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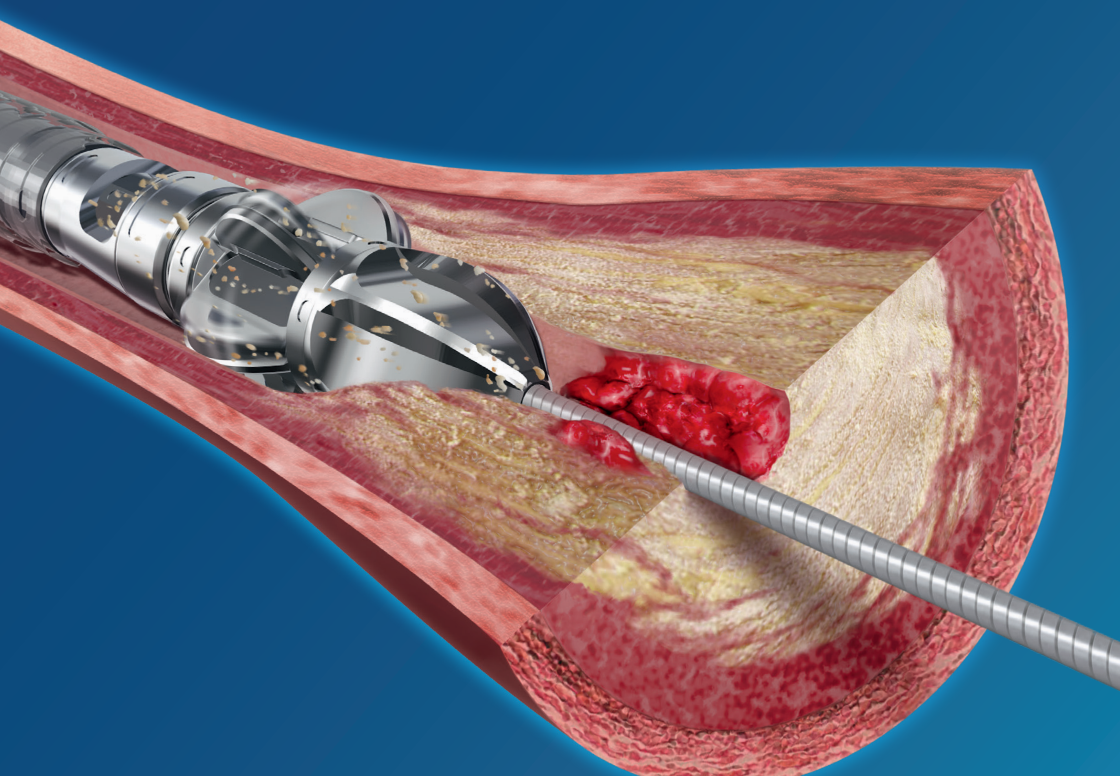


Leading endovascular experts provide their insights on the evolving role of atherectomy.


Robert Beasley, MD


Jos C. van den Berg, MD


Thomas P. Davis, MD


Lawrence A. Garcia, MD


William A. Gray, MD


Akiko Maehara, MD


J.A. Mustapha, MD


Sonya S. Noor, MD


Nicolas W. Shammas, MD


Thomas M. Shimshak, MD

Expert Panel Discussion on Atherectomy and Vessel Prep: What Roles Do They Play In My Practice?

Endovascular Today sat down with a multidisciplinary panel of esteemed interventionists to discuss their current practice paradigms for atherectomy, including the hot topic of Vessel Prep prior to drug-coated balloons and other adjunctive therapies.

MODERATOR

Craig McChesney
Publisher
Endovascular Today
Wayne, Pennsylvania
Mr. McChesney may be reached at cmcchesney@bmctoday.com.

PARTICIPANTS

Robert Beasley, MS, MD
Director, Vascular/Interventional Radiology
MSMC Vein Center, and Wound Healing Center at Mount Sinai Medical Center
Miami Beach, Florida
He has disclosed that he is a trainer and/or advisor for Abbott Vascular, Bard Peripheral Vascular, Boston Scientific Corporation, Cook Medical, Cordis Corporation, Cardiovascular Systems Inc, Endologix, Gore & Associates, Lake Region Medical, Lombard Medical, Medtronic, and Spectranetics Corporation.
Dr. Beasley may be reached at robert.beasley@msmc.com.

Thomas M. Shimshak, MD
Interventional Cardiologist
Heart and Vascular Center
Florida Hospital Heartland Medical Center
Sebring, Florida
He has disclosed that he receives honoraria from and is a consultant and speaker for Volcano Corporation and Boston Scientific Corporation, and does training programs for Volcano Corporation.
Dr. Shimshak may be reached at tshimshak@gmail.com.

Sonya S. Noor, MD
Clinical Associate Professor
Department of Surgery
University of Buffalo
Buffalo, New York
She has disclosed that she is a consultant for Boston Scientific Corporation.
Dr. Noor may be reached at snoor@kaleidahealth.org.

Thomas P. Davis, MD
Director, Cardiac Catheterization Lab
St. John Hospital and Medical Center
Detroit, Michigan
He has disclosed that he is a consultant to Boston Scientific Corporation, Avinger, Roxwood Medical, Volcano, Medtronic, Cardiovascular Systems Inc., Cordis Corporation, and Bard Peripheral Vascular.
Dr. Davis may be reached at (313) 343-4612; tpdavis60@aol.com.

J.A. Mustapha, MD, FACC, FSCAI
Metro Health Hospital
Wyoming, Michigan
Michigan State University
Lansing, Michigan
He has disclosed that he receives honoraria from and is a consultant to Bard Peripheral Vascular, Boston Scientific Corporation, Cardiovascular Systems, Inc., Medtronic, and Spectranetics Corporation.
Dr. Mustapha may be reached at jihad.mustapha@metrogr.org.

All physicians were compensated for their time associated with this panel discussion and/or article.

***EVT:* In your practice, have you treated enough patients using the combination of atherectomy and drug-coated balloons (DCBs) (or other adjunctive therapies) to be able to say if your outcomes are better, worse, or about the same compared to treatment with other contemporary therapies such as stenting, specialty balloons, etc.?**

Dr. Mustapha: Luckily for us, we use ultrasound 100% in terms of bettering our therapy. One of the things that we've done so far [that] we've seen a difference with is debulking the target vessel pretty much to the wall, where you can actually go in, prep the vessel, deliver the DCB, and see under ultrasound that the DCB is actually in complete contact with the vessel wall, giving you a 1:1 ratio between the

> ... for the first time, we have seen fewer patients coming back with restenosis since DCBs have been out, and atherectomy does make a big difference in those patients ...
> —Dr. Mustapha

DCB and the vessel wall. I've got to tell you, for the first time, we have seen fewer patients coming back with restenosis since DCBs have been out, and atherectomy does make a big difference in those patients if you want to get a proper vessel prep prior to [using a] DCB.

Dr. Shimshak: I think the problem is, like all the trials, [what we see in the] real world is different in terms of the endpoints and the patient population that we deal with day in and day out. I think if we limit the scope of DCBs to short or intermediate-length lesions, there is clear benefit. What I struggle with is making the leap for long superficial femoral artery (SFA) disease—chronic total occlusions that are 20 or 30 cm. That is a huge amount of disease that you're dealing with. In those patients, I think atherectomy, coupled with whatever other device, gives you optimal luminal gain and is the way to go. That's why I think vessel preparation is so key. You may be able to achieve [good results in a long lesion] with a DCB, but I think that's a good place for stenting, and I still believe stenting has a role in those long segments of disease.

Dr. Davis: When we were in the DCB trials, we were treating a very different population of patients' lesions. Historically, I can say that I know a few patients who have come back when I've just used DCBs [to treat them]. I haven't seen many of the [patients treated with] atherectomy and DCBs, at least in my own sense of it, but we are collecting our data, and I think at the 1-year mark we'll know a little bit better. I think we need a little bit more time to go by to have a better answer to that question.

I think back over the European data and what Professor Thomas Zeller sees, and you've got to take what he says with a lot of stock. He truly is a believer in [atherectomy and DCB], and that's what he does in his practice.

Dr. Beasley: You see some tremendous results. Early on, I remember a couple of my patients who I treated with atherectomy and DCBs when they first became available. Those patients have not shown any restenosis, reocclusion, or redevelopment of plaque that I can see, and these are patients that I follow closely on external ultrasound in the office.

In my lab, I'm using [multiple DCBs] at a time on a patient and hopefully getting a 70% to 80% success rate, where we don't have to place a stent. If we do have to place a stent, then you're placing a bare-metal stent over an area that already has drug on it.

EVT: What is the role of atherectomy in your current practice? Does it depend on the type of adjunctive therapy you are using?

Dr. Beasley: I use atherectomy in almost every case that has anything to do with any type of peripheral vascular disease—any type of critical ischemia or revascularization model. If [the vessel] has plaque, an occlusion, or a stenosis, I use atherectomy to prepare the vessel.

