ADVERTORIAL

BioMimics 3D—The Swirling Flow Stent: Four experts share their views

Thomas Zeller

Thomas Zeller, MD, is Director of the Department of Angiology at Universitäts-Herzzentrum Freiburg-Bad Krozingen in Bad Krozingen, Germany. He has disclosed that he is a member of the Veryan scientific advisory board and receives speaking honoraria and institutional study grants from Veryan.

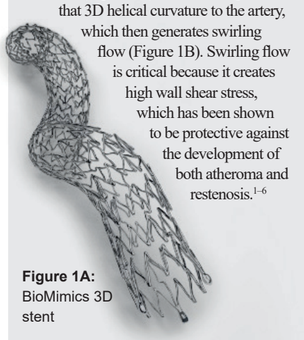

Figure 1A: BioMimics 3D stent

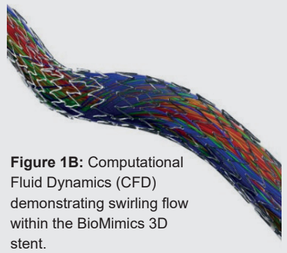

Figure 1B: Computational Fluid Dynamics (CFD) demonstrating swirling flow within the BioMimics 3D stent.

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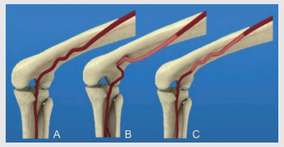

Figure 2:
A. Unstented SFA shortening into a gentle S-shape on knee flexion.
B. A straight stent unable to shorten on knee flexion.
C. BioMimics 3D stent shortening with the vessel on knee flexion.

Professor Zeller, you have had the longest experience with the BioMimics 3D stent, as you were the principal investigator of the MIMICS first-in-man study, and were the first to implant the device. Could you provide some detail about the technology of BioMimics 3D?

Zeller: The BioMimics 3D nitinol stent is unique because it has a true 3D helical centreline (Figure 1A). The stent imparts that 3D helical curvature to the artery, which then generates swirling flow (Figure 1B). Swirling flow is critical because it creates high wall shear stress, which has been shown to be protective against the development of both atheroma and restenosis.[1–6]

You have been involved in many femoropopliteal studies, and have seen new technologies come and go. When you first heard about the interesting science behind the technology of BioMimics 3D, did you think that it would translate into clinical benefit?

Zeller: It is often the case that a novel technology does not bear fruit, and so I was initially curious about the potential outcomes. It seemed quite likely that the biomechanical benefits of BioMimics 3D could be realised, the stent's ability to shorten with the vessel upon knee and hip flexion is intended to mitigate the risk of vessel kinking and stent fracture (Figure 2). The stent is highly resistant to fracture when subjected to the types of longitudinal forces seen in the superficial femoral artery (SFA) and popliteal artery.

It was less clear what effect, if any, would derive from the swirling flow. The MIMICS study included a randomised arm in which the market-leading straight stent of the time (LifeStent, CR Bard) was the control; it was designed as a pilot study to identify potential device performance trends. An independent core-lab reviewed all imaging. Compared to the straight-stent control arm, the BioMimics 3D stent arm had significantly improved primary patency at two years and significantly reduced clinically driven target lesion revascularisation (CD-TLR) between one and two years.[7] It is likely that this difference was due to the long-term protective effect of swirling flow inhibiting development of restenosis.

You are now the European principal investigator for the MIMICS-2 study. Do you choose to use the BioMimics 3D in non-study cases?

Zeller: BioMimics 3D is my first choice in all indications when a stent is required in femoropopliteal lesions except when there is heavy calcification. I have now used hundreds of BioMimics 3D stents in both study and non-study patients since that first-in-man case and the reason is simple: I am more and more convinced that the swirling flow that is generated is protective, that it preserves patency and does so for a prolonged period. It is becoming clear that when a drug-coated balloon (DCB) is chosen as the primary therapy, adjunctive deployment of BioMimics 3D can support longer-term preservation of patency due to swirling flow.

Michael Lichtenberg

Michael Lichtenberg, MD, is Director of the Angiology Department at the Vascular Centre Clinic Arnsberg, Germany. He has disclosed that he receives study support from Veryan and is a member of the Veryan scientific advisory board.

Dr Lichtenberg, you are the principal investigator of the MIMICS-3D pan-European Registry. Why did you want to take on this role?

Lichtenberg: I have been using the BioMimics 3D stent consistently for two years, and it is now my "go-to" stent for use both in primary stenting and in conjunction with a DCB. In that time I have become impressed with the performance of this device. It is very easy to use, and as time has passed it has become clear that the patients are not coming back for reintervention at the rate that I might expect with any other bare metal stent. A recent health economics article has shown that BioMimics 3D was associated with the lowest lifetime costs and the highest number of quality of life years (QALYs) in the UK and Germany when compared to drug-eluting stents (DES), DCBs, bare metal stents (BMS), and angioplasty with bailout BMS.[8] This, of course, is due to the low reintervention rate for BioMimics 3D. I wanted to be involved in a larger scale, real-world registry to find out if the high rates of freedom from CD-TLR that I was seeing in my centre, and that were reported in the Mimics randomised trial, could be consistently reproduced in a larger population.

