Interim Data From the VISION OCT Image-Guided Atherectomy Trial

Interview by Jennifer Ford

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At the 2015 EuroPCR meeting, clinical investigators presented 30-day interim results from the VISION trial, a study designed to evaluate the safety and efficacy of the Pantheris OCT image-guided system (Avinger, Inc.) to perform directional atherectomy for removal of plaque from diseased lower-extremity arteries. Interim results as of the date of the meeting showed that following Pantheris treatment, residual stenosis of less than or equal to 50% was achieved in 96% of lesions, surpassing the primary efficacy endpoint performance goal. Both Ankle Brachial Index and Rutherford classification outcome measures showed statistically significant improvement across all patients undergoing 30-day follow-up. Safety data at the time of procedure and through 30 days also indicated an extremely favorable acute safety profile, with 0 dissections and 0 perforations related to the use of the Pantheris catheter in the Per Protocol cohort as adjudicated by an independent clinical events committee (CEC). The study's primary safety endpoint is defined as freedom from a composite of major adverse events (MAEs) in less than or equal to 43% of patients through 6-month follow-up. While not representative of 6-month results, 7% of patients in the VISION trial had experienced an MAE through 30 days. Avinger completed patient enrollment in the VISION clinical trial in March 2015. Data collection and analysis is ongoing for the 6-month follow-up period. Following availability of 6-month data, primary endpoint analysis results will be used to support a 510(k) application with the FDA.

At the 2015 New Cardiovascular Horizons meeting, *Vascular Disease Management* spoke with trial investigator Patrick Muck, MD, a vascular surgeon from Good Samaritan Hospital in Cincinnati, Ohio, and Avinger founder and CEO John B. Simpson, MD, about the trial and the Pantheris system.

Dr. Muck and Dr. Simpson have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Muck reports consultacny, stock ownership, and reimbursements from Avinger. Dr. Simpson reports employment, board membership, stock ownership, and reimbursements from Avinger.

VDM: What is the distinguishing feature of the Pantheris device?

Simpson: The key element of the device is we've been able to incorporate on-board imaging using optimal coherence tomography, which is a fiber optic-based imaging system, in a way that allows us to image the cutter edge so we know exactly what the device is doing, real time, during the procedure, when the cutter is being used in a passive mode just for imaging. This is profoundly different from anything we've ever had because historically we've had only fluoroscopy to look at the artery, and fluoroscopy gives you a shadow view of the channel for blood flow, but it doesn't tell you anything — it's just not capable of resolving anything that relates to how the disease is distributed in the vessel. Knowing that is pivotal when working on the vessel — to know how the disease is actually being distributed and the plaque is being distributed in the arteries. It's as though we have a little camera on the cutter and it allows us to see what we're doing real time, which raises the safety and efficacy profile of the procedure in a very dramatic fashion.

VDM: What was the impetus for the development of the device?

Simpson: With fluoroscopy, we had a lot of perforations — not horrible perforations with some of the previous devices but really noticeable perforations — and unfavorable outcomes. Also, if you cut too deep in the artery wall, the restenosis and recurrence rates are high. We've known that for a long time, but we've never been able to avoid doing it, and now for the first time we can do both: we can cut appropriately but, sometimes more importantly, not too deeply. It was a combination of those two things that haunted me a bit and I just kept thinking that there had to be a better way to get more information and to add more precision to raise the safety profile of the intervention that we're doing. I'm trained as a cardiologist, so our target is to eventually get into the coronary arteries but we're starting off in the peripheral vessels. You never want a perforation in any vessel, and while they can be managed almost routinely in the peripheral arteries, they can be a disaster and potentially fatal in the coronary arteries. So as we move closer and closer to the coronary arteries we want to make certain that our on-board imaging will raise the safety profile.

VDM: Could you give us an overview of the design of the VISION study?

