Quotes from 1998 panel discussion of trial design for ablation catheters for AF

From page 114 (appropriate treatment for AF):

DR. TRACY: I think that we are still so early in the learning curve with atrial fibrillation, we don't know anything about what lesions we really need, anything about what locations we need, whether they need to be transmural or not. We don't know anything about it at all, so far, as far as I am concerned.

From page 151 (acute procedural endpoint):

DR. CURTIS: I guess the question is how do you know when to leave the lab? How do you know when you have done enough, got a good enough result, or you think that you can stop and you are going to say, "Well, now I am going to see if my patient is cured."

DR. SIMMONS: It is going to depend on what kind of catheter they brought. If they bring some basket barbed-wire thing that you put the pulse through and you take it out and you are done, then that is the end of the procedure. But if they are asking you to do something anatomical that is descriptive, maybe repetitive fluoro-images or something.

The study is yet to be defined. We can't answer that question. Nobody has brought forward anything for us to look at.

DR. CURTIS: That's right. I don't think there is an acute outcome that you can say is the gold standard that people are going to have to adhere to in order to know whether the procedure works. Maybe none of those are important. I don't know.

I would imagine each company designing a study is going to want some goals to come out of the lab with and it may be inducibility or not. I think the gold standard still here is going to be whether patients suffer symptomatic recurrences. With some of these studies, we may learn what matters more.

If one company goes for noninducibility and that helps or doesn't help and another one goes for evidence of block with linear lesions and that helps, that would give you some answers there. But there isn't anything in the literature that tells us what the right answer to this is right now.

You have to say that we don't know that inducibility or noninducibility at the end of the procedure is going to make a difference.

From page 158 (assessment of success after ablation):

DR. CURTIS: It is just a plan that you are making. I think if you have to resume antiarrhythmic drugs, I guess you either have a complete success--you have a patient have a recurrence but then you put them on antiarrhythmic drugs and nothing else happens, that would be a partial success because they are now controlled whereas they weren't.

Or you put them on antiarrhythmic drugs and they are still having episodes. You may be splitting hairs to say whether that is a partial success because they are having less than they used to or you just downright call it a failure because you went through an ablation therapy and you still have episodes.

I think it would be awfully hard to figure out how you were going to finagle saying that, "Well, they had two episodes in the three months before they started but they only had one in six now on my drug and so, therefore, I have got a partial success." I think that would be hard to say.

DR. TRACY: Some of the literature is reporting that as partial success. I agree. It is another one of the ambiguities of this whole thing, when does it slide from a partial success to a failure.

DR. PORTNOY: If a patient is having fairly frequent symptoms so we have some good data, which number would you be more comfortable with for c., for example, a 50 percent decrease in frequency or a 75 percent decrease in frequency, just to give us sense for what do you think is clinically relevant.

DR. TRACY: At least 75 percent, I would say. You have to demonstrate a very significant decrease.

DR. CURTIS: Probably something like that.

DR. SIMMONS: I would go for 75, too.

DR. VETROVEC: I have some trouble with b., though, increased time to first recurrence of atrial fib. Since we are not going to have very good baseline data no matter how hard we try, that number is going to be a very funny number.

DR. CURTIS: I don't like that either. I don't think that should be an endpoint. I think that gives you some ballpark as to how we are thinking about this.

From page 160 (length of follow-up):

Question #13. "What is an appropriate follow-up period for evaluating recurrences of arrhythmias to be used in assessing the chronic performance of the investigational ablation system; three months, six months, one year or something else? Minimum, six months?"

DR. TRACY: Longer.

DR. SIMMONS: Longer, I think.

DR. TRACY: A year. After the blanking period.

From page 177 (right-sided ablation):

DR. CURTIS: There may be a lot of value to that anyway because if you are talking about new catheters and you are learning how to use them and all the rest of that, to have to go to a right- and left-sided ablation at one setting is going to be an incredibly long and difficult procedure.

There probably is a lot of value to saying the first X number of patients, we are going to do on the right side only. That doesn't stop you from going back to the left side later on if you are not controlling the arrhythmia.

I think there is some reason to think--there is certainly data in the literature that suggests that right-sided lesions alone just don't work out as well as also approaching the left side. So I think that is probably, ultimately, going to be necessary unless some new techniques get developed.

But that probably would be reasonable to at least start on the right side with new catheters.

DR. VETROVEC: Point of information. Are patients with paroxysmal arrhythmias more likely to respond to just right-only compared to people with more chronic arrhythmia where they have more dilated atria, or does that make any difference?

