vascularnews

App

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ACT 1 subgroup analysis shows benefit of carotid artery stenting for women and highly atherosclerotic patients

New ACT 1 subgroup analysis demonstrates that in female patients the rate of ipsilateral stroke is lower with carotid artery stenting (CAS) compared with endarterectomy (CEA), while in highly atherosclerotic patients stenting seems to deliver better overall long-term results than endarterectomy.

The data were presented by Gary Ansel (Columbus, USA) at the Vascular Interventional Advances 2017 conference (VIVA; 11–14 September, Las Vegas, USA), with Ansel noting that the results for female patients are significant as they are discordant with those reported in the CREST trial, while the findings for highly atherosclerotic patients are concordant with data from the CAPTURE 2 trial. Furthermore, the ACT 1 patient cohort represents the largest dataset of randomised asymptomatic carotid stenosis patients treated by experienced operators since the CREST trial.

Gary Ansel

ACT 1 was a prospective, multicentre, randomised trial to support the approval of the Xact rapid exchange carotid stent system and the Emboshield embolic protection systems (both Abbott Vascular) in asymptomatic extra-cranial carotid atherosclerosis patients—the largest randomised trial of its kind to investigate asymptomatic patients. The trial randomised 1,453 patients 3:1 to CAS:CEA and followed them to five years, finding that the treatments were non-inferior at one year (p=0.01) and that at five years there was no difference in any stroke or survival between the groups.

The current analysis evaluated the performance of CAS and CEA in the gender and varying atherosclerotic disease burden subgroups.

The gender subgroup included 212 women and 278 men with no difference in baseline risk factors between the two groups. There was no difference in ipsilateral stroke-free survival rates between the male CAS (96.9%) and CEA (97.9%) patients between 31 days and five years post-procedure (p=0.54). For female patients, the CAS group had a five-year ipsilateral stroke-free survival rate of 99.2% compared with 96.5% in the CEA group (p=0.02).

The patients in the atherosclerotic subgroup were divided into four groups: carotid only (n=161), carotid plus coronary artery disease (CAD; n=141), carotid plus peripheral artery disease (PAD; n=65), and carotid plus CAD plus PAD (n=109). There was no difference in other risk factors between the groups at baseline.

Ansel reported that there was no difference in the rate of a composite of 30-day death, stroke, and myocardial infarction or ipsilateral stroke from 31 days to five years between the carotid only, carotid plus CAD and carotid plus PAD groups. However, in the carotid plus CAS plus PAD group—those with the highest atherosclerotic burden—the five year event-free survival rate was 93.9% for CAS compared with 85.6% for CEA (p=0.04).

This trend was also observed when looking only at ipsilateral stroke at five years, with no difference between the first three groups, but carotid plus CAD plus PAD patients exhibiting a five-year freedom from ipsilateral stroke of 97.8% with CAS and 91.8% with CEA (p=0.04).

"We look forward to the results of CREST 2—even though it will not directly compare the groups analysed here—to learn more about these groups of patients," Ansel said.

Commenting on the data, Alison Halliday (University of Oxford,

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Aloke Finn: DCB particulate embolisation **Page 22**

Stéphan Haulon: Profile **Page 26**

Radiation exposure during EVAR causes DNA damage in operators

Research carried out at the St Thomas' Hospital Campus of the King's Health Partners Vascular Unit, London, UK, and published in *Circulation*, shows evidence of cellular DNA damage in operators performing endovascular aneurysm repair (EVAR), particularly in those carrying out complex procedures.

The health implications of prolonged low dose radiation exposure are frequently a topic of discussion amongst vascular interventionalists, who are performing a growing number of fluoroscopically guided procedures of increasing complexity. Anecdotal evidence points to an alarming pattern of premature, atypical malignancies in high volume operators. However, in the absence of large, prospective registries relating radiation dose to long-term health effects, a causal link with prolonged exposure cannot be established.