Muck: For the first time ever we had a trial with image-guided atherectomy utilizing OCT. So OCT is obviously not a radiation source so that's a benefit, but the biggest benefit of this trial is that for the first time ever you can actually see inside the artery, see what you want to remove, see what you want to keep, no different than what I do in the operating room. As a surgeon I do over 120 endarterectomies a year. And surgery is all about tissue planes: you want to remove the disease but you also want to leave the healthy tissue, and for the first time now you can actually see inside the artery and apply the same surgical principles with an endovascular approach. You can remove what you want to remove, and leave what you want to leave. It's no longer blind atherectomy.

VDM: You think that Pantheris is changing a clinical paradigm for imaging?

Muck: I don't think there's any question it's going to change the paradigm. With this, not only can you see inside the vessel but also you can see the layers of the vessel, see where the plaque is removed, see what needs to be removed, and leave the healthy tissue behind. What physician doesn't want more information about their patient and their disease process? This is an unquestionable paradigm shift.

VDM: Could you share a few highlights from the data of that just came out?

Muck: Thus far at 30 days there have been no dissections, no pseudoaneurysms, and no perforations related to the use of the Pantheris in the per protocol cohort. Again I think that's all related to the fact that you can actually see inside the vessel and you can avoid healthy layers but you can also remove the disease as well.

VDM: So how will this fit into the interventionalist's armamentarium and their decision-making?

Muck: There is not one device that fits all – you have to individualize for patients – but I think that as we move forward we're realizing that stents and permanent implants are not always best. The attitude of "leave nothing behind" is definitely taking over. So we will use this to remove tissue, remove the plaque, and then also apply some biologic agent like a drug-coated balloon or a drug agent to the lesion and I think that's where it's headed.

VDM: So the Pantheris device offers a radiation-free solution to atherectomy?

Simpson: I often ask the question, "Raise your hand if you want more radiation exposure." There are some physicians who are not nearly as sensitive to these issues and they should be; they think it's merely a hazard of the trade. But eventually the hazard of the trade will take a toll and they're going to want to avoid that, and OCT gives them that opportunity. I believe that the day will come where we can do the entire intervention, other than getting the device in place, everything else will be without fluoroscopy or radiation exposure for the physician or for the patient.

Muck: Radiation exposure to patients, physicians, and the team is something we don't pay enough attention to. Now there are reports of left-sided multiglioblastoma in cardiologists. This OCT imaging does not use radiation, so it's less exposure for us, for patients, and for the whole team. In the future we'll need to look at ways to reduce radiation exposure and with the OCT imaging that Dr. Simpson has created, you can see the inside of the vessel and all three layers and you're doing it without radiation or harm to the patient or physician. I've spent seven years learning surgery, essentially seven years in surgery school learning how to do endarterectomies, preserving tissue planes and removing disease, but keeping the healthy. Hats off to Dr. Simpson who has now brought a surgical procedure such as endarterectomy into the endovascular world. He never ceases to amaze me.

Simpson: There is increasing evidence that there are all kinds of malignancies associated with sustained

radiation exposure and it's exacerbated now that we're being more aggressive working in the peripheral vessels because the way that labs are set up. The x-ray tube is much closer to where the physician is standing when they're working on the leg. Radiation exposure is still serious for physicians working in the coronaries but you're working on the heart which is a couple feet away from the groin. This is the reverse. It requires no radiation, no x-ray radiation, anything like that to do OCT. And, in fact, the fluoroscopic images will frequently lead you astray, so there's no real reason to use fluoroscopy during the atherectomy process.

VDM: What did you find to be the most remarkable finding from the 30-day results?

Muck: If you look at the overall tissue analysis from 164 patients, less than 1% of the tissue that's removed is adventitia. That shows how precise this is, so to me that's the most remarkable result, almost as important as the safety of it. As I mentioned previously there were no dissections, perforations, or pseudoaneurysms, so I think it's without a doubt a paradigm shift, and you're talking to someone who up until the last year or two didn't believe in atherectomy. It seemed like a blind process, where you don't know what you are removing or injuring.