DR. TRACY: There is a little bit of information on that but, again, there is not enough information--and I think some of the studies are in the packet that we received. I don't think that we know that well enough. I don't think we have characterized things well enough to state that with any degree of certainty.

DR. VETROVEC: If that were true, then it would be to recommend that the first ones be done on the paroxysmal arrhythmias to get experience on the right side. You could always go back, if you had to, but you wouldn't be jeopardizing the patient maybe to the same degree you would if you know, in chronic, you have to do both sides.

DR. CURTIS: Aside from the small subset of focal A-fibs that are in the pulmonary veins, I don't think we know for sure that anybody can just be done on the right side.

Let's do 15 because I think it is still getting into these right- versus left-sided issues. "Is there a clinically appropriate way to conduct a staged anatomical approach for treating A-fib patients? For example, could patients be treated only in the right atrium and then, if symptoms persist one month post-ablation, a left-sided A-fib ablation could be performed?

"Is it appropriate to conduct a study in the right heart only for A-fib ablation or does the literature suggest that A-fib ablation should be performed in both the right and left hearts?"

We were talking about these catheters and their initial use and using it in the right side only to get some experience with it, and that would probably be a good way to have a small feasibility study. Let's say you did that and you didn't see any particular problem. You were able to maneuver the catheter and the device worked in your system and all that.

Then you are talking about the clinical-trial design of the various ways to do it; right-sided ablations in all patients; go to the left if they fail. You might want to have a trial where some patients get right-and-left-side right up front versus a right-sided only. That would be another way to do it.

DR. TRACY: I agree. Otherwise, you are talking about something that gets pretty complex. If you say, okay, when you first do this, you can only do this on the right side and then, since you can't really be sure what is going on for the first X number of weeks, then X number of weeks go by and you are pretty sure, after watching them for another month or two, that it really didn't work, and then you go back on the left side.

So you are getting pretty boxed in at that point. You have got a lot of time going by here. So, again, I think to limit it only to the right side is not necessarily the right thing. I think maybe comparison. I think it is going to depend on the catheter design what seems to be appropriate for that particular device.

From page 185 (appropriate lesion set):

DR. CURTIS: Let's go to No. 16. "Is there an optimal lesion set for treatment of A-fib? If not, can an multicentered study be conducted using more than one prescribed lesion set or should a feasibility study be conducted to optimize the prescribed lesion set prior to multicenter expansion?"

I think one problem I could foresee that we should think about is there is always a chance that one company guesses better than the other one, and put one extra linear lesion in the left side, or did something a little bit different from another company and has some other different outcome.

Is it their catheter? Or is it the lesion set? If it is the lesion set, then anybody's catheter who can do that, it ought to be effective for. You would hate to see somebody have done a two- or three-year study with, whoops, the wrong lesion set and you get the questions about generalizability.

If this company's lesion set works and I have got a catheter and I can do that kind of stuff, do I still have to go back and do that study again in order to know that it is going to have the same kind of outcome in order to get the labeling indication.

DR. TRACY: We are struggling to figure out exactly what it is that needs to be done. We don't even know. So I think it makes designing a study very, very difficult because we don't know very much about even what it is that we are trying to accomplish.

DR. CURTIS: I would have to say I don't know what the optimal lesion set right now is so you don't know that answer. There is not one in the literature, the catheter-based MAZE 3 is the way to go. Nobody knows that so you can't say you have got an optimal lesion set right now.

Could you do more than one? It might well be worthwhile for a company to have more than one to see if the extra effort involved in putting two more lesions on the left side makes enough of a difference that it is going to affect what we consider the success of the procedure.

So I think having more than one lesion set probably would be not a bad way to go.

A feasibility study to optimize the prescribed lesion set--a feasibility study is going to be hard-pressed to tell you the long-term outcomes with that sort of thing. You might have some safety data from it and get some information.

DR. SIMMONS: I agree. I disagree with one thing you said. If a company comes and does a lesion set and then someone else does a slightly different lesion set, it doesn't mean that their catheter could actually be approved because now they can do that second lesion set. It might be a completely different problem with the catheter tip or the material or the way--so, if they guess wrong, it is probably too bad, isn't it? It is a shame, but that is the way it will have to be. But I agree.

DR. TRACY: It is the kind of situation where you would hope that, ha ha, industry would be communicating so that if somebody knew that lesions in such-and-such a location never worked that they would tell everybody so that nobody wastes anybody's time doing things that don't work.

We are subjecting people to lots and lots of radiation, lots and lots of effort. I think this is really calling on the scientific community as well as the industry to really be forthright about what information they are gathering so that people don't waste their time and expose patients to unnecessary risk.