation is. This is a relatively sophisticated group of folks on the call, but…, but ablation really is the direction of energy into the prostate that goes back to using things like cryoablation going back even 20 years ago, but interestingly if we look at where HIFU has gone, you know, globally, that technology has been under development over the last 20 some light years; and the first HIFU treatments were done using the EDAP device in…, in France as early as 1995 for prostate cancer and…, and…, and as has been said, many treatments have been done, you know, certainly in Europe and in the Asian…, Asian area. In the United States, there has been very limited use obviously except for two very small clinical trials that were under the.., under the auspices of the FDA, which were both sponsored by the manufacturers. Okay?

Dr. Stephen Scionti – Now, I had the opportunity with the salvage trial to be one of the lead proctors overseeing a lot of the training that some of the clinical trial sites during that and that was in the Sonablate case at the clinical trial that was done for the treatment of radiation-recurrent prostate cancer. It was a relatively number…, small number of patients treating very…, the very difficult clinical problem of radiation recurrence. In the EDAP trial, that was a primary trial that was designed to compare low-risk prostate cancer treatment to cryotherapy; and interestingly, they never could enroll the cryotherapy arm and today its pretty clear that we would never consider using cryotherapy in low-risk prostate cancer and you remember that both these trials were designed many, many years ago before our…, our thinking on prostate cancer changed, but those trials were essentially trials that couldn't really be fully…, fully enrolled and really…, really when they came to the FDA advisory panel meeting about a year or so ago, October 2014.

Dr. Stephen Scionti – In the case of the EDAP trial, they were all low-risk patients and…, and…, and the panels…, and the panel basically said they are all low-risk patients. We probably should be treating some of these men and how do we interpret this data; and in the case of the Sonablate trial, about a third of the patients for low-risk recurrent patients who may have the same…, same concerns realized that in salvage population, there were a lot of side effects in that trial as would be expected treating radiation-recurrent patients with any modality. So, what that led to in support to understand the process, the FDA had really a change in their…, in their methodology that opened up something called a 510(k) de novo pathway for new devices and it wasn't specific the HIFU, but HIFU would fit into this in the United States and what the agency was allowed to do because of a rules change was to look at published prospective trials from outside of the United States. So, they looked at data that came out of Britain, out of Japan, data that came out of France and Germany and as long as the data could be verified going back to what are called case reports, initial case report forms, then the FDA would accept that data in its decision making process about whether or not this technology had…, was…, had any effect at all, was ineffective, and wasn't safe. So, that's…, that's the pathway using this 510(k) de novo pathway by which the Sonablate device was able to obtain approval. In the FDA…

Mike Scott – If I may just…, if I may just stop you.

Dr. Stephen Scionti – Yeah.

Mike Scott – You were…, you were talking about data like the…, the arm at (inaudible) stature in the UK. I…, I believe there is a 1% in Japan who is…, who…

Dr. Stephen Scionti – Uchida, yeah, the Uchida with the others.

Mike Scott – …introduced the significant amount of data, those…

Dr. Stephen Scionti – Right. About a thousand cases. Yeah.

Mike Scott – (Inaudible) we are talking about. Correct?

Dr. Stephen Scionti – Right and…, and EDAP submitted Dr. Christian Chaussy's data as well as Gelet and…, and…, and Sebastien Crouzet's data, so there was…, both manufacturers relied on large databases maintained in some of those primary markets and submitted those databases, which were gone back and verified by the…, by the FDA. Okay? Now, the FDA stayed away from specifically a cancer indication and…, and…, and I don't know what the nature of the negotiation was, but they…, what they asked the…, what they examined the data for was does the technology…, does the treatment ablate prostate tissue? In other words, is there evidence that when you apply energy with HIFU to the prostate and you go back and subsequently re-biopsy that area, do you obtain a negative biopsy of that area in a high percentage of patients? In other words, do you effectively ablate the target tissue? Okay? And so, that's…, that's not the question of whether one cures prostate cancer. Its a question of whether one can ablate tissue and therefore the FDA's indications specifically says for prostate tissue ablation and they make no claims at all or labeling regarding cancer specifically and so it's the how it's used in the United States and what one can say about the use of prostate cancer.

Dr. Stephen Scionti – A manufacturer, whether it be SonaCare who makes the Sonablate device or whether it be EDAP who makes the Ablatherm device, neither manufacturer will be able to make advertisements or claims regarding the treatment of their devices, specifically for prostate cancer. They can talk about prostate ablation. Now, clinicians, physicians can use the technology, however, in their best medical judgment they think fit to treat whatever that particular condition. So, one could theoretically treat benign prostate enlargement. One could treat high-grade PIN lesions. One could treat atypical precancerous or atypical small acinar proliferations or ASAPs or one could treat prostate cancer. Now, it's the how it's going to be used in the United States, I don't think we'll see any significant use for benign prostate enlargement because there's much easier ways to treat the disease and I also can't imagine that, you know, we'll use it very much to treat high-grade PIN lesions because we are going to observe those in almost every case. We will observe those in every case anyway. So, I…, I think you will see a lot of the use of the device for prostate cancer, which is with the FDA guidelines of…, of ablation, but it's not. It's clear to understand that the FDA guideline does not address prostate cancer. The FDA makes no claims about its success rate in treating prostate cancer. That is something that, you know, with the clinicians and with…, with the…, with the real, with the aggregation of clinical outcomes, those statements will be able to be made in the future at least from US stand, but it's not there right now. One can't make the cancer claims specifically.