I'm a user of pretty much all the atherectomy devices, so depending on the location of the lesion, the position of the lesion, and the type of the lesion, I'll use a particular atherectomy device. I know with DCBs, you want to debulk and expose the vessel wall to that drug. With stenting, you want to give the stents a chance so that the stent's drug can appose itself to the wall the best possible way it can. So, I pretty much use atherectomy at all times.

Dr. Noor: I started using atherectomy early in my fellowship training so I took to it really easily—it wasn't as difficult to learn when you have already adopted other techniques, and at that time, it was really just angioplasty and stenting. I really like the philosophy of atherectomy, which has luminal gain and removal of the plaque, allowing the vessel to be more compliant with minimal trauma. Everything else that we do to the vessel in order to get luminal gain causes more injury and trauma and sets you back a year from now, when you have disease recurrence.

I use atherectomy, depending on the lesion, almost everywhere. In the femoral, popliteal, or below-the-knee distribution, atherectomy is probably my first line of defense. It then allows you to decide how you want to treat after. I'm not a big stenter; however, I will use focal stenting, depending on how much lesion or disease is left behind. I think it's a great platform for DCBs and possibly drug-eluting stents (DESs) once we have a little bit more data.

Dr. Mustapha: I try to marry each atherectomy device with the type of lesion or plaque that I'm facing at the time. In our institution, we use extravascular ultrasound, and that has been extremely helpful. We evaluate the plaque that we're dealing with and actually make a decision on which type of atherectomy device we're going to use based on what we saw. [Under fluoroscopy,] we tend to undersize the vessel significantly, especially in the SFA/popliteal and tibial vessels. Based on what we see on ultrasound, we are able to debulk or modify the vessel [plaque] more accurately.

Dr. Shimshak: For me, it really comes down to plaque burden. When you begin to look at these vessels from a physical standpoint, you begin to realize why balloon angioplasty has failed at the most basic level. Remember, you cannot achieve an adequate lumen just by compressing that material. By the same token, even if you are an aggressive stenter, you [may] not be able to achieve optimal luminal dimensions of the stent even with the highest-performing stents today without preparing that vessel, in my opinion. I think balloon angioplasty is not enough. As Dr. Noor said, there is no question that as we begin to embark on preparing the vessel with balloon angioplasty when these vessels are highly calcified, there's a high incidence of dissections that are generated, which impacts patency and the durability of whatever intervention you perform.

Dr. Davis: To add onto that complexity, as years go on, we all push the envelope in terms of the types of vessels we're willing to treat. As the complexity of lesions increases, I think atherectomy really is almost imperative in those types of lesions—long calcified lesions, thrombotic, and mixed lesions. As we push the limit, that's where we need it more.

Dr. Mustapha: Intimal calcification is different than medial calcification. Intimal calcification is the one that actually causes the problem for us, in particular if you deploy a stent without prepping the vessel properly—this is where you see the stent kinked. Intimal calcification has a significantly higher density of calcium deposit in it versus medial calcification. This is where the term "debulking" versus modifying the plaque comes into play. Knowing what kind of lesion you're dealing with is extremely important. Sometimes you may not be able to debulk it, so you modify it, and you will be able to dilate it.

Dr. Shimshak: To Dr. Mustapha's point, 360° calcification cannot be approached with angioplasty or any other device short of debulking. In my practice, the other traditional subset, as Dr. Davis alluded to, that we backed off from and now are pushing the envelope on, would be common femoral disease. I don't think every [case of] common femoral disease needs to be treated with endarterectomy. I think there are subsets that can be treated with endovascular techniques, and I think intravascular ultrasound (IVUS) is the guide for that, correlated with angiograms.

ATHERECTOMY AND DCBs: A Q+A WITH DR. NICOLAS W. SHAMMAS

Nicolas W. Shammas, MD, MS, FACC, FSCAI
President and Research Director, Midwest Cardiovascular Research Foundation; Adjunct Clinical Associate Professor, University of Iowa; and Consultant and Interventional Cardiologist, Cardiovascular Medicine, PC
Davenport, Iowa
He has disclosed that he received related research and educational grants for the Midwest Cardiovascular Research Foundation from Boston Scientific Corporation, Medtronic, and CSI; and is a trainer for the JETSTREAM Atherectomy System, is on the speakers' bureau for Boston Scientific Corporation, and is a member of the JET steering committee.
Dr. Shammas may be reached at shammas@mchsi.com.

***EVT:* In your practice, in which lesion types are you choosing to perform vessel prep with atherectomy prior to DCBs?**

Dr. Shammas: I use atherectomy frequently prior to DCBs or plain old balloon angioplasty in any lesion > 10 cm long, any total occlusions (if you cross intraluminally), or calcified plaque—irrespective of length.

Why do I do this? We have seen that these particular lesions are high risk for dissections and stenting, and I try to use a no-stent strategy in my lab as much as possible to keep the vessel intact for potential future treatments and avoid potential stent-related problems. With that no-stent strategy, atherectomy has become very important in my lab. If you look at the lesions that have the highest predictor for the need for stenting and the lesions that are more likely to dissect, they are calcified long lesions, total occlusions, and complex lesions (TASC C and D). With that in mind, these particular vessels are treated with atherectomy in my lab almost routinely. I have been performing atherectomy for over 15 years now, which has reduced my stenting rate to < 10%. Atherectomy is quite the tool to allow me to have the best acute procedural success.

***EVT:* Do you think thrombus is underappreciated in peripheral artery lesions? How important is clearing the thrombus barrier prior to utilizing DCBs?**

Dr. Shammas: Clots can be of different ages, and different age clots bind paclitaxel in different ways and allow diffusion of the drug in different ways, creating a milieu that is highly unpredictable to how much drug can penetrate into the vessel

EVT: Despite a lack of level 1 data, what inspires your confidence in using atherectomy prior to DCB? What would you say to peers of yours who have not yet incorporated vessel prep with atherectomy into their practice, prior to using DCB in certain lesion types?

Dr. Noor: It's unfortunate that atherectomy doesn't have good level 1 evidence. It's probably a failure on all of our parts that there isn't good level 1 evidence that allows you to compare such a good modality of treatment with other standard modalities out there. But if I had to do every case with level 1 evidence, I would only get half my cases done, realistically.

It does take time. The problem with atherectomy is that there is a learning curve, and it's a steep learning curve. There are multiple devices out now, so it's difficult to be able to learn each one of them, but if you would pick one or two, you could use it. It's not as easy and fast as angioplasty and stenting—it's a labor of love—but I think you offer your patients a very good solution.

> As the complexity of lesions increases, I think atherectomy really is almost imperative in those types of lesions—long calcified lesions, thrombotic, and mixed lesions. As we push the limit, that's where we need it more.
>
> —Dr. Davis

Dr. Beasley: When you take a look at IVUS and see the concentric luminal gain after atherectomy, and you take the Fanelli results into account, and then the dispersion of the balloon and paclitaxel into the wall, when you improve the wall apposition—it's an argument you make without level 1 evidence, but it's an argument that I think that most reasonable folks can understand.

Dr. Shimshak: I think it's a leap at this point; we don't have the robust datasets that we want. I think it will come, but the message I would convey to people who are not yet embracing atherectomy, to help them understand the power of that therapy, would be to begin to use IVUS if they're not using IVUS. I think that is the key element in understanding the utility of this approach. Then, be guided by atherectomy coupled with other new technologies that do have more proven efficacy.

wall. In my mind, the presence of a thrombus is equal to unpredictability of drug absorption into the vessel wall. If we can take care of the thrombus and remove it as much as possible, I think that would create more homogeneous, predictable drug diffusion into the target lesion.

With that in mind, I use the JETSTREAM™ Atherectomy System (Boston Scientific Corporation), because it's also approved for thrombectomy. I use it to treat both fibrous plaque and thrombus, and I try to remove as much of this plaque-thrombus burden as I can safely. The presence of a thrombus is also a high predictor for distal embolization, so particularly in total occlusions, I tend to use filters on a routine basis because we know very well that embolic debris will likely occur during the treatment.

EVT: How important is creating concentric lumens or circumferential lumens with atherectomy in order to create a uniform landing zone for DCB?

Dr. Shammas: My own particular preference is to maintain the rotational cutting within the intima and the superficial media rather than go deep into the media and the adventitia. There is a very interesting study that was recently published in the *Journal of Endovascular Therapy* that discussed the impact of deeper cuts into the media and the adventitia.[1] Strikingly, it showed that a very high rate of patency loss would occur when you cut very deep into the media and adventitia, supporting the hypothesis that restenosis, to a large degree, originates from the outer and deeper layers of the artery. To me, atherectomy is about vessel modification and about getting the least amount of deeper trauma into the vessel wall. I think this is a very important concept and raises the question of whether rotational cutting may lead to less restenosis than random directional cutting.