The authors of the paper (B Modarai *et al*. *Circulation* 2017; doi: 10.1161) say that the standard method for measuring exposure to the operator employs personal monitors that record cumulative dose in an isolated body area, often not in real time. The safe dose limits set for occupational radiation exposure use a linear no-threshold model that assumes the risk of cancer increases in a linear manner with the exposure. Furthermore, these safe limits are extrapolated from cancers that develop after much higher dose irradiation in survivors of atomic bombs and those exposed to nuclear accidents. "In truth, we know

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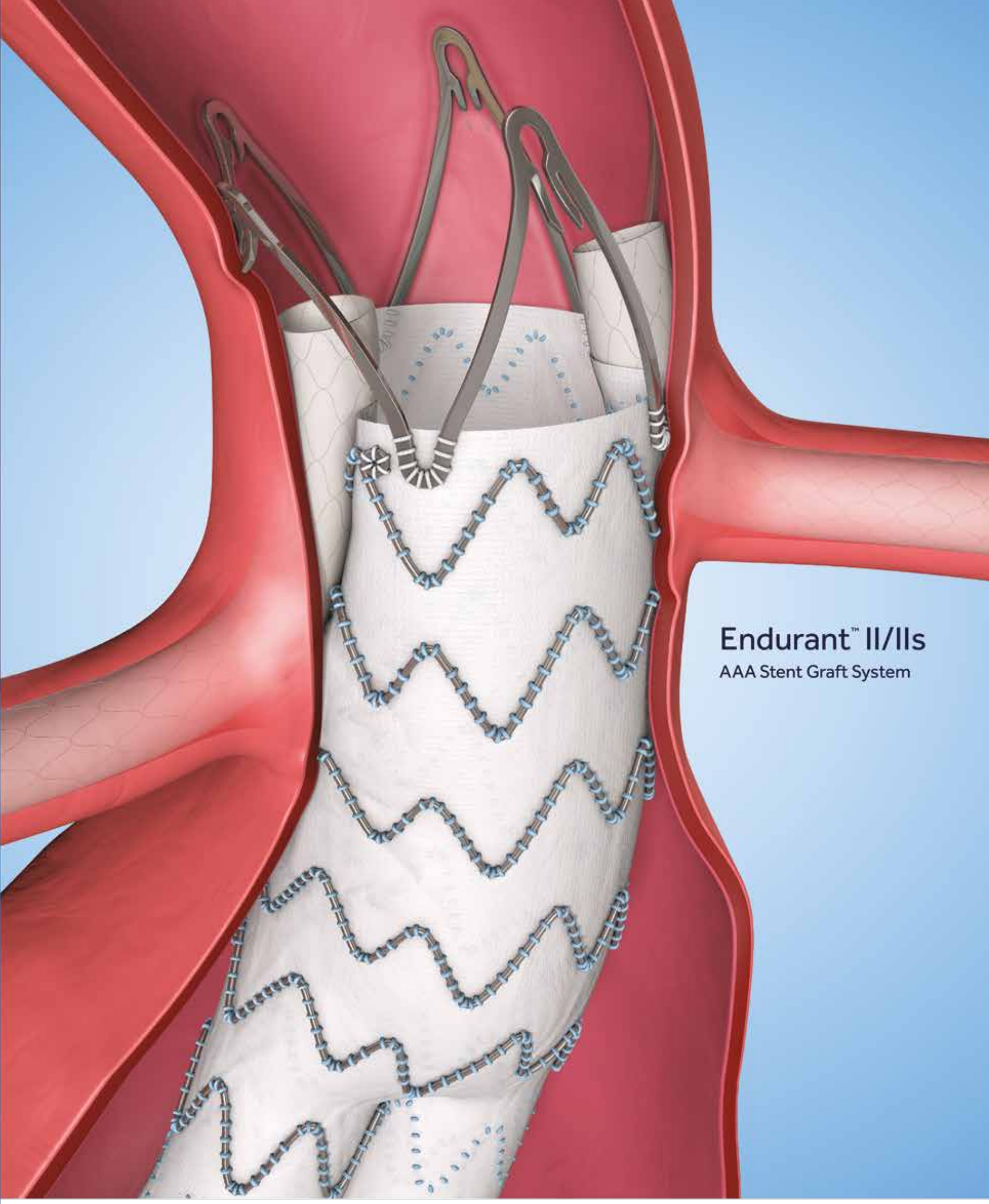

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New Global Vascular Guidelines for chronic limb ischaemia to be published Q1 2018

At the European Society for Vascular Surgery (ESVS) meeting (19–22 September, Lyon, France), *Vascular News* spoke to Florian Dick (University of Bern, Bern, Switzerland) about the new Global Vascular Guidelines for chronic limb-threatening ischaemia, which were presented to delegates as part of the scientific sessions. Dick told *Vascular News* about the main message behind the guidelines, and how they will form a framework around which the evidence base can grow. The guidelines are expected to be published online in the first quarter of 2018.