Mike Scott – (Low Audio) have what I will describe as extensive experience of…, of carrying out HIFU, who are now going to be bringing that skill into the United States? Based on some of the data I have seen, there is a clear indication that it takes a while to learn how to do this really well, probably as with surgery and everything else like this. There are some people who will just be more talented than others and will be able to do it better.

Dr. Stephen Scionti – That's true.

Mike Scott – I am curious whether the opinion leaders among your case tried to develop some form of registry system to track stature of the (inaudible) and how you are thinking about (inaudible) with the…, with the manufacturer, how you are thinking about the appropriate training and maybe not certification, but at least, you know, mentoring of those who want to learn how to do this well because essentially…

Dr. Stephen Scionti – Yeah.

Mike Scott – … there are significant number of patients here.

Dr. Stephen Scionti – Oh, lucid. You are absolutely correct. You are absolutely correct and those are major challenges and.., and I think it's a major challenge to any new technology. So, yes, so let me tell you, you know, this is…, again I am going to give you some of my opinion. You are quite correct that that the American urologists will try and jump into this very quickly and…, and some may have…, may have gone through weekend course, some may have done one or two procedures over the last 10 years in international locations, and there will be a handful of people, a relative handful of people that have got a…, a significant clinical experience. In other words, they are comfortable with the technology, you know, in terms of how to carry out the treatment. What I will say is that what happens in the treatment room is only half…, half the part of getting a successful outcome. Proper patient selection is really critically important, not every patient is a candidate, #1.

[00:14:47] (Dr. Stephen Scionti) – So, understanding where HIFU fits is an important part of training, understanding how to deliver the treatment is an important aspect, and then how to care for that patient post training and…, and post treatment, and then how to monitor that patient are important aspects and…, and those will be the challenges. So, the manufacturers can't legislate what the physicians do. I think they…, they…, they don't…, they don't have the ability to tell someone in a…, who…, who happens to get their access to a device in some remote area, they can't treat a patient. What…, what its incumbent upon urologists, even professional societies do, I think is to…, is to require, you know…, you know, really train in their credentialing. So, you are starting to see this occur. So, one of the…, one of the systems that I am…, I am becoming involved with is a…, a company that's now forming. It's called Vituro Health and…, and…, and I am a…, I am negotiating right now. My role is that of Medical Director, and some of the things that I have said are critically important in order for me to do that is that we need to create a registry because that's something we have never been able to do. There's never been the financing the manufacturer with support as before, but now with cases going on in the United States, there is a requirement to track the data in a…, in a…, you know, not in a hotchpotch way but a very formal way in which every data point is being recorded and…, and that…, that can be done if you have got physicians as part of, you know, a program where there as a condition for using the device, they have got to agree to participate in the registry, so that's…, that's one…, that's one thing…, that's one thing that's going to happen. The second thing…

Mike Scott – Would you be planning…, would you be planning to do that with some sort of external oversight in a manifestation with one of the major prostate cancer centers or the university or something?

Dr. Stephen Scionti – Well, whether it's with university or whether it's with…, with…, or whether that's with a…, something like what…, with Endocare or the cryotherapy manufacturers did with an external…, external sort of monitoring database, one of the two I think is important, but you have got to track outcomes, #1.

Mike Scott – Yeah.

Dr. Stephen Scionti – #2, I…, I think, very important, you have got to assure that the physicians that are doing the procedure as part of one's organization have been properly trained with proper proctoring, QA, proper patient selection, and proper support and…, and that…, that really…, that really is…, is very important because if you have poor patient selection, then patients who are the ones who would optimally benefit get treated and then that doesn't help the patient and it certainly won't help the technology in the United States. So, I think it's…, it's something that has to be done in a very organized way, will only be done if physicians are part of a larger organization. So, there's…, there's two or three organizations like this beginning right now in the US and I think all are thinking the exact same thing, realized for only about, you know, three or four weeks post approval. So, a lot of this is under…, is under construction as we speak.

Mike Scott – Sure.