Michael Lichtenberg

The results from that ongoing registry will be presented in due course. In the meantime, can you describe your centre's experience with BioMimics 3D?

Lichtenberg: I recently presented the preliminary results of 121 patients in the Arnsberg registry at LINC 2017. The six-month results show 95% primary patency and 95.8% freedom from TLR. Of note is the finding that there was no statistical difference between the popliteal artery and the SFA in terms of primary patency. These results are extremely impressive and equate to the very best DES results. Where the two technologies differ, however, is that the drug effect of a DES will wear off, whereas the swirling flow generated by BioMimics 3D does not.

Why do you think swirling flow is so important, and how does it affect your clinical practice?

Lichtenberg: It is generally recognised that flow within an artery is laminar and that because of the helical curvature of arteries, flow is also naturally swirling. This results in an increase in the velocity of blood against the vessel wall and a rise in wall shear, which is beneficial to the vascular endothelium and reduces the risk of both atherosclerosis and restenosis. Swirling flow is most often identified within the larger proximal arteries, which may explain the lower prevalence of atherosclerosis and restenosis in these proximal arteries compared to that occurring in infrainguinal vessels. The BioMimics 3D stent is designed to impart helical curvature to the SFA and popliteal arteries, thus inducing swirling flow. Both swirling flow and the use of antiproliferative drugs have been shown to be effective at maintaining patency by inhibiting neointimal hyperplasia through complementary mechanisms. Consequently, I choose to use BioMimics 3D when primary stenting is indicated and also as the ideal partner to DCBs when adjunctive stenting is required.

Gunnar Tepe

Gunnar Tepe, MD, is Head of Diagnostic and Interventional Radiology at the Academic Hospital RoMed Clinic of Rosenheim in Rosenheim, Germany. He has disclosed that he is a member of the Veryan scientific advisory board and receives speaking honoraria from Veryan.

Professor Tepe, you have been involved in several high-profile DCB studies. Is it the case that DCBs are used preferentially in your practice?

Tepe: We have learned a lot from the DCB studies and as a result have developed techniques to optimise angioplasty when using DCBs. Nonetheless, we have come to realise that there are limitations to DCBs and that they cannot be used to the exclusion of other technologies. Some form of scaffolding is required in a significant proportion of SFA disease, and a stent that is resistant to kink and fracture, that can shorten with the artery while maintaining its radial strength, and that can improve long-term patency is ideal when a scaffold is required.

Besides the need to provide scaffolding, what are some other considerations regarding DCB use that would necessitate either primary stenting or the adjunctive combination of a stent with a DCB?

Tepe: Calcium is one of the obvious limitations for DCB use. The pivotal DCB trials showed improved performance versus simple angioplasty, but that occurred in a tightly selected set of lesions that excluded severe calcification, cases of significant dissection following predilation, and cases in which lesion predilation could not be completed.[9–13] Since only 12% to 26% of the lesions were total occlusions, and since diligent lesion preparation was performed in all cases, this non-calcified simple disease was unlikely to recoil after angioplasty and the bailout stent rate was only 2.5% to 7%. When the same DCBs are used in routine clinical practice, as documented within the global registries, the lesion patency and CD-TLR rates remain good. However, we need to be cautious in the interpretation of these data. These real-world patients present with disease that is more complex than that occurring in those recruited to the pivotal trials, and the rate of stent use is higher at 28% to 35.5%. So in these more clinically generalisable cohorts, we are most likely measuring the outcome of DCB plus stent. The stent rate is clearly related to both lesion length and the chronic total occlusion (CTO) rate. In IN.PACT Global, for instance, when lesion length exceeds 25cm, the stent rate is 53%, while in total occlusions the stent rate is 47%. This is why, in my daily practice, for everything other than simple, short lesions, I use either DCB plus a stent or primary stenting.

Gunnar Tepe

What stent do you choose in these situations?

Tepe: I began to use BioMimics 3D consistently just over a year ago, and since then, I have only had one patient return for a TLR. One memorable case in the early days of using BioMimics 3D was a patient who had previously had a straight, bare metal stent occlude in one limb. When the patient needed treatment of the contralateral limb, I did everything I could to avoid placing a stent in order to avoid another occlusion. I used a DCB, then plain angioplasty, then lithoplasty (Shockwave Medical) plus DCB, but after each of these interventions the lesion occluded within three months. When I finally decided that I would have to use a stent, I chose to use BioMimics 3D plus a DCB, and 12 months later the vessel is patent and the patient has no symptoms. My explanation for the positive results with BioMimics 3D are the same as those expressed by Professor Zeller and Dr Lichtenberg—it is all due to swirling flow. Now whenever a stent is needed, BioMimics 3D is our first choice.