EVT: What type of clinical data would you like to see in the future regarding atherectomy and DCB?

Dr. Shammas: Peripheral vascular intervention lags behind the coronary world by years, and the reason for that is the lack of good, randomized data. I'd like to start seeing a move from just registries—which are also important—but, we need to move into the world of randomized trials that are powered enough to prove a point.

We need to be able to prove and get the message out there that atherectomy devices added to a DCB can be highly effective in reducing acute failure, and at the same time will likely have an impact on the long-term patency and reduction of target lesion revascularization. I would also like to see a trial of atherectomy with DCB versus DCB only that is powered and large enough to at least show that the additional vessel prep and the additional vessel modification would lead to better outcomes acutely as well as in the long term. ■

1. Tarricone A, Ali Z, Rajamanickam A, et al. Histopathologicial evidence of adventitial or medial injury is a strong predictor of restenosis during directional atherectomy for peripheral artery disease. J Endovasc Ther. 2015;22:712-715.

Dr. Mustapha: Stents did not always have level 1 evidence. Eventually, atherectomy will have level 1 evidence, and operators who don't use atherectomy today will hopefully see the value of atherectomy then. We had an atherectomy study [DEFINITIVE LE, Medtronic] that had a patency rate similar to stenting, so you already have something that tells you atherectomy is as effective as stenting in certain situations.

Many operators are reluctant to make the shift toward atherectomy utilization. In part, it could be due to the ease of use of a stent and/or not wanting to invest the time using atherectomy. In my opinion, atherectomy is the first tool to think of when trying to achieve the most effective vessel prep.

Dr. Davis: I go back to my Stone Age days when I was just using balloon angioplasty in the coronary [arteries], and then stents came out, and we always [thought] we shouldn't stent all the time, we should do bailout stenting. [Then] all of a sudden, stenting became this phenomenal thing. Then DESs came out, but because of the cost, you only used them in certain areas and at certain times. Now, if you don't put a DES in there, you're committing malpractice unless there's a good reason not to. So I think part of this is cost—costs have come down, and I think we've gotten used to the outcomes there.

I think drug delivery is here to stay, and right now, we have DCBs as our delivery system. Who knows where the technology is going to go and what's going to be the best delivery system, but that's what our system is.

***EVT:* How are you currently making the decision on which atherectomy device to use for vessel prep prior to using a DCB?**

Dr. Shimshak: Calcium is critical to remove and prepare the vessel, but I also think it's plaque burden. Whatever device offers you the ability to debulk varying morphologies is my go-to device. There aren't very many that fit that bill. Most of the atherectomy devices are better for some things than others, but in my clinical practice, the JETSTREAM™ Atherectomy System (Boston Scientific Corporation) gives you predictability for varying lesion morphologies. Even for the non-IVUS users, I think there's comfort in that, if you don't understand the extent of disease, the device will perform admirably regardless of what kind of morphology you've encountered—soft plaque, eccentric, concentric, varying degrees of calcium, thrombus—it provides functionality for all those lesion morphologies.

In my practice, I would say over 90% [of the time, the] atherectomy device that I select off the shelf is JETSTREAM, for the reasons that I've already discussed. It gives me high performance for varying lesion morphologies, it's predictable, and it has a safety profile that's desirable. The aspiration is key, and I find it to be very desirable regardless of where I am.

> ... in my clinical practice, the JETSTREAM Atherectomy System gives you predictability for varying lesion morphologies.
> —Dr. Shimshak

Dr. Noor: Any time you performed a peripheral vascular intervention and you're concerned about thrombus, it's almost a contraindication to do anything because before, if you embolized the thrombus, we didn't have a lot of options. We had to lyse it and then you had to go back in and treat the underlying lesion.

But with newer technology, you can still go in and lyse it or use the AngioJet™ Thrombectomy System (Boston Scientific Corporation) and then treat it with atherectomy, or use JETSTREAM, which allows you to do both [atherectomy and thrombectomy, due to JETSTREAM having an indication for both]. The concept of being able to treat the thrombus and the underlying disease at the same time is very attractive not only for the patient and the time spent in the lab, but also from a cost standpoint. There are a lot of advantages to doing that, and your complication rate hopefully is lower with or without a filter, depending on how comfortable you are using one or not.

Dr. Davis: There is a lot more thrombotic disease that we just don't recognize in these lesions. Dr. Shimshak, as you've noticed, too, that's why by IVUS, with the virtual histology, you see it. When you do an OCT, the thrombotic areas are much more evident. A surgeon would probably recognize it more than we would, but as interventionists, you don't really recognize exactly how much thrombus you're dealing with on occlusive disease in the SFA.

Dr. Beasley: For the great majority of the SFA, [I use] rotational atherectomy because you have the benefit of not only being able to get a really nice channel, but also a very concentric luminal gain that you can then use for your adjunctive treatment modality, be it DCBs or stenting. You also have that aspirational component where you can at least be sure of yourself that you're pushing through and debulking this plaque. ■

The European Experience With Drug-Coated Balloons and Vessel Prep

With a 5-year head start using DCBs before US physicians, Prof. Jos van den Berg shares his take on best practices with this tool, as well as the available data.

Jos C. van den Berg, MD, PhD
Head of Service of Interventional Radiology
Ospedale Regionale di Lugano, cede Civico
Lugano, Switzerland
Associate Professor of Radiology
University of Bern, Switzerland
He has stated that he has no financial interests related to this article.
Prof. van den Berg may be reached at jos.vandenberg@eoc.ch.

***EVT:* As someone who has had the opportunity to use drug-coated balloons (DCBs) for a number of years, what would you say to the US physicians who are looking to understand how well DCBs work?**

Prof. van den Berg: When we started using DCBs 5 years ago, we actually didn't know anything about how they worked or whether they worked. So in that respect, being a little bit late may be an advantage, because we know now how they work. When we started, not having any data, we were just using those balloons in difficult lesions. We now have, more or less, the picture that it also works in primary lesions—at least TASC A and B.

***EVT:* Is that knowledge you've gleaned from the randomized studies or from your own practice?**

Prof. van den Berg: It's mainly from the randomized studies. Seeing that it worked in my own practice also helps, but I think when you have the confirmation from larger randomized trials, then you can really be confident that the new technique is working.

***EVT:* From a clinical standpoint, what are some of the salient points about vessel prep that you have learned over the past several years?**

Prof. van den Berg: Vessel preparation can be very helpful. In patients who don't have [a lot of] calcification in the vessel wall, you can do it with just optimal balloon angioplasty. In cases where patients have highly calcified SFAs, then you probably need to do something additional [such as atherectomy].

Regarding optimal balloon angioplasty, I think it's important to be very meticulous with your technique. A lot of people just inflate a balloon rapidly and deflate very rapidly, and that's one of the things that probably enhances the incidence of restenosis by creating this trauma to the vessel wall. By gently inflating the balloon, you really give the vessel some time to adapt to the balloon, not creating much vessel wall injury. By leaving the balloon inflated for a long time, recoil will probably be much less. We know this from studies in the past, in the 1980s and 1990s, when stents were not available, and people had balloon angioplasty as the only tool. Even in the long lesions with long dissections, you can actually get rid of the complication of dissection with a long balloon inflation. That is something we had forgotten about when long stents became available for the SFA.

***EVT:* In heavily calcified lesions, what are some of the additional steps that you try to take?**

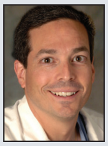
Prof. van den Berg: One of the problems with the heavily calcified lesions, as we know from the Fanelli study, is that the calcium is really interfering with the good results of DCBs.[1] You probably need to get rid of (or crack) the calcium in order to enhance the results in those specific patients. Fanelli et al made a classification from grade 1 to 4, and they really saw a drop off in primary patency in the grade 4 lesions that had calcium all around the vessel wall, almost at 360°. So, the idea is to get that out in order to get better results with the DCBs.

There are some data from a small study from Cioppa et al[2] in Italy that indicate that by using atherectomy to take out the calcium and then following up with a DCB

(Continued on page 18)

The Data Behind Atherectomy and Drug-Coated Balloons

Dr. Lawrence A. Garcia shares his thoughts on what is needed most from future trials and reflects on his key learnings in this space.



Lawrence A. Garcia, MD
Section of Interventional Cardiology and Peripheral Interventions
St. Elizabeth's Medical Center
Boston, Massachusetts.
He has disclosed that he does research for and is a noncompensated consultant for Abbott Vascular and Medtronic; is a noncompensated consultant for Bard Peripheral Vascular, Cook Medical, TriVascular, and Boston Scientific Corporation; is a compensated consultant for St. Jude Medical; and has equity in CV Ingenuity, Primacea, Spirox, Tissue Gen, Arsenal, Syntervention, Essential Medical, and Scion Cardiovascular.
Dr. Garcia may be reached at lawrence.garcia@steward.org.