Dr. Stephen Scionti – For example, in our center in Sarasota, we will begin treatments the first week in December. Initially, I will be involved either performing or overseeing every single treatment that occurs in

the center. So, I will review every case. I will be personally involved with overseeing every case and…, and…, and…, and until a physician has done at least…, at least six cases with…, with…, with proper oversight, they won't be allowed to work independently. So, that is the sort of attention that's going to be placed in order to get good outcomes. Now, the risk is…, and…, and…, and, Mike, I think you hit this…, the nail right on the head here. The risk is that there will be people who get their…, companies who will get their hands on technology and they'll…, they'll…, they'll move them around the United States, the different centers, without a whole lot of concern about quality or about proper outcomes and…, and I think that's a terrible mistake. So, I think it's the patients…, patients out there have got to be savvy enough to ask questions off their physicians. Hey, what's your experience level? You know, how comfortable are you? How many of these have you done and what's your…, who's your…, what's your backup? Who are you working with? Did they help you, you know, with.., with getting proper training? How have you been trained? Who have you trained with? Unfortunately, right now in the US, there's not a lot of experience sitting at our universities. For example, when I was at NYU, I was at NYU for a couple of years full time and we are involved in the salvage trial in which we…, we had a…, we were only allowed to…, each side could do no more than about eight cases because they wanted to spread out. So, there's no real high concentration of experience in any of the universities in the United States at this point and so, I think you'll see a lot of this evolve, but it's not there right now. So, those will be the challenges, but it's something that I am certainly well aware of that there is a need for.

Mike Scott – So, I…, I think you have given us a very nice introduction. I appreciate that. Thank you. One of the things that obviously is going to be an issue is…, is coverage for this treatment and I…, I am curious if you have been…, if you can share with us any information about the issues about that, in the sense that, you know, obviously there are different types of abuse of the…, of the technology that when we consider to be essentially really valuable, I mean in other words, even though the outcomes after salvage, if you…, after radiation were not world shatteringly wonderful. It is clearly better than a lot of the other options.

Dr. Stephen Scionti – That's correct.

Mike Scott – …and so, you know, and the other question is…, is…, is coverage going to be available for a repeat if a patient needs that? So, that…

Dr. Stephen Scionti – Yeah.

Mike Scott – …that would be one of the things I am interested in. The other one is the whole question of a conversation with a patient who is a good candidate for active surveillance.

Dr. Stephen Scionti – Yeah. That's a…, that's good…, that's a great point.

Mike Scott – Why do you not think it might be a good idea?

Dr. Stephen Scionti – No, that's a great point. So, let's…, let's take the…, the insurance coverage, then we'll go back to the surveillance. At this point in time, there are no commitments from any insurers in the United States at this point in time to cover the procedure. Okay? Now, that will change, but its going to take time and the only way that is going to occur is by presenting one insure at a time with an understanding that is technology, but they are going to want to see and this is why…, this is why a US-based database registry will be important. The insurers want to see outcomes as well. So, this is going to take some time until we see insurance approvals or payment across the board, I would estimate, its a guess, I would estimate it might take four or five years, but on a case-by-case basis, I think we will be able to see individual patients get coverage on a case-by-case appeal basis, making the.., you know, a case-by-case appeal for patients and so, working direct with the insurance companies is something that is going to be very important to do and the manufacturers are going to have to really take a major role in that as well because they are obviously going to have a lot more procedures with their technology if there is a reimbursed insurance cover.

Dr. Stephen Scionti – Now, as to re-treatments, it's…, it's anyone's guess as to how that's going to be covered. Right now, one of the manufacturers treating in the…, in the, you know, in the Caribbean market on

the SonaCare had a policy in place that they would…, they would treat patients who needed a second treatment at a reduced price, but those international sites are closing, as we speak, because most…, most patients in the US don't want to go to the Bahamas, they don't want to go to Mexico and so the demand, I think, will go away very quickly for international sites and with that we are going to have to really address, you know, reimbursement issues where people need second treatments.

Dr. Stephen Scionti – HIFU, like every other treatment that we do, including radical surgery, has a biochemical and a pathologic recurrence rate without question…, without question and the higher the Gleason grade, the higher the recurrence rate is and that's true of every treatment. So, we are going to have the need for patients that require salvage therapy and…, and sometimes HIFU is an appropriate salvage therapy, sometimes it's not, but that…, getting…, getting those insurance issues reimbursed will be one of the first priorities I think in the US, but it will initially be on a case-by-case basis and what I am telling my patients right now is they…, they really can't expect insurance reimbursement at this point in time and don't go down this path with the…, the hope that they'll talk the insurance company into it because we just don't know that that will happen.

Dr. Stephen Scionti – Now, active surveillance, that's an intriguing question because in my mind active surveillance patients are active surveillance patients and…, and so no treatment…, no treatment no matter how non-invasive really…, really is…, is…, is…, should be a substitute for active surveillance because there is no treatment that's got zero side effects. It doesn't exist. So, if a patient truly has low-volume, low-grade, low-risk disease, then we can talk about by which parameters, but truly clinically insignificant disease, that patient then becomes in my mind an excellent candidate for surveillance and that's not the patient that needs any treatment at all. So, just because HIFU has…, or may be less invasive than surgery doesn't mean we ought to treat insignificant disease because a treatment is still a treatment. That's my philosophy.

Mike Scott – Would you consider that to be true? I mean there's a small number of patients for who the whole concept of living with a…, a cancer in their prostate is…, is a very traumatic experience.