Florian Dick

What is the main message of the new global vascular guidelines for chronic limb-threatening ischaemia?

FD: The central message is to approach the patient in a holistic way with a planned scheme; patient risk, limb threat assessment according to the so-called WIfI concept and anatomic assessment according to GLASS afterwards. Only then you can decide on how to treat the patients, as you have a basic matrix to predict risks and outcomes. Then you put in your differential treatments and you assess again. You have the chance to follow the patient in a very structured way, and make sure (i.e. measure) that what you are doing leads to improvement. If it does not, you change your treatment approach. It is very much an approach copied from the oncology world, where you have an objective TNM staging system and you restage and restage until you are sure your approach is effective.

How were these guidelines decided when there is a lack of level 1 evidence?

FD: It is true that these guidelines do not reflect existing evidence, but the aim is to provide a universal scheme or a matrix to use in validation trials or evaluation. This is a framework to put upcoming evidence into. It consists of several 'boxes' according to a three dimensional matrix, where you enter the limb threat measured by WIfI—wound, ischaemia, foot infection—stages, the patient risk and the vascular anatomy. Ideally you would have clusters of patients and you would test your therapeutic approaches in each of these boxes to decide which patient would benefit most from what treatment. But we are not there yet, so we provide the framework for systematic assessment of the patient, the problem, and to follow through to outcomes.

How have the other specialties that work on revascularisation of the lower limb been brought together to incorporate the guidelines?

FD: This has been sponsored by the three leading vascular surgical societies—the European Society for Vascular Surgery (ESVS), the Society for Vascular Surgery (SVS), and the World Federation of Vascular Societies (WFVS). It has been written and conceived by an expert panel consisting of all the medical specialties that treat vascular patients, including vascular surgeons, interventional radiologists and cardiologists, vascular physicians and podiatrists. It was difficult to organise the collaboration between these large societies and it would not have been possible to include more official societies and all their needs. There was the follow-up consensus paper of TASC III which eventually did not work out between the several specialties. But many decided to follow this new initiative, which is less lesion based but uses an holistic patient approach.

How does this differ from the TASC approach?

FD: This is a different approach to TASC, which goes lesion by lesion and how each of them should be treated technically. The new view is to evaluate the whole limb, the whole patient first and see what the patient really needs. You want to integrate the whole patient risk regarding perioperative outcome and the problem of the limb (not only its perfusion) to be able to treat the patient's situation, not only a lesion. What the patient wants is to keep the foot functioning, not hurting, and without wounds. The patient does not care about whether the lesion is treated or not. They want to have a functioning leg that does not hurt and does not have any lesions.

Who are the architects of the guidelines?

FD: The driving force came from the three co-editors, Michael Conte, Andrew Bradbury and Phillippe Kohl, each of whom represent one of the sponsoring societies. Joe Mills is one of the leading people behind the WIfI concept, which is a huge leap forwards because it moves away from a purely perfusion perspective, and integrates all the other factors associated with limb threats. It integrates not only ischaemia or perfusion (the "I"), but assesses also wound and foot infection. John White is one of the central coordinators, and Rob Fitridge and Kal Suresh both represent the World Federation to make sure the perspective stays global. Jean-Baptiste Ricco, the former editor-in-chief of the *European Journal of Vascular and Endovascular Surgery (EJVES)* and myself were elected to represent the European perspective on this truly global initiative.

Can you explain the GLASS classification and its use?

FD: The GLASS—global anatomic staging system—classification really relates to the arterial path down the limb. After the step back to see the holistic scheme which integrates the person and the problem (wound, perfusion and infection), you need to go into more detail for the anatomic scheme of the arterial path. With GLASS we have a matrix that assesses the two levels (fem-pop and tibial) regarding arterial vascularisation options with the aim of restoring one path to the foot.

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ACT 1 subgroup analysis shows benefit of carotid artery stenting for women and highly atherosclerotic patients

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Oxford, UK), principal investigator of the ACST-2 trial and president of the European Society for Vascular Surgery, said, "I welcome the addition of newer evidence in this area."