***EVT:* What type of trial data do you want to see moving forward in the atherectomy and drug-coated balloon (DCB) space, and why? What type of "real world" questions might the data help to answer?**

Dr. Garcia: What we really need now is head-to-head comparisons. At the end of the day, everybody is going to be looking for superiority trials.

I suspect that for a superficial femoral artery (SFA) or an infrapopliteal segment, which is so inhospitable for everything we do endovascularly, that as long as you get a primary patency and the pattern of restenosis is less aggressive than what you first started with, then the therapy for that is a lot cheaper. What you spend up front becomes absolutely critical to the health care dollar downstream, and that's where I think we're going to win or lose on a lot of these head-to-head trials.

The combination therapy of atherectomy and DCB has a large cost, but if the downstream side is that you have a 91% primary patency, and of those 9% that fail, they fail in focal ways, then the downstream reintervention for any patient who needs it is a balloon. [This is more cost efficient] as opposed to having a similar up front cost [with a stent] and having a failure that may become an occlusion, which may then require more expensive reintervention, so your health care dollar just got wasted. I think that is where we're going with ACO models and primary payers—we're going to have to focus a lot on the health care economics.

***EVT:* You have been intimately involved in both atherectomy and DCB trials. What have you learned in your experience that you're applying to your practice today about both of those?**

Dr. Garcia: We've championed atherectomy for a lot of years, and I still believe that the technology, in and of itself, particularly for the SFA, is a very viable and valuable commodity for how we treat our patients when it comes to treatment for claudication. The DCB world, I think, is the holy grail. A lot of us in the United States have seen other parts of the world, particularly Europe and Asia, get DCBs for so many years, and we felt left out. However, once DCBs got here, I think many of us have gravitated to using them in these anatomic locations, particularly the SFA.

In my particular practice, I have found that the combination of therapy, both with atherectomy as well as with DCB is very useful. My hope is that our anecdotal experience translates scientifically when testing combination therapy versus DCBs alone, or against what should be considered the standard right now, which is Zilver PTX's (Cook Medical) 5-year data. Eventually, we have to go against other therapies, and if the endoprosthesis wins, then it will save a lot of time, but we should prove it. If it fails, and atherectomy is proven to be best with the combination therapy, then we should gravitate toward that.

In my particular practice, I've always been somebody who likes to leave nothing behind, and it's interesting to see the worldwide consensus come back to the folks who used to stent a ton and now say that they are leaving nothing behind. I think we've all learned that once you put a stent in there, it's in there forever, and you have to deal with it in some way, shape, or form in the future. ■

Effective Debulking With the JETSTREAM™ Atherectomy System

Strategies for effective treatment of PAD in the era of drug-coated balloons and contemporary stenting.

BY THOMAS M. SHIMSHAK, MD, FACC, FSCAI

Peripheral artery disease (PAD) is a major cause of morbidity and mortality in the United States, affecting 8 to 12 million people. The incidence of PAD increases in the presence of well-defined atherosclerotic risk factors, including cigarette smoking, diabetes mellitus, hypertension, hyperlipidemia, and advanced age, and is estimated to affect > 20% of adults aged 55 years and older. When symptomatic, PAD may adversely have an impact on functional capacity, ability to work, and quality of life. Furthermore, PAD is associated with significant social and economic costs[1] and increases the risk of future cardiovascular events.

Advances in percutaneous catheter-based therapies have led to improved early and late clinical results in symptomatic patients.[2] Successful percutaneous revascularization improves quality-of-life measures, functional capacity, amputation rates, and survival in patients with intermittent claudication and critical limb ischemia. Use of adjunct devices and improved procedural outcomes have resulted in an increase in the number of PAD patients treated with endovascular therapy. The number of endovascular procedures has doubled for patients with intermittent claudication, and it has increased fourfold in patients with critical limb ischemia.[2]

Endovascular therapy of the superficial femoropopliteal arterial segment has historically been challenging. Although overall procedural results have been favorable, late results have been limited by unacceptable high restenosis rates and recurrent symptoms. The atherosclerotic disease process in the femoropopliteal arterial segment is often diffuse with complex histologic morphologies, including soft or fibrous tissue, thrombus, and superficial and deep calcium. In addition, chronic total occlusions (CTOs) are common (Table 1).[3] These factors have limited the utility of balloon angioplasty alone for sustainable favorable results and have led to the use of alternative therapies, including stenting (bare-metal, drug-eluting, and covered nitinol stents), atherectomy, and more recently, drug-coated balloons (DCBs).

TABLE 1. LESION LOCATION AND CHARACTERISTICS*

Variable	No. (%) or Mean ± SD
Stenosis	1,334 (62.4)
Chronic total occlusion	615 (28.8)
In-stent restenosis	188 (8.8)
Mean length, mm	100.8 ± 9.4
Location	
Femoral	660 (30.9)
Popliteal	266 (12.4)
Tibial	513 (24.0)
Bypass graft	59 (2.7)
Multilevel	389 (18.3)
TASC classification	
A	297 (13.9)
B	632 (29.5)
C	592 (27.7)
D	616 (28.8)

**Based on data from Shrikhande GV, Khan SZ, Hussain HG, et al. Lesion types and device characteristics that protect distal embolization during percutaneous lower extremity interventions. J Vasc Surg. 2011:53:347-352.*[3]

The JETSTREAM Atherectomy System (Boston Scientific Corporation) is intended for use in atherectomy of the peripheral vasculature and to break apart and remove thrombus. It consists of a sterile, single-use catheter and control pod and a reusable power console. The catheter is compatible with an 0.014-inch wire

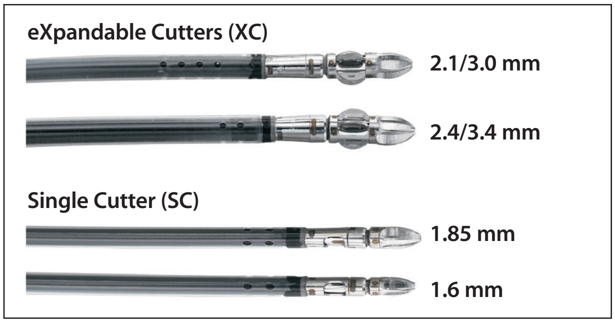


Figure 1. The JETSTREAM Atherectomy System cutters. Two different expandable cutter (XC) catheters are available in sizes 2.1/3.0 mm and 2.4/3.4 mm. The single cutter (SC) catheters have fixed, nonexpandable cutters and are available in two sizes, 1.6 mm and 1.85 mm. All catheters are 7-F sheath and 0.014-inch guidewire compatible (including the Boston Scientific Thruway Guidewire. It is also approved for use with Atherectomy Lubricants, such as Rotaglide™ Lubricant).

(including the Thruway™ Guidewire [Boston Scientific Corporation]) and 7-F sheath. It consists of a five-flute, front-end cutting tip that rotates at 70,000 to 73,000 RPM. Catheters are available in a variety of sizes, including two with nonexpandable cutters (1.6 mm or 1.85 mm), and two catheters with expandable cutters (2.1/3.0 mm, and 2.4/3.4 mm) (Figure 1). The JETSTREAM Atherectomy System is designed to treat a variety of lesion morphologies including soft, fibrotic, calcified, and/or thrombus. By virtue of its property of differential cutting, it preferentially cuts atheromatous disease, while sparing normal tissue. It also incorporates dynamic and continuous aspiration of particulate debris and thrombus, a feature that reduces distal emboli and improves device and procedural safety. Although other atherectomy systems have demonstrated effectiveness in removing calcium, the JETSTREAM Atherectomy System is unique in terms of combining differential cutting with dynamic aspiration (Table 2).

CASE PRESENTATIONS*

Case 1: Diffuse Distal SFA and Popliteal CTO

A 78-year-old woman presented with severe, limiting, intermittent claudication of her right leg. She had undergone complex endovascular therapy of her left leg several months earlier, after presenting with an ischemic great toe ulcer. The ulcer had healed, but she had limiting exertional right calf pain, which had been present for more than 6 months. Previous CT angiography had demonstrated wide patency of the right common and external iliac arteries, common femoral artery (CFA) and profunda, and proximal right superficial femoral artery (SFA). The distal right SFA was diffusely diseased, and the popliteal artery was chronically occluded.

The interventional procedure was completed using antegrade access with a 7-F sheath, demonstrating a diffusely diseased, calcified distal right SFA with multiple subtotal stenoses. The proximal portion of the popliteal artery was chronically occluded with reconsti-

TABLE 2. COMPARISON OF PROPERTIES OF DIFFERENT ATHERECTOMY DEVICES

	JETSTREAM™ Atherectomy System (Boston Scientific Corporation)	Diamondback 360™, Stealth 360™ Atherectomy System (Cardiovascular Systems, Inc.)	SilverHawk™, TurboHawk™ Plaque Excision System (Medtronic)	Turbo-Elite Laser™ Atherectomy Catheter (Spectranetics Corporation)
Front cutting	✔			N/A
Differential cutting	✔	✔		N/A
Active aspiration	✔			
Concentric lumens	✔			
Lesion morphology:				
Calcium	✔	✔	✔ (large vessel only)	✔
Thrombus	✔			✔

Sources: Endovascular Today Buyer's Guide 2014. JETSTREAM System Brochure, Boston Scientific Website, 2014. Boston Scientific, 2014. Diamondback 360 product website, CSI, 2014. Covidien website, Directional Atherectomy products, 2014. Turbo-Elite Laser Atherectomy Catheter Instructions for Use, May 2014.

**Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.*

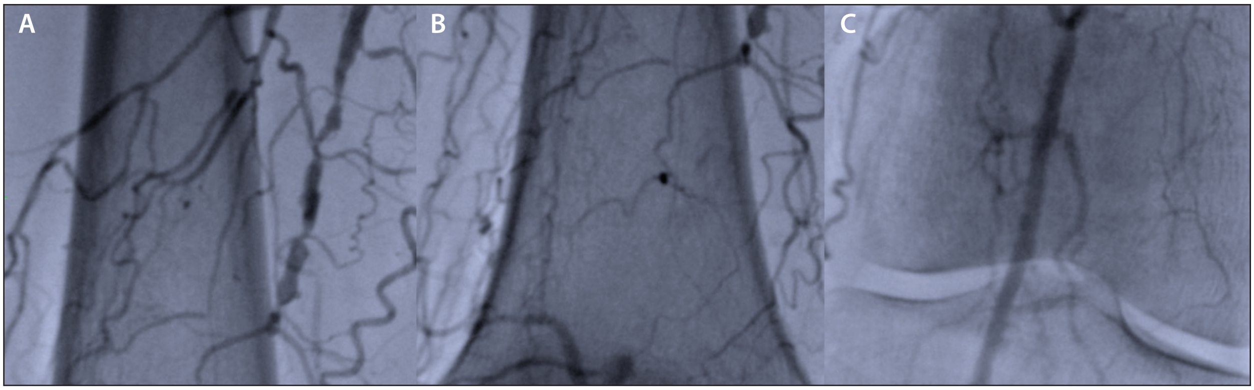


Figure 2. Distal right SFA (A). CTO of the proximal popliteal artery (B). Reconstituted midpopliteal artery (C).

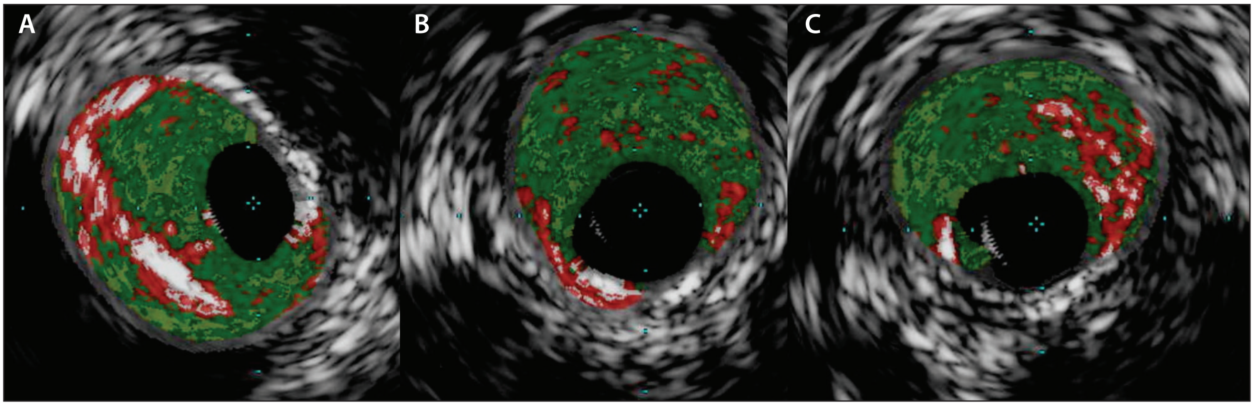


Figure 3. IVUS using virtual histology of the popliteal artery following recanalization and predilatation. Eccentric dense fibrocalcific plaque with scattered thrombus and an extensive arc of superficial calcium encompassing > 270° (A). Eccentric fibrocalcific plaque and scattered associated thrombus (B). Predominantly fibrous plaque and localized thrombus and superficial calcium (C).

tution of the midportion of the popliteal artery via collaterals (Figure 2). The distal popliteal artery had a discrete subtotal stenosis. There was diffuse infrapopliteal disease, characterized by an occluded distal peroneal artery and proximal occlusion of the posterior tibial artery. The anterior tibial artery was widely patent.

After administering 2,500 units of intravenous (IV) heparin, a 0.018-inch, 300-cm-long, 30-g Victory™ Guidewire (Boston Scientific Corporation) was used to recanalize the CTO using a 4-F angled Glidecath® (Terumo Interventional Systems). The wire tip was directed freely into the anterior tibial artery with fluoroscopic guidance. After recanalizing the occluded popliteal artery, an additional 5,000 units of IV heparin were administered to achieve a therapeutic activated clotting time. After exchanging for a 0.014-inch guidewire, the popliteal artery and distal SFA were then dilated with a 2- X 150-mm balloon catheter, performing multiple overlapping inflations encompassing the mid and proximal popliteal artery and distal SFA. The 0.018-inch guidewire was exchanged for a 0.014-inch, 315-cm-long BareWire (Abbott Vascular) delivery wire. Intravascular ultrasound (IVUS) was then performed using the 2.5-mm Eagle Eye® Platinum IVUS catheter (Volcano Corporation). Virtual histology and Chromaflo (Volcano Corporation) were used to assess the disease severity, extent of calcium, lesion morphology, and vessel dimensions and found severe fibrocalcific disease with mixed thrombus and extensive superficial calcium encompassing a > 270° arc of calcium (Figure 3).

The JETSTREAM Atherectomy System was used to debulk the lesion and remove calcium. Prior to introducing the 1.6-mm cutter, a 4- to 7-mm Emboshield NAV6® (Abbott Vascular) was deployed in the distal popliteal artery. The 1.6-mm cutter was advanced manually just proximal to the disease. The device was then activated, and two passes were made, encompassing the entire length of the diseased segment. This was followed by additional passes with the 2.1- to 3-mm cutter. Adjunctive angioplasty of the distal SFA and proximal popliteal arteries was performed with a 4-mm Chocolate® balloon (Cordis Corporation). A 4.5-mm

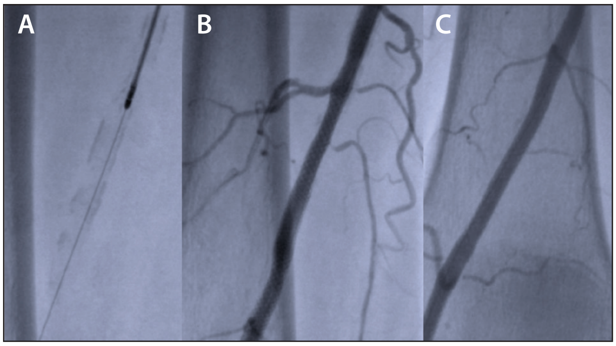


Figure 4. The JETSTREAM Atherectomy System was used on the right distal SFA, which had associated calcium (A). Final arteriogram of distal SFA after using the JETSTREAM Atherectomy System, angioplasty, and stenting (B). Final arteriogram of the popliteal artery after using the JETSTREAM Atherectomy System and balloon angioplasty (C).

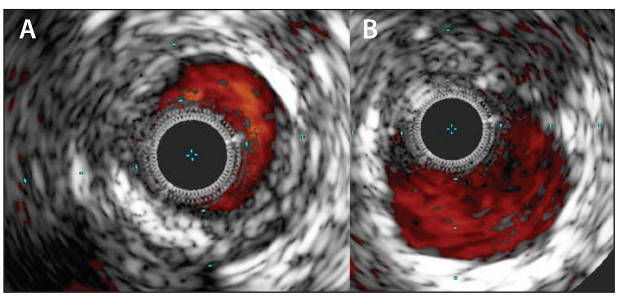


Figure 5. IVUS images of the popliteal artery after JETSTREAM Atherectomy, adjunctive balloon angioplasty (A), and stenting (B). Posttreatment IVUS showed significant calcium and plaque removal and an increase in luminal cross-sectional area compared to pretreatment.