Dr. Stephen Scionti – Oh, God! Right. Now, so…, so let's… So, again, that's a… You have got to look at this on a case-by-case basis, right? And so what I…, what I am…, what I am trying to say that we should use a minimally invasive treatment across the board for low-risk patients because with the idea that well, we…, you know, we should at least do something for them, but you are correct. I see patients in the office everyday who really…, it's their choice to not live with the disease, but yes, they wouldn't accept a radical prostatectomy, for example. So, I think…, I think…, yes, I think that becomes an option for them, but this is discussion that…, that the…, that the doctor must have with his patient. You know, it's…, it's about finding their disease. Its about understanding the true extent of the disease. Its about characterizing the disease and laying out them for that…, that patient what the risk of options are, ranging from active surveillance all the way to, you know, different forms of treatment. There's no question that patients who have surveillance, you know, capable disease have radical prostatectomies. That happens for sure because the patient decides they don't want to watch that disease. So…., but I think it's about having that one on one, very detailed, a very personalized discussion with that gentleman and talking about what their options really are and taking into consideration the characteristics of the disease, their age and of course in prostate cancer, preferences…, patient preferences still play a major role in the direction that…, that…, that one takes. So…

Mike Scott – I have…, I have one more slightly off-the-wall question for you and then I am going to ask some of the other panelists to participate. So, my off-the-wall question is, we know that a small number of patients with severe chronic recurrent prostatitis and I am talking about really severe…

[00:27:28] (Dr. Stephen Scionti) – Yeah.

Mike Scott – …have been successfully treated with radical prostatectomies. Have you ever treated such a patient with HIFU?

Dr. Stephen Scionti – You know, honestly, no, I haven't. You know, we really limited the…, the treatment

in…, in the international locations to men with histologic prostate cancer. So, I think that's new territory and…, and…, and frankly, I honestly don't know how they would respond and here's the problem, is that many times severe chronic prostatitis, you know, the chronic pain associated with that syndrome often times will…, will…, will persist even when you…, when you have treated the prostate and so I…, I think that's something that's going to require…, that's something that really is a formal research study. So, that sort of thing, because the…, because I think its really unknown as to the outcome and where ablation fits, that would be something that I think would have to be studied pretty rigorously in order to answer that question. Potentially, it could be helpful, but I really don't know at this point.

Mike Scott – Okay. So, we…, we have three panelists with us today – Allen Edel who…, who has a great deal more experience of…, of management of patients with radiotherapy than I do; Tony Crispino, who is the SWOG patient representative on the SWOG GU panel; and Jim Wickstrom, who I…, there's some rumor that you may have treated him. So…

Jim Wickstrom – Yeah.

Dr. Stephen Scionti – I think I know Jim.

Mike Scott – So, maybe Allen, are you there?

Allen Edel – Yes.

Mike Scott – Perhaps you would like to…

Allen Edel – I am.

Mike Scott – …see if you have some…, couple of questions for Dr. Scionti.

Allen Edel – Sure. One question I have is about that Uchida study you mentioned. They reported five-year biochemical recurrence-free survival of 48% for the Sonablate 200 model and then over time it came up to 82% for the Sonablate 500TM model and I was wondering is…, is that due to technological advances and if so, what were they because that's an astounding improvement or is…, is it practitioner expertise just coming along the learning curve and what…, what advances…, what further advances would you like to see in the technology in the future?

Dr. Stephen Scionti – That's…, that's an excellent…, excellent question. Okay. So, to answer your question, I…, I think it's…, there have been major technological advances. There's no way we can discount the fact that the practitioner got better. So, there is a bit of both going on there, but the major advance is that Sonablate 200 was a very primitive device that can only treat the prostate and I don't want to get too technical here, but it treated in a 60-degree sector window, which means that you had to…, you know, you had to treat the standard prostate instead of three zones in at least six, if not eight zones. Now what that did is it left a lot of possibilities for missing tissue, we didn't have complete overlap. There was tissue that wasn't treated. We know that once we start to deliver energy to the prostate, the prostate is going to swell. It's going to change size. So, we designed a HIFU treatment, we are capturing the series of ultrasound images and then we are…, we are…, we are designing their treatment to…, to…, to cover a series of captured images. Now, the minute you turn the machine on and start to treat somebody, the prostate changes size and shape. So, it's a very dynamic process, but you are using a treatment plan that you designed at some point earlier in the procedure and so if the prostate is changing size and shape, what was happening in those early days is the energy was going to a target that was old, in other words the target changed, you didn't recognize it. So, one of the first major advances made technically with the Sonablate was that it had what's called a restacking feature. It had the ability to…, after five to seven minutes of treatment or so or at numerous intervals, to take a brand new series of images and realign the treatment with the new images and then adjust the treatment to the changing target, adjust the image to the changing target, very important because now you can continue to conform the energy to the changing target. That was one of the major advances as

you went from the Sonablate 200 to the Sonablate 500.