The ACST-2 trial will compare CEA with CAS for long-term stroke prevention, and will enrol patients with tight asymptomatic carotid stenosis. Halliday explained, "In ACST-2 we hope to complete recruitment of 3,600 patients (with over 1,000 women) by the end 2019, so we will be adding evidence from many more randomised patients. Data on women, and particularly on younger women, has been particularly interesting since results from ICSS and now from ACT 1 suggest they may benefit more from CAS than CEA."

"For those with a high atherosclerosis burden, these data are especially encouraging," Halliday told *Vascular News*. "We have recruited large groups of patients with diabetes and with known heart disease in ACST-2, trial follow-up is now three and a half years, so the five and 10-year results of these trials will be of particular interest as long-term durability of carotid procedures is essential to guide future practice."

Radiation exposure during EVAR causes DNA damage in operators

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very little about the biological effects of chronic, low-dose occupational radiation exposure," they say.

Bijan Modarai, reader and consultant vascular surgeon, and co-workers, Tamer El-Sayed and Ashish Patel, also found that use of shielding—especially leg shielding—seems essential protection during such cases.

DNA damage to operators was quantified by measuring the lymphocyte expression of γ-H2AX; a histone protein created by DNA double standard breaks and phosphorylated ATM (pATM); a DNA damage response marker. Lymphocytes are exquisitely radiosensitive and therefore ideal cells to use for monitoring the biological effects of exposure. Expression of γ-H2AX and pATM on lymphocytes was quantified preoperatively, immediately postoperatively and 24 hours postoperatively.

Screening time was significantly longer for complex EVAR procedures than for standard EVAR, resulting in a higher radiation dose area product (DAP) over the course of the procedure. The study showed that complex EVAR procedures were associated with higher levels of DNA damage, with a marked spike in the immediate postoperative period, before falling back to normal levels within 24 hours. Sampling of operators after standard EVAR showed a milder increase in DNA damage markers immediately postoperatively, while open repair showed no increase.

Bijan Modarai

Ashish Patel

Tamer El-Sayed

Radiation exposure to the legs is significant and appears to be a danger. Radiation was measured under a lead apron, over a lead apron, and on the legs during complex and standard EVAR. During standard EVAR, radiation under the lead apron was 0uSv (range 0–3uSv), over the lead was 11uSv (range 4–74uSv), and to the legs was 92uSv (range 43–203uSv). For complex EVAR, radiation under the lead apron was 2uSv (range 0–13uSv), over the lead was 27uSv (range 4–1504uSv), and to the legs was 145uSv (range 16–416uSv).

The induction of γ-H2AX and pATM in operators reflects these high levels of radiation exposure, with a sharp spike post-procedurally without leg pad protection.

In a separate part to the study, blood from six different operators who had not had any exposure to radiation in the previous 48 hours was collected and exposed in vitro to the same radiation dose. The expression of γ-H2AX varied on operators' lymphocytes irradiated with the same dose, with blood from some individuals consistently producing high levels of this marker of DNA damage.

This is the first study to find evidence of cellular DNA damage in operators after performing EVAR and hints at the potential utility of a biodosimetric approach to measuring the effects of radiation exposure. Directly measuring cellular response rather than conventional dosimetry could identify operators who are prone to radiation damage and who may have a lower "safe" limit than radio-resistant operators. Factors such as age, gender, previous exposure, and diet may also impact the response to radiation. It must be stressed, however, that a greater understanding of the long-term consequences of the raised expression of γ-H2AX and pATM in irradiated lymphocytes is required before conclusions can be reached about its relationship to cancer risk.

New Global Vascular Guidelines for chronic limb ischaemia to be published Q1 2018

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Essentially, GLASS looks at the distribution and the severity of the different lesions along the whole limb, and grades them against the chances of success with endovascular treatment.

How is the question of bypass versus endovascular being addressed in the guidelines?

FD: The guidelines are essentially based on the available information we have. Besides a few registry and observational analyses most information comes from the BASIL (Bypass versus angioplasty in severe ischaemia of the leg) trial conducted in the UK, where we saw that patients with a positive prognosis and a life expectancy of over two years will benefit from bypass surgery, because it is more durable with a more direct revascularisation. But again, the new guidelines only provide the scheme and a matrix where we have to yet fill in the knowledge; it is a framework that needs to be filled with evidence.