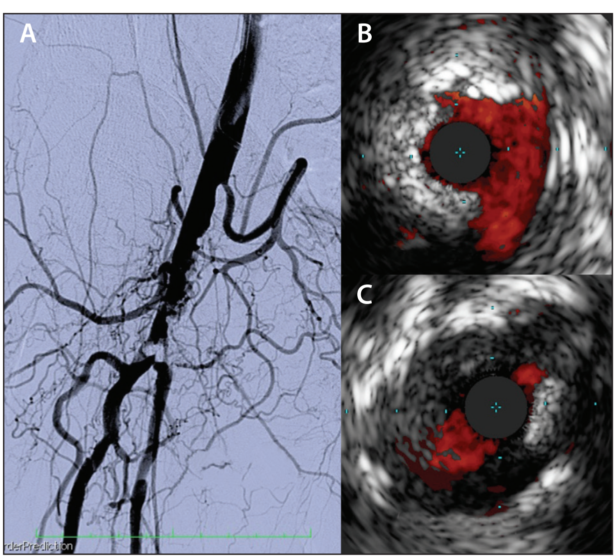


Figure 6. Angiogram of the right CFA, SFA, and profunda artery (A). IVUS images of the CFA (B) and SFA origin (C).

braided self-expanding stent was deployed in the distal SFA with minimal elongation. Final angiogram and IVUS demonstrated wide patency and full stent apposition (Figures 4 and 5). The distal popliteal lesion was also treated with the 2.1-mm JETSTREAM Atherectomy System. The patient's postprocedure course was uneventful. She was discharged the following day and remained stable and symptom free at 6-month follow-up.

Case 2: Complex Calcific Disease in the CFA, Profunda, and SFA

An 84-year-old man presented with severe, bilateral exertional calf discomfort after walking < 1 block. Noninvasive evaluation included a resting ankle-brachial index in the right leg of 0.68. He underwent CT angiography, which demonstrated discrete, high-grade disease of the right CFA and of the proximal and distal right SFA. He had two-vessel runoff below the knee, consisting of the anterior tibial and peroneal arteries. He was referred for selective right iliofemoral arteriography and runoff and possible endovascular therapy. Contralateral access from the left femoral artery using a 6-F Flexor® Ansel sheath (Cook Medical) was used. Selective right iliac arteriography demonstrated highly calcified, complex disease and critical obstructive disease of the right SFA with an eccentric subtotal (95%) stenosis. There was also high-grade disease at the origin of the profunda artery, with an eccentric 85% to 90% stenosis. The CFA was extensively calcified and had significant distal disease just proximal to the bifurcation (Figure 6). The patient was given 5,000 units of IV heparin, and the right SFA was crossed with a 0.014-inch 30-g Victory™ Guidewire. A second 0.014-inch, ChoICE™ PT Guidewire (Boston Scientific Corporation) was directed into the profunda artery using a two-wire technique. A series of sequential balloon inflations were then performed with 2.5-mm and 3-mm X 20-mm balloons, dilating the CFA-SFA origin, followed by the CFA-profunda arteries. The balloons were inflated to 10 to 12 atm, and full balloon expansion was achieved.

At this point, the CFA, SFA, and profunda artery were evaluated with the 2.5-mm Eagle Eye® Platinum IVUS catheter. IVUS demonstrated a dense, extensive arc of superficial calcium of the SFA, encompassing > 270° of the luminal circumference (Figure 6). Based on the arteriographic findings and the IVUS data, the JETSTREAM Atherectomy System was used. A 4-F Glidecath® was advanced over the 0.014-inch-long guidewire into the mid-SFA. The 0.014-inch guidewire was exchanged for a 0.035-inch, 300-cm Supra Core® (Abbott Vascular) guidewire. The 6-F sheath was then exchanged for a 7-F Flexor Ansel® contralateral sheath, which was advanced

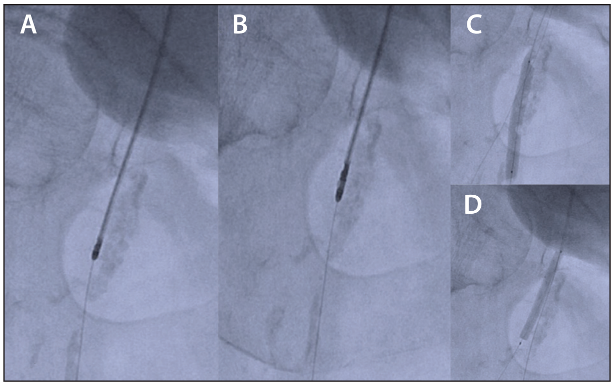


Figure 7. The 1.85-mm SC JETSTREAM cutter (A) and 2.1- to 3-mm XC JETSTREAM cutter (B). Balloon angioplasty of the proximal CFA-SFA after JETSTREAM Atherectomy (C). Balloon angioplasty of the CFA-profunda artery after JETSTREAM Atherectomy (D).

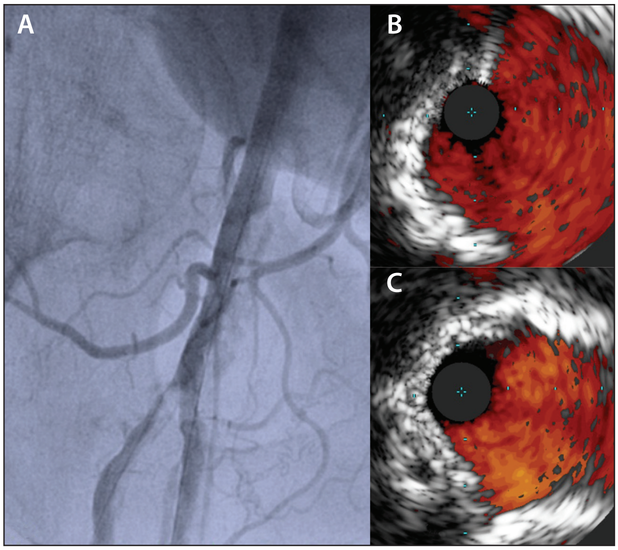


Figure 8. Final angiogram of the right CFA, SFA, and profunda artery (A). Final IVUS image of the right CFA (B). Final IVUS image of the right SFA origin (C).

to the distal right external iliac artery. An additional 2,500 units of IV heparin were administered to achieve a therapeutic activated clotting time. The Glidecath® was reintroduced over the Supra Core® wire to the mid-SFA. The 0.035-inch wire was then exchanged for a 0.014-inch, 315-cm BareWire, which was advanced to the distal SFA, and a 4- to 7-mm Emboshield NAV6® was then deployed. The guidewire in the profunda artery was removed. The CFA and origin of the SFA were then treated with the 1.85-mm SC JETSTREAM catheter, followed by the 2.1- to 3-mm XC JETSTREAM catheter (Figure 7).

After withdrawing the JETSTREAM catheter over the wire, repeat arteriography demonstrated significant improvement in the SFA, with < 50% residual disease. There was persistent high-grade disease at the origin of the profunda artery. The SFA was then dilated with a series of prolonged, low-pressure inflations using the 5-mm balloon (Figure 7C) and 6-mm Chocolate® balloon catheter. The CFA was ultimately dilated with a 7-mm balloon catheter (Figure 7D). A 0.014-inch ChoICE PT wire was then directed into the profunda artery, and the origin was then dilated with a 5-mm balloon catheter. Finally, kissing-balloon inflations were performed in both the profunda and SFAs. The final arteriogram demonstrated wide patency of the CFA and SFA and moderate eccentric disease of the proximal profunda artery (Figure 8A). Repeat IVUS of the SFA and CFA demonstrated a significant reduction in plaque burden, calcium, and an increase in cross-sectional area (Figure 8B and 8C).

DISCUSSION

Both cases demonstrate the effectiveness of the JETSTREAM Atherectomy System in treating complex, calcified PAD. Preatherectomy IVUS characterized the location and extent of the lesion-specific calcium and the complex morphology of the disease. These cases also demonstrate that lesion morphology and complexity may not be fully appreciated by angiography alone. IVUS characterizes vessel size, extent and severity of disease, and morphologic features, including the presence and location of calcium. The JETSTREAM Atherectomy System is effective in removing plaque and calcium, resulting in significant luminal cross-sectional area. It was particularly effective for highly calcified disease of the CFA and SFA. Despite the severity and complexity of the disease in this challenging location, a favorable procedural result was achieved with combined atherectomy and balloon angioplasty.

Why Is Calcium Removal Important?