Dr. Stephen Scionti – A second and very important change was the ability to incorporate what's called tissue change monitoring or TCM, that's a TCM version. So, as ultrasound energy goes from a transducer up into the prostate, there is some absorption and attenuation of energy on the way to the focal zone or to the target. Okay? And so, as that occurs, there is really…, was no way to assure there is the proper deposition or absorption of energy in the target zone as opposed to have been absorbed in the pre-target zone when the area between the target and the…, and the rectal wall and so tissue change monitoring is a mechanism by which the software is able to measure the…, the physical characteristics of the tissue on ultrasound before and after the treatment pulse and documented, agreed to which the characteristics changed. Okay? Now that has been documented in vivo in a study that was done by Dr. Marberger in which they were able to correlate actual temperature changes in the focal zone with the measured TCM changes.

Dr. Stephen Scionti – So, from practical standpoint, as one is doing the treatment with TCM, one delivers treatment to an area and in real time, on the fly, as we treat, we are getting a direct readout from the software about whether each little volume of tissue we treat is getting the appropriate energy and whether it's changing. If it doesn't, we can go back and on the fly re-treat that zone. So, when we leave the procedure room, we have a better assurance that the area that's been targeted has absorbed…, has absorbed enough energy to cause a treatment change. That's been very important. One of the other changes that happened physically in the device is the size of the treatment lesion also increased between the Sonablate 200 and 400 and now we had available, for example, the ability to make a 12 x 12 x 3 lesion and what that did technically, allowed us to treat little larger prostates with more overlap between the zones. So, those three…, those three advances, you know, going to a stacking mode, going to larger lesions, going to tissue change monitoring were major technical advances. Now, those were in place even several years ago because Uchida has reported on outcomes using TCM and…, and TCM was introduced and he first began to use it somewhere around 2011 or so, 2010 and 2011.

Dr. Stephen Scionti – As for the future, I think anyone who knows some of the work I do, I am a major advocate of using MRI to define the disease as well as to help design treatment. So, one of the major advances we are seeing now is the integration of MRI fusion into the treatment platform. So, in other words, we can use MRI to tell us several things. We can help us to understand prostate anatomy better. We can help us to understand the location of the neurovascular bundles; and we can help us to identify, you know, the locations of the most significant tumor location in the prostate. That information then can be superimposed on to the ultrasound images to help in treatment planning and I think that's a major advance. So, that…, that is, the future for that really exists now because that technology has been integrated into both manufacturers' platforms. The Sonablate platform has it and will have it in the United States; and the EDAP platform, they call their platform the focused one that has MRI integration, is available in Europe and it's my understanding that EDAP will plan to make that available soon in the United States as well.

Mike Scott – Okay. I want to make sure we have plenty of time for questions from…, from the patients that are on the line other than the panel. So, Tony, do you have one question for Dr. Scionti?

Tony Crispino – Thank you, Dr. Scionti, for a very comprehensive explanation. It's very helpful. The question I come on over, being somebody who works in the clinical trial background (inaudible) clinical trial setting, I hear your explanation that while the procedure is approved in the US, there is only so much claim about what you can say you are doing with it. How is this addressed directly with…, with the patient and how do you explain to them that why you can't say cancer specific, perhaps what you can say at this particular (inaudible) what you can tell that patient is very helpful.

Dr. Stephen Scionti – Oh, no! I think that's a great point and that's…, that's why I tried to make that point earlier and tried to, you know, walk through what the FDA, you know…, you know, language was. I think it's very important. You know, at this point, making…, you know, having a conversation with a patient and…, and again, it's all about being full disclosure here. To say that we have proof that we can cure your prostate cancer, that…, that…, that…, that can't be…., that's not substantiated. Okay? I talk… As an ablations person, I

talk about ablating disease, ablating…, ablating regions of abnormal tissue, ablating tumor. That's…, that's short of…, that's short of claiming cures. So, I…, I think patients have to understand what ablative therapies can do and what they can't do. Okay? So, if we can…, if we can take a targeted area and turn it biopsy negative, does that prove that there…, there won't be a recurrence? No. Does that prove that there can be just a recurrence, no, and I think those kind of conversations have to be had. So…, so I think it really comes down to the conversation. Now, what will we see in the United States? We are going to see all kinds of things said to patients and…, and there's no question about that. You know, that subtle distinction and maybe for us it's the…, those of us on the…, on the call, it's not terribly subtle, but for a lot of physicians, they won't get that distinction between ablation and…, and…, and true cancer treatment. So, I think you will see a lot of what you are referring to and what you are probably concerned about, I think you will see some of that going on in the US. I think those of us that are in a position of, you know, medical direction and leadership are very clear about the language we use and what we tell patients.

Mike Scott – And, Jim, do you have question for Dr. Scionti?

Jim Wickstrom – Well, good question. I… He's actually answered my questions very well. I would just like to say that I kind of backdoor'ed prostate cancer by having physicians stand over me and tell me he has got an appointment on Friday at one of my surgery, which is a little challenging emotionally and I did my due diligence by interviewing dozens of patients and that's how I learned everything and before you hear a whole lot of the patient groups and their complaints and their feelings that are very personal because losing…, for a man to lose his ability to urinate, control the urination or impotence is just challenging; and as Dr. Scionti pointed out, you have got to do one on one work with people and so many physicians are not trained to do this. They move on to the next patient as we all know; and since the urology community is in conflict with itself in so many ways, having this less invasive treatment of HIFU available is so powerful. So, that's all I wanted to say.