Simpson: In my opinion, the most exciting thing is that we've treated 164 narrowings, and we've had not a single perforation, and that just makes me euphoric. This means a lot to a physician to not have to worry about cutting holes in these arteries any longer. And we've had no dissections, and that's how balloon angioplasty works. The whole interventional space will now have to change. Historically, we've always been very aggressive inside the artery with balloons and stents and we push everything around and stuff gets torn and displaced and "squished," and then that leads to this inflammatory response that occurs inside this artery that causes the artery to re-narrow. So now we're taking a whole new approach, we don't do any of that. Now we just clean the artery out and there's no disruption to the deep-wall components, to the adventitia. It's like you sneak in you sneak out and nobody knows that you were there. And that's the part that makes it so exciting because it makes it so safe as well as so efficacious.

And also, only about 1% of plaque removed was "deep-wall" component that we don't want to remove. In other studies, and in studies I have done myself, deep-wall component usually makes up 30% to 40% of what is removed. So to be able to go from up to 40% down to 1% for what you don't want and to have 0 perforations, this is going to set a whole new bar. There will be a learning curve for physicians, but in the end the procedure takes no more time; if anything it will take less time and there are fewer complications.

VDM: So what are some tips for physicians who might think that it would be difficult to implement?

Simpson: The learning curve is probably 5-10 patients. You need to study the imaging, you need to learn how to interpret the images on the OCT. They're kind of similar to ultrasound and most physicians have been using ultrasound for a long time. The resolution

is 10-fold higher than that of ultrasound. If you get a new quarterback, he needs to study the playbook, and just like that, physicians need to study the images in advance and they need to be aware of what the images are really showing because you have to interpret the images directly to take full advantage of the opportunity and if you're sloppy with your image interpretation, and sloppy with the implementation, not that it's unsafe but it's not as safe and as effective as it can be if you're really precise and committed.

VDM: And do you think OCT technology can be expanded into other peripheral vascular therapies in the same sort of application?

Simpson: Well I think we would…we're definitely in the process of exploring that but now I think the sweet spot for OCT will remain vascular in my opinion. I mean you can use it in the GI tract and the pulmonary system but and you know OCT is widely used in ophthalmology, that's really where it started. In the vascular space, I think that it will have a really solid home and the important thing about the way we configure our device, we also have to manage the blood, the disadvantage for OCT it doesn't see through blood very well, the great advantage of it is almost having a microscope, in terms of what you're able to see. Almost like microscopic detail of the artery wall while you're working on it. If you get the blood out of the way and we have really novel ways of managing that and that's not glamorous at all but it's pivotal to getting the images that we need for the physicians to make the good decisions and it has to be really easy to use and I think easy to use did not characterize the device in the VISION trial but it absolutely characterizes the next generation device and we can re-design several elements just to concentrate just on that feature to make it easier to use so…and we've still been able to maintain the same efficacy and safety profile.

VDM: Is there a future study in the works for the new generation device?

Simpson: We will stay focused and concentrate on everything we need to do to get FDA approval. Following that though, of course, I have enormous enthusiasm for comparing this device to other devices. We also created a very smooth lumen and it's a very smooth surface inside the artery and a much smoother surface than anyone else in this space. We can document this smooth surface with OCT, and it is much smoother than anyone else in this space can accomplish, perhaps with the exception of the SilverHawk, but the dilemma that we face with the SilverHawk is that it goes too deep. It does leave a smooth surface, but it goes too deep and that's troublesome. We get a large trough, we get a really smooth surface, we give a really good channel for blood flow that is really smooth, and we can do all though without putting the medial adventitia at risk, so it's a natural device to compare to everything else that's out there — drug-eluting balloons, stents, SilverHawk, CSI, Pathway. I'm eager to see more results.