So the WIfI and GLASS approaches help give clarity on how to predict critical limb-threatening ischaemia trial outcomes?

FD: Exactly. This is a predictive arrangement and now we have to validate it with outcomes. It also proposes a set of standardised outcome measures that make sense clinically, but that can also be measured objectively and compared. This is all about creating a framework for comparisons, across different institutions, different techniques of revascularisation and different countries. The most important aspect we want to integrate is that the concept does not concentrate on North America or Western Europe; it integrates the views of the whole world, so these truly are global vascular guidelines. This also makes it difficult because the means and resources that are available for these patients are highly different in different regions of the world. Health systems are very different; we have to integrate those thoughts as well, not only to have a perspective for very high income countries where they can invest everything into these patients, but to integrate the views of the majority of patients globally. For example, India, China, and Asia more generally have a very important place in it because they have high prevalence of diabetes and they may not have the same means. It really provides a framework for comparisons and it will be a living document that will grow with evidence and get more specific. However, at the moment it does not give you an exact guideline on what to do technically in each instance but instead on how to approach a patient. I think this is the primary sense of these guidelines, but with time and re-evaluation, they will grow into practical clinical (and technical) guidelines.

The Guidelines Steering Committee

Where will the guidelines be published?

FD: This document will be endorsed by the ESVS and SVS, as well as the WFVS. They will come out as a conjoint publication in the *EJVES* and the *Journal of Vascular Surgery*, so there is a lot of interest from both major societies to have a consensus document that will hopefully be generally accepted and live. It comes with a lot of tools, with apps where you can easily calculate your stages and your grades and this would then be used of course to follow your own patients to categorise them and add some outcome data. Only if we produce and generate more and valid evidence we will learn how to apply these schemes, and how to serve our patients best, eventually.

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DETOUR 1 trial shows 88.9% six-month patency following SFA percutaneous bypass for long lesions

A sub-analysis of the DETOUR 1 trial—the largest prospective series evaluating the percutaneous treatment of superficial femoral artery (SFA) lesions with lengths of 25–45cm—has shown that, with optimal positioning, the Detour system (PQ Bypass) achieved 88.9% primary patency at six months with a low 30-day rate of major adverse events (MAEs). The sub-analysis was of the 50 patients (53 limbs) in the "extreme lesion" subgroup with lesions >25cm long.

Presenting the data at the Vascular Interventional Advances 2017 conference (VIVA; 11–14 September, Las Vegas, USA), Sean Lyden (Cleveland, USA) said, "Percutaneous bypass using the femoral vein as a pathway may end up being an important step forward in the treatment of long segment SFA disease."

Long-segment femoropopliteal disease has poor outcomes due to complex anatomy. Intermittent mechanical stresses (extension, compression, contraction, torsion and flexion) limit the efficacy of stents, while extrinsic compression from calcium, hardened plaque and total occlusions mean it is impossible for an implant to achieve its truly stated diameter. All this results in a high incidence of restenosis and reocclusion, resulting in decreased patency, Lyden explained.

Current methods of surgical bypass for long-segment disease result in long hospital stays and high rates of wound complications, rehabilitation and readmissions. Endovascular treatment for TASC C/D patients produces lower patency rates alongside longer procedure times with many devices used per procedure. Percutaneous bypass, Lyden said, was first pioneered 15 years ago, and has proven durability out to four years' follow-up.

The Detour stent graft is designed to achieve results comparable to open bypass, employing the femoral vein as a pathway for a modular stent graft bypass. During the procedure, fluoroscopy is used to deploy a series of stent grafts from the popliteal artery into the femoral vein, and from the femoral vein into the SFA in a continuous, overlapping fashion through two independent anastomoses. The final result is a large lumen, endograft bypass that delivers unobstructed, pulsatile flow from the SFA ostium to the popliteal artery and restores blood flow to the lower extremities.

Sean Lyden

The prospective, multicentre, non-randomised, single-arm DETOUR 1 trial enrolled 77 patients (81 limbs) treated at eight global sites. The investigators employed a CT core laboratory, duplex ultrasound core laboratory and an independent medical review of safety endpoints.

The trial is especially notable in that, unlike past studies, the majority of enrolled patients had lesions >10cm, with an average of 29.7cm. In the long-lesion subset, the average DETOUR 1 lesion length was 33.8cm, while other studies have limited analysis to lengths <25cm.