Mike Scott – So, Dr. Scionti, I have one last question for you before we…, I give this back to Priya for her to…, to bring in the…, the other people on the line. That…, that relates to the use of HIFU in focal therapy. I assume you have some experience of at least trying this and I am curious, you know, whether you think that this is a…, a really serious opportunity to expand the potential for focal therapy.

Dr. Stephen Scionti – The…, the answer is yes and I'll elaborate just for a moment.. Again, I don't want to steal everybody's time here. I…, I am very much… You have had…, you have had Professor Emberton on here as a guest on this…, on this forum and…, and…, and I am one of his disciples, you might say. Okay? I have worked with Mark, met numerous…, numerous committees. We have been on the faculty for a lot of courses that we've…, we've talked together and…, and I believe in properly selecting patients, this is the key that focal therapies are real opportunity. Now, the challenge of focal therapy is diagnostics. If one tries to select patients for focal therapy based on a systematic 10 or 12-core ultrasound-guided biopsy, it will fail because that diagnostic technique is not capable of selecting out patients who truly have focal disease. There's no question that there are patients with an index lesion and clinically insignificant disease or (inaudible) elsewhere in the prostate, but you have got to work hard to find those with advanced diagnostics and…, and much like the…, the Hashim Ahmed and Mark Emberton, in our center we really advocate 3D MRI systematic and fusion biopsy and…, and really a careful…, careful selection of men who are candidates for focal, but yes, in those patients there's no question that on the side effect side, there is a marked decrease in side effects. What we don't know long term is how many of those patients will develop disease in the preserved part of the prostate and that's the question. I am very confident in the ability to destroy an index lesion. We know that we can do that in excess of 90% of the time by…, by biopsy documentation. What we don't know is to preserve tissue. What chance does that preserved tissue have for developing significant prostate cancer over 5 years, 10 years, 15 years? That question is unanswered. That is the…, that's the controversy about focal therapy. So, and I think if…, if certainly…, we are certain to have discussion I think on this in this…, in this debate many times, but I think it's an opportunity if done with careful diagnostics.

Mike Scott – Okay. Well, I think you have been very forthcoming and…, and very…, very frank with us, which has been very nice, so that's great and, Priya, I am going to throw this back to you now for questions from

the…, the audience on the phone.

Priya Menon – Thank you, Mike. That has been a very eye-opening discussion, I think. We have a list of questions, Dr. Scionti, sent in by our listeners. Some of them are just coming in. I will just… We will just quickly go through them. We have about 15 minutes to address these. We have a couple of questions asking about the side effects and recurrence rates of HIFU. So, maybe you can take a few minutes to explain that.

Dr. Stephen Scionti – Okay. That's… Again, that's really central to our discussion. I think the…, I think the first thing to understand is that with recurrent rates, they…, they really are…, they are very… Recurrence rates are proportional to the grade and stage of disease across every single treatment. There is no question about that. So, if people are making claims about any treatment and saying, if I have got a…, a…, a Gleason grade 7 stage T2b prostate cancer and I treat it with any technology, whether it be surgery, radiation, or HIFU, and again at 98% biochemical recurrence-free rate, that's…, that's…, that's just incorrect. That's not going to happen with any modality today. So, I…, I think that what I tell patients is that, you know, once we understand grading and staging, we can give them an estimate of where recurrence rates are published at and I…, and I think some of the data specially out of the longer-term work from Uchida, from Crouzet, from…., from Chaussy really suggests those biochemical disease recurrence…, biochemical disease recurrence rates are pretty favorable. Now, are they… Has anyone ever done…, ever done a prospective head-to-head comparison? No. And so, it's very dangerous to make statements about HIFU being superior to anything. In terms of recurrence rates, you cannot say that. Now, side effects are related to two things. How much of the gland you have to treat? Its related to where you put energy. It's also related to experience. If one…, if one targets the rectal wall with this technology, there is a risk for rectal injury. Having said that, proper training should avoid that and…, and that should become a very rare event with proper training. So, side effects really depend on practitioner experience. They also depend on the grade and severity of the disease. If one's trying to treat bulky extraprostatic disease, there will be more side effects. There is no question.

Mike Scott – And…, and what sort of rate of…, of…, of good erectile function would you expect to get in, say, you know,(inaudible) T7 T2b case today?