Timothy Sullivan

Timothy Sullivan, MD, is Chairman of the Department of Vascular and Endovascular Surgery and Medical Director of the Abbott Northwestern Vascular Center, Minneapolis, Minnesota, United States. He is the US principal investigator for the MIMICS-2 study.

Professor Sullivan, as you are a US physician, your access to devices is different from that of the other contributors. How does this impact your treatment options?

Sullivan: It is true that the United States lags behind Europe and some other regions of the world with regard to early availability of new technologies. At the same time, there is no shortage of devices available for femoropopliteal intervention, and treatment of patients with infrainguinal occlusive arterial disease remains a challenge for clinicians in terms of choosing the most appropriate modalities. Vascular clinicians are fortunate to have access to a wide armamentarium of devices and procedures, especially as new endovascular devices are developed. We need to be vigilant in looking for improvements in this area so that we can offer our patients the optimum care based on rigorous scientific evidence.

Why did you decide to take on the role of US principal investigator for the MIMICS-2 study?

Timothy Sulivan

Sullivan: Even though the pivotal DCB trials had positive results, there are clear limitations to the blanket use of DCBs in the SFA. In common clinical practice, primary stenting is necessary for certain indications, and a stent is also required in a significant proportion of DCB-treated lesions. In both scenarios, it is logical to use a device with good outcomes that not only provides the scaffolding that DCB-only therapy lacks, but could also extend the period of low incidence of CD-TLR past the initial 12 months when DCBs are effective. The BioMimics 3D stent has been demonstrated, in a randomised controlled trial, to have better patency and a reduced CD-TLR rate when compared to a straight nitinol stent.

Can you tell us about the MIMICS-2 study, including the endpoints and progress?

Sullivan: BioMimics 3D is already CE-marked and available for sale in Europe. MIMICS-2 is a prospective, single-arm, multicentre trial of 271 patients in 47 investigational sites in the USA, Japan and Germany which was designed to provide clinical data to support approval of the product in the USA and Japan. The study has three-year follow-up and includes a 12-month primary patency effectiveness endpoint. The principal investigators are Thomas Zeller (Bad Krozingen, Germany) for Europe, Masato Nakamura (Tokyo) for Japan, and myself for the 35 sites in the United States. Thanks to the excellent support and enthusiasm among our panel of investigators, enrolment was the fastest ever in a femoropopliteal stent study and was completed in October 2016. Now that enrolment in MIMICS-2 is complete, our department (unlike the departments of my European colleagues) no longer has access to this novel device, and I wait with interest to see the primary endpoint results when they become available later this year.

References
1. Caro CG, Fitz-Gerald JM, Schroter RC. Arterial wall shear and distribution of early atheroma in man. Nature. 1969;223:1159-1160.
2. Carlier SG, van Damme LC, Blommerde CP, et al. Augmentation of wall shear stress inhibits neointimal hyperplasia after stent implantation: inhibition through reduction of inflammation? Circulation. 2003;107:2741-2746.
3.Caro CG. Discovery of the role of wall shear in atherosclerosis. Arterioscler Thromb Vasc Biol. 2009;29:158-161.
4.Chiu JJ, Chien S. Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives. Physiol Rev. 2011;91:327-387.
5.Malek AM, Alper SL, Izumo S. Hemodynamic shear stress and its role in atherosclerosis. JAMA. 1999;282:2035-2042.
6. Qin F, Dardik H, Pangilinan A, et al. Remodeling and suppression of intimal hyperplasia of vascular grafts with a distal arteriovenous fistula in a rat model. J Vasc Surg. 2001;34:701-706.
7. Zeller T, Gaines PA, Ansel GM, Caro CG. Helical centerline stent improves patency: two-year results from the randomized MIMICS trial. Circ Cardiovasc Interv. 2016;9(6):e002930. doi: 10.1161/CIRCINTERVENTIONS.115.002930.
8. Kearns BC, Thomas SM. Cost-effectiveness of superficial femoral artery endovascular interventions in the UK and Germany: a modelling study. BMJ Open. 2017;7(1):e013460. doi: 10.1136/bmjopen-2016-013460.
9. Tepe G, Laird J, Schneider P, et al. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. Circulation. 2015;131:495-502.
10. Laird JR, Schneider PA, Tepe G, et al. Durability of treatment effect using a drug-coated balloon for femoropopliteal lesions: 24-month results of IN.PACT SFA. J Am Coll Cardiol. 2015;66:2329-2338.
11. Scheinert D, Schulte KL, Zeller T, et al. Paclitaxel-releasing balloon in femoropopliteal lesions using a BTHC excipient: twelve-month results from the BIOLUX P-I randomized trial. J Endovasc Ther. 2015;22:14-21.
12. Schroeder H, Meyer DR, Lux B, et al. Two-year results of a low-dose drug-coated balloon for revascularization of the femoropopliteal artery: outcomes from the ILLUMENATE first-in-human study. Catheter Cardiovasc Interv. 2015;86:278-286.
13. Rosenfield K, Jaff MR, White CJ, et al. Trial of a paclitaxel-coated balloon for femoropopliteal artery disease. N Engl J Med. 2015;373:145-153.