Calcium is common in patients with PAD, and its presence adversely affects procedural results and long-term outcomes. The presence of calcium necessitates greater balloon inflation pressures, resulting in an increased rate of dissections after balloon angioplasty. Despite using high balloon inflation pressures, the presence of calcium and excessive plaque burden may limit stent expansion.[4-7] The presence of severe calcium limits the long-term effectiveness of DCBs by interfering with effective drug absorption. In a recent analysis, 12-month patency of femoropopliteal arterial segments following treatment with a DCB was 50% for lesions with calcium encompassing 270° to 360°, versus 100% for lesions with calcium from 0° to

90°. Compared to lesions with less severe calcium, excessive calcium was associated with lower ankle-brachial indices, greater late-lumen loss, and high target lesion revascularization.[8]

Benefits of the JETSTREAM Atherectomy System

The JETSTREAM Atherectomy System is effective in removing calcium in femoropopliteal disease. The safety and effectiveness of this device in removing moderate to severe superficial calcium in de novo femoral and popliteal arterial occlusive disease was evaluated in the JETSTREAM Calcium Study.[9] This prospective, multicenter registry used IVUS before and after atherectomy to characterize the efficacy of the JETSTREAM Atherectomy System in removing calcium. The study demonstrated a significant reduction in stenosis diameter (86%, preatherectomy; 37%, postatherectomy; and 10%, postadjunct therapy) and an increase in luminal area (pre: 6.6 ± 3.7 mm^2; post: 10.0 ± 3.6 mm^2; $P = .001$). In addition, calcium removal was responsible for 86% ± 23% of the increase in luminal area following treatment. The ability of the JETSTREAM Atherectomy System to remove plaque (including superficial calcium) improves luminal diameter and cross-sectional area. These luminal gains are further enhanced by adjunct balloon angioplasty (plain-old balloon angioplasty or caged balloons). By virtue of plaque modification and calcium removal, the JETSTREAM Atherectomy System may lead to improved stent results using conventional self-expanding nitinol stents.

Finally, the ability to remove calcium may also improve late results following use of adjunctive DCBs. The DEFINITIVE AR study,[10] a prospective, multicenter, randomized pilot study, evaluated the use of SilverHawk™ and TurboHawk™ (Medtronic) directional atherectomy systems and Bayer HealthCare's peripheral paclitaxel-coated angioplasty catheter with Paccocath® technology. It was designed to assess the clinical benefits of plaque removal using this device, followed by treatment with a DCB with an endpoint of 12-month angiographic patency. DEFINITIVE AR demonstrated higher technical success and a lower incidence of flow-limiting dissections following this treatment strategy compared to using a DCB alone. Additionally, directional atherectomy combined with a DCB improved patency in long and severely calcified lesions. Primary patency rates for the long (> 10 cm) lesion subset at 12 months as evaluated by duplex ultrasound were 96.8% in patients treated with directional atherectomy and antirestenosis therapy (DAART) compared to 85.9% in patients treated with a DCB alone. Primary patency rates at 12 months in severely calcified lesions, per core lab assessment, were 70.4% in DAART patients, compared to 62.5% in patients treated with DCB alone. DAART resulted in 94.1% primary angiographic patency when more plaque was removed with directional atherectomy (< 30% residual stenosis was achieved), compared to 68.8% patency when less plaque was removed (> 30% residual stenosis) before treatment with the DCB.

CONCLUSION

PAD is complex and diffuse, and it is often associated with calcium deposition. The presence of calcium may limit the effectiveness of balloon angioplasty, stenting, and DCBs. Calcium has also been associated with increased rates of dissection following balloon angioplasty. The JETSTREAM Atherectomy System is effective in removing calcium and leads to improved luminal dimensions and cross-sectional area. Plaque modification using the JETSTREAM Atherectomy System may lower complication rates (dissection) and improve early and late results using adjunctive balloon angioplasty, stenting, and/or DCBs. ■

Thomas M. Shimshak, MD, FACC, FSCAI, is an interventional cardiologist for the Heart and Vascular Center, Florida Hospital Heartland Medical Center, in Sebring, Florida. He has disclosed that he is a consultant and speaker for Volcano Corporation, and Boston Scientific Corporation; and performs training programs for Volcano Corporation. He receives honoraria from Volcano Corporation, and Boston Scientific Corporation. Dr. Shimshak may be reached at tshimshak@gmail.com.

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Key Learnings From the JETSTREAM Atherectomy Calcium Study

Insights from the authors on removing severe superficial calcium to achieve significant luminal gain in femoropopliteal arteries.

BY AKIKO MAEHARA, MD; GARY S. MINTZ, MD; AND WILLIAM A. GRAY, MD

The recently published JETSTREAM Calcium Study was a prospective, single-arm, multicenter study to evaluate the effect of the JETSTREAM™ Atherectomy System (Boston Scientific Corporation) when treating severely calcified peripheral arterial lesions in the common femoral, superficial femoral, or popliteal arteries causing claudication.[1] The main question was whether the JETSTREAM Atherectomy System was effective in removing calcification. This was evaluated using both quantitative and qualitative intravascular ultrasound (IVUS), by comparing pre-intervention and postatherectomy IVUS images. The two major findings were as follows: The JETSTREAM Atherectomy System removed and modified moderate to severe superficial calcium to achieve significant lumen gain as standalone therapy; and adjunctive balloon angioplasty after calcium modification with the JETSTREAM Atherectomy System showed further lumen increase without major complications. In this study, the JETSTREAM 2.1/3.0 mm device was used for all procedures without distal protection. There were no major adverse events up to 30 days postprocedure.

WHY AN IVUS STUDY IS UNIQUE

Calcium was screened by angiography to identify moderate to severe obstructive intraluminal calcification in the common femoral, superficial femoral, or popliteal arteries. Lesions were evaluated by IVUS. Patients identified by angiography as possible candidates were included in the final analysis only if there

...major findings were as follows: The JETSTREAM Atherectomy System removed and modified moderate to severe superficial calcium to achieve significant lumen gain as standalone therapy.

CASE STUDY 1: COMMON FEMORAL*

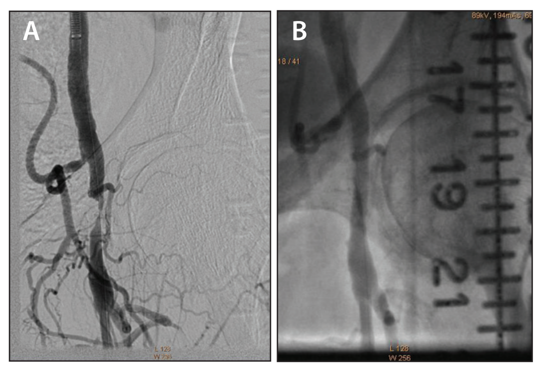

Figure 1. Before (A) and after (B) successful revascularization of a highly stenotic left common femoral artery.

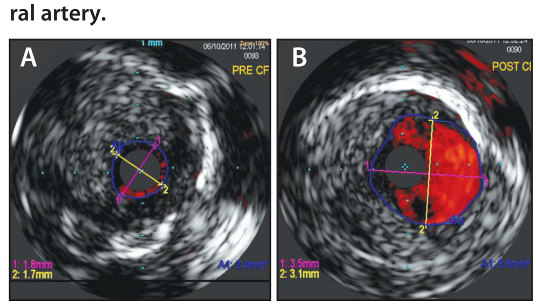

Figure 2. Pre-atherectomy IVUS image of the common femoral artery (lumen area = 2.4 mm²) (A) compared to post-JETSTREAM image (B) illustrates impressive luminal gain and a circumferential lumen created with standalone JETSTREAM Atherectomy (lumen area = 8.6 mm²). Boston Scientific images on file from the JETSTREAM Calcium Study.

**Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.*

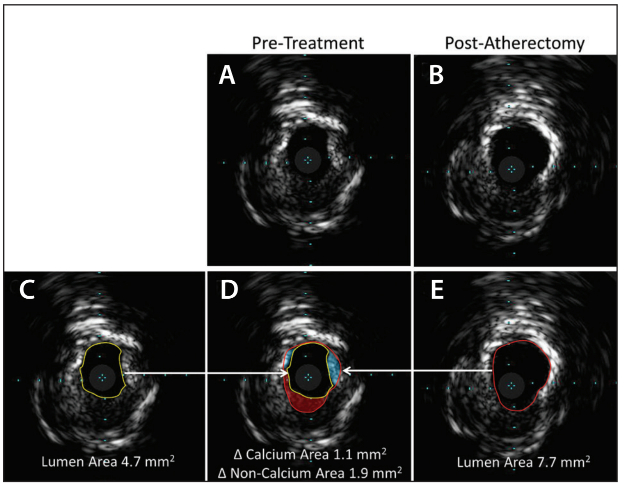

Figure 3. Method of intravascular ultrasound analysis of calcium reduction. The pretreatment IVUS (A). The corresponding postatherectomy IVUS image (B). The analysis sequence is shown at the bottom. After identifying and matching the slices with calcium reduction, the lumen borders for both pretreatment (yellow circle: lumen area = 4.7 mm^2) (C) and postatherectomy images (red circle: lumen area = 7.7 mm^2) (E) were contoured, and the two were overlaid (D). By comparing the two contours to the visual assessment of plaque, lumen gain (3 mm^2) could be attributed to a reduction of calcified plaque (blue area = 1.1 mm^2) or to a reduction of noncalcified plaque (red area = 1.9 mm^2). Reprinted from Maehara A, Mintz GS, Shimshak TM, et al. Intravascular ultrasound evaluation of JETSTREAM atherectomy removal of superficial calcium in peripheral arteries. EuroIntervention. 11(1), 96-103, Copyright 2015, with permission from Europa Digital & Publishing.