Dr. Stephen Scionti – Yeah. No. Good question. I think that depends on whether or not you can…, you can spare the neurovascular bundles and in making that decision, I use MRI extensively. So, you'll see in the radical prostatectomy community, a lot of the…, a lot of surgeons beginning to use MRI to make those decisions. I believe MRI is helpful to make those decisions as well. So, if the tumor is bulging the capsule near the neurovascular bundle, I don't think…, think you can preserve that bundle with any treatment at all. So, to tell a patient with a T2b lesion that the lesion is infringing upon the neurovascular bundle, to promise that patient potency is incorrect because if you do that, you are going to spare tumor. Now, the converse is if the tumor really is well demarcated, interior to the capsule, away from the bundle, the patient is a candidate for nerve sparing and we treat the entire prostate. We can look at about 80% of those men having a functional erection by three to six months out. If one does a totally focal procedure, a minimal procedure, treats one or two…, a 1- or 2-cm lesion well away from the bundles, that patient can expect better than 90…, better than 90% return to potency very quickly, but it depends on the disease, depends on the location, and…, and I think this is where the diagnostics are really important in terms of giving patients proper advice.

Mike Scott – Thank you. Priya?

Priya Menon – Thank you, Mike. Dr. Scionti, John writes in from the UK. He says, I am in the UK where HIFU is approved on the NHS. For low-volume, low-risk Gleason's 6 men like me, is this treatment the best currently available and with minimal side effects?

Dr. Stephen Scionti – Okay. So…, so, John, the real question is…, is…, is how old are you and are you a candidate for active surveillance and is that really…, is…, is active surveillance, you…, you can't have fewer side effects in active surveillance but understand that there is a lot of psychological load that goes with active surveillance. So, yes, I mean…, may you be an excellent candidate for HIFU, yes, prostate size is critically important. If you have got a small lesion, a small prostate, you may be an excellent candidate. If you've got

a small tumor and a very large prostate, you would be a very poor HIFU candidate. So, it really goes down to an understanding about the load of disease, the location of disease, the volume of disease and I think the UK is really taking the lead. A lot of the folks may have taken the lead with MRI imaging and so, you know, I think, you know, looking at some of the work done at the University College of London by Mark Emberton and his colleagues, I…, I really would encourage you to look because if you have got Gleason's 6 disease and its…, it's a large enough tumor, and its well seen, you may be a candidate for a focal ablation. So, you know, I…, I think going back to a personalized approach is very important.

Priya Menon – Thank you, doctor. The next question is from Mike, who asks, can results for HIFU treatment be expected to be similar for areas outside the prostate, like seminal vesicles, lymph nodes, bladder neck as normal treatment to the prostate bed?

Dr. Stephen Scionti – The short answer to that is no. HIFU is an…, is an ablative treatment, is best used for very localized disease. If the…, if the advantage to HIFU is low side effects, treating men with advanced disease, especially in neighboring structures, is going to produce lot more side effects. So, in my practice, if I see a patient that's suspected of having extensive seminal vesicle involvement or tumor encroaching on the bladder neck or certainly any risk of lymph node involvement, I am…, I am generally referring those patients to my radiation therapy colleagues. We are not treating those patients with HIFU. So, again, It's really not designed for extensive disease. Now, interestingly, Christian Chaussy has published some work out of Germany looking at a series of patients with bulky advanced disease and…, that is the disease palliation mode and reports that they have…, they have done fairly well, but that's certainly not where we think about HIFU classically and I…, and I don't think that's where we ought to see used in the United States.

Priya Menon – Thank you, doctor. The next question is, EDAP's Ablatherm was also FDA approved on November 9th. They have a fully robotic model with MRI imaging, focal one, that is also expected to be 510(k) clear. Could you please comment on this?

Dr. Stephen Scionti – Yeah. We talked about that little while ago. Yes.

Priya Menon – Yeah.

Dr. Stephen Scionti – You know, I…, I think it's an excellent platform. The…, the Ablatherm platform has been extremely well studied. The focal one has got MRI integration. They will get a 510(k) on that and I…, and I think it's really going to be…, it's really going to be more of the experience of the surgeon than it will be of which particular machine they use. Both machines are capable of getting excellent outcomes. I think it really comes down to proper patient selection, proper execution by an experienced surgeon, and proper care of that patient postop, but I am excited to see…, I am excited to see their…, their technology in the United States because I think that…, that…, that surgeons need to have a choice and use which platform they feel is going to suit their needs the best. But, yeah, I…, I think that's very important that we have both of these available.

Priya Menon – Thank you, doctor. There is a caller on line. Person calling in from (206)XXX-XXXX, you are on air. Please ask your question.

Caller 1 – Okay. Can you hear me?

Dr. Stephen Scionti – Yes, we can.

Priya Menon – Yeah.

Caller 1 – Oh, good. This…, this is Mike from Seattle. Doctor, I have talked to you before, about six weeks ago and you answered one of the questions I had about seminal vesicle treatment with this new machine. In my case, that's…, that's when I am going to have to do a bilateral treatment, both the right and left, and I wondered if you actually had done that when you were in the, you know, grant came in Bahamas

experience, but I think, like you said, you just answered that, but have you ever actually done that?

Dr. Stephen Scionti – Okay. So, done a complete…, a complete gland treatment or treating well within the seminal vesicles?

Caller 1 – Just the seminal vesicles, the biopsy and the C11 choline, just to refresh your memory, they were okay on the prostate, confirmed by biopsy that there is nothing there.

Dr. Stephen Scionti – Yeah. So…, so…, so again, you know, you look at the optimal patient for HIFU, it's a localized diseased patient, right? But, if we have got an isolated lesion that we know and it's just into a seminal vesicle area and we can see the area, there's no reason we can't put energy there. The problem is…, the…, the risk is that once we see seminal vesicle disease and this is…, this is true of any treatment, any localized treatment, even though our…, our…., our studies for metastatic disease are negative, there is a very significant risk at least microscopically of disease that's been disseminated throughout the blood stream or disseminated into the lymph nodes or the bone scan and its not been picked up by these assays. So, the short answer is, if we see an isolated lesion even if it's in the seminal vesicle, we can target it. The real… The uncertainty is…, is good as the studies are for metastatic disease. The studies don't totally exclude metastatic disease; and if there is disease that's distant and not being detected, then treating a seminal vesicle lesion, for example, won't be curative at all because the disease is elsewhere and that really is because we don't have…, even given some of the assays you mentioned, we still don't have a totally sensitive test for microscopic disease that's well outside of the prostate, it still doesn't exist today and that's the challenge.

Caller 1 – Okay.

Priya Menon – Thank you, doctor. There's another caller on line. Caller using (703)XXX-XXXX, please ask your question.

Caller 2 – Hey, hello, Dr. Scott. Thanks for very informative talk. I would like to know, are you tracking your own results systematically as in all consecutive patients? If so, would you care to share your results or do you expect to be able to announce your results at some time?

Dr. Stephen Scionti – Okay. So, you know, over the last 10 years, patients have been treated in eight different foreign countries literally from all over the world without a…., without a university research team behind me, but this exists in the UK, for example, or with…, in…, in Japan with Dr. Uchida. So, do I have some results? Yes. Are they…, are they robust to the point where there's no missing data points? No, that's just been impossible to do. So, going forward with the introduction in the United States and in formal…, formal protocols, formal companies behind this, that will be much more feasible to do. Okay? Now, what I do have and what we are working on pulling together is I have a subset of patients. They have been well tracked with focal treatments. In focal treatment, you know, I am very insistent and anyone that's seen me for a focal treatment has heard me say this, is that we are going to follow patients very carefully and I am going to insist on MRI follow up and a biopsy at the one-year mark to document the…, the complete ablation of the tumor as well as to look at the rest of the prostate to be sure there has not been development of the tumor in the remaining healthy tissue. That's a fairly robust series that we are actually trying to put together right now. So, I think we are going to see a lot more of that. Now that should get centralized in one location with people, you know, that are…, are much more organized in that manner, but as you can imagine, you know, with…, with people treated at eight different centers over 10 years, that's been very difficult to do.

Caller 2 – And, Dr. Scionti, how many patients are in that focal therapy series roughly?

Dr. Stephen Scionti – Rough…, rough right now with good data, we have got about 90 patients.

Caller 2 – And how long is the…, how long is the series, in other words, you know, what…

Dr. Stephen Scionti – The first patients was treated about four years ago.

Caller 2 – Okay. Thank you.

Mike Scott – So, I have one more question before we end the call and…, and that is, this is now the third…, we have now had one…, two types of HIFU approved, one of which is the inside tech equipment that has been…, was originally approved for the treatment of…, of metastatic pain. Do you expect the HIFU being used more in the palliative area or in due course in the sense that it can probably be targeted in ways to treat isolated lesions, where radiation can't be used?

Dr. Stephen Scionti – You know, the potential is certainly there. The potential is most definitely there. For…, for…, for example, for bone tumors and bone pain, any area that one can target is potentially there. So, what I think now that we have technology available in the United States, I think you are going to see…, under clinical trial protocols, I think you are going to see that studied and…, and that certainly…, that certainly is…, is an area for…, for expanded use and where I think it can be of benefit, but I…, I think it has…, that has to really be studied in an organized manner and now that there are platforms that will be available will be at universities that will be at centers where this work can be done. It's just…, it's just… I think you will see that being used outside of the urology department.

Mike Scott – Well, thank you very much indeed for your time, Dr. Scionti. I am going to hand this back to…, to Priya for us to sign off, but you have been very forthcoming this evening and I think people have learned a lot about the opportunities that may exist in the near future and in the longer term as well. Thank you.

Dr. Stephen Scionti – Well, thank you for the invitation to be on the show.

Priya Menon – Dr. Scionti, it has been wonderful listening to you. The approval of HIFU is hopefully definitely going to be a turning point for treatment of prostate cancer in America. With that note, I would like to wrap up today's CureTalks. Thank you, Mike, Allen, Jim, and Tony. This talk is available on CureTalks' website. Please visit curetalks.com for details on upcoming talks. Thank you, everyone.

Thank you, Dr. Scionti. Good night!

Thank you, everybody.

Dr. Stephen Scionti – Thank you. Good night, everyone.