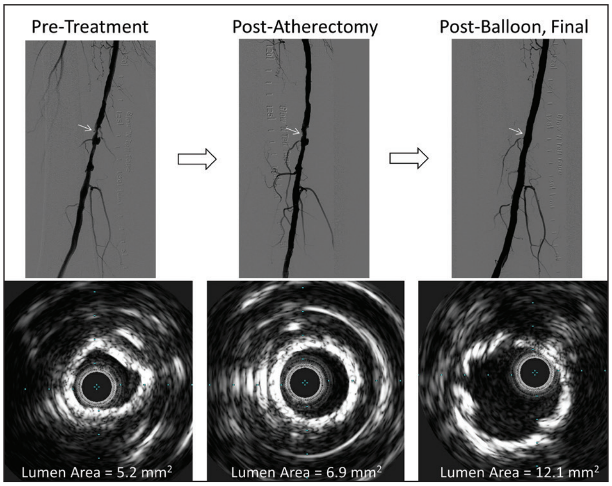

Figure 4. Representative case of pretreatment, postatherectomy, and postballoon final images. The lumen increased from pretreatment (5.2 mm^2) to postatherectomy (6.9 mm^2) to postballoon (12.1 mm^2) without dissection. Reprinted from Maehara A, Mintz GS, Shimshak TM, et al. Intravascular ultrasound evaluation of JETSTREAM atherectomy removal of superficial calcium in peripheral arteries. EuroIntervention. 11(1), 96-103, Copyright 2015, with permission from Europa Digital & Publishing.

was superficial calcium that had an arc > 90° and a length > 5 mm. Overall, 55 patients were screened; however, only 26 patients met the inclusion criteria. Half of the lesions identified angiographically as having moderate to severe calcification did not have severe superficial calcium (calcium within the lumen) at the lesion site as determined by IVUS. In these lesions, superficial calcification existed only in nonstenotic segments, or only deep calcification (calcium within the vessel wall) was present at the stenosis site. Therefore, the first finding of this study was the limitation of peripheral angiography to detect and localize calcification in peripheral arterial lesions. Deep calcification may not affect luminal gain (ie, create a stenosis). Therefore, the differentiation between superficial and deep calcification and their respective roles in severe stenosis is important when evaluating the true efficacy of any atherectomy procedure and device. These findings are similar to the data reported by Mintz et al in coronary artery lesions.[2] In that study, IVUS detected calcium in 841 of 1,155 coronary artery lesions (73%), while angiography detected calcium in only 440 (38%). Therefore, the overall sensitivity of angiography relative to IVUS was 48%, with a specificity of 89%.

> At the slice with the maximum calcium reduction, the lumen area increased from 6.6 ± 3.7 mm^2 preintervention to 10 ± 3.6 mm^2 (P = .001) after atherectomy.

SIGNIFICANT LUMINAL GAIN ACHIEVED WITH JETSTREAM ATHERECTOMY

For the patients who were ultimately included in the study, first the preintervention and postatherectomy IVUS lumens were outlined. Second, the postatherectomy IVUS images were overlaid onto their respective preintervention images. Assuming there was no change in total arterial area, the change in lumen area was attributed to either calcified plaque or noncalcified plaque removal (Figure 3). At the slice with the maximum calcium reduction, the lumen area increased

CASE STUDY 2: DISTAL SFA/PROXIMAL POPLITEAL*

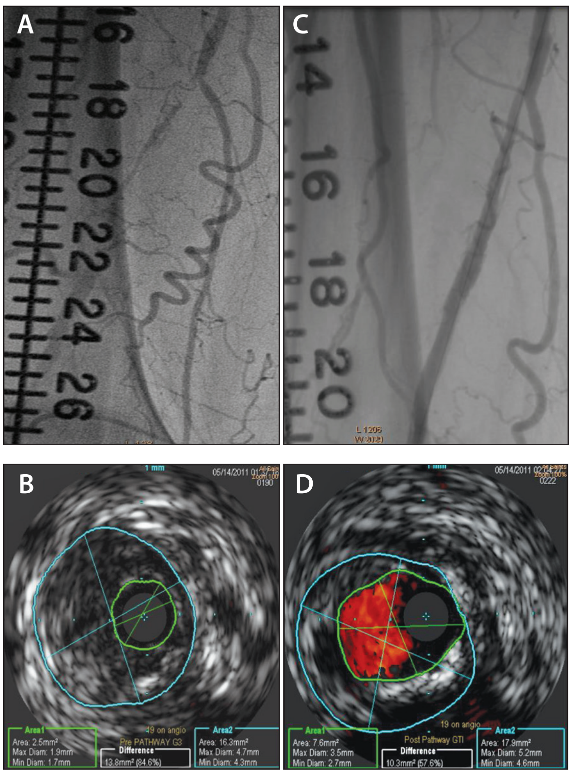

Figure 5. Successful debulking with the JETSTREAM Atherectomy System in a distal right SFA/proximal popliteal artery lesion (A). The pre-atherectomy IVUS image (B) reveals a lumen area of 2.5 mm². The post-atherectomy images (C and D) reveal a lumen area of 7.6 mm² and impressive debulking with JETSTREAM Atherectomy even before adjunctive therapy. Boston Scientific images on file from the JETSTREAM Calcium Study.

from 6.6 ± 3.7 mm^2 preintervention to 10 ± 3.6 mm^2 (P = .001) after atherectomy. The decrease in calcium area, measured as 2.8 ± 1.6 mm^2, was responsible for 86% ± 23% of the lumen area increase. Additionally, the arc of reverberations increased from 25˚ (range, 15˚–35˚) to 70˚ (range, 46˚–95˚), P = .001, indicating device-related modification of calcium. Therefore, the second lesson was that the JETSTREAM Atherectomy System increased lumen dimensions by calcium removal as well as by calcium modification (increase in reverberations).

VESSEL EXPANSION WITHOUT VESSEL DAMAGE

In the 11 lesions that had postadjunctive balloon IVUS images, the minimum lumen area increased further from 7 mm^2 (range, 6.4–7.8 mm^2) after atherectomy to 11.9 mm^2 (range, 10.3–13.5 mm^2) after adjunct balloon inflation (P < .01). However, the prevalence of dissections also increased from 3/11 after atherectomy to 8/11 after adjunct balloon inflations (P = .03). However, the maximum angle of the dissection flap was minor (42° [range, 17°–66°]) with a preserved lumen area (15.6 mm^2 [range, 13.4–17.7 mm^2]) within the dissection. The dissections were non-flow limiting. Also, the higher resolution of IVUS imaging versus angiography most likely led to a higher detection rate. Thus, the third and final lesson was that the JETSTREAM Atherectomy System allowed additional lumen increase by facilitating vessel expansion without significant vessel damage (ie, dissection), presumably because of calcium modification. A representative case is shown in Figure 4.

CONCLUSION

Severely calcified lesions may cause damage to the polymer/drug coating of a drug-eluting stent, resulting in inadequate drug delivery.[3,4] Although there is accumulating evidence in coronary artery intervention showing that calcified lesions have worse outcomes compared to noncalcified lesions,[5,6] the clinical impact of superficial calcium removal in peripheral artery disease in respect to effectiveness of drug-coated balloons or drug-eluting stents needs further investigation.[7] ■

Akiko Maehara, MD, is with Columbia University Medical Center and the Cardiovascular Research Foundation in New York, New York. Dr. Maehara has disclosed that she receives a grant from and is a consultant to, Boston Scientific Corporation.

Gary S. Mintz, MD, is with the Cardiovascular Research Foundation in New York, New York. Dr. Mintz has disclosed that he receives grant support and is a consultant for Boston Scientific Corporation and Volcano Corporation.

William A. Gray, MD, is with Columbia University Medical Center in New York, New York. He has disclosed that he is a consultant to Boston Scientific Corporation. Dr. Gray may be reached at (212) 304-5697; wg2131@columbia.edu.

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**Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.*

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in very heavily calcified occlusions and long lesions, you can get good results with patency rates of 90% at 1 year.

EVT: In your experience, what is the best way to remove calcium from these particular lesions?

Prof. van den Berg: I think you need some kind of mechanical atherectomy. I'm using laser atherectomy a lot, but in these cases merely as a tool to modify the calcium because we know that laser is not really good at completely removing calcium.

EVT: Are there particular characteristics of the balloons that you use for percutaneous transluminal angioplasty that you find to be advantageous?

Prof. van den Berg: I typically use semicompliant balloons that give me a little bit of space to play around with the diameter. By using the compliance chart, the diameter of the balloon can be adapted to the diameter of the vessel wall. It's very important to be aware of the fact that when you use compliant or semicompliant balloons when there is a tight stenosis, in the areas where the balloon opens up more than in the area of the tight stenosis, the vessel wall might get injured much more at the proximal and distal end of the balloon (ie, the dogbone effect). That might, again, be a factor that is influencing restenosis in the long term. ■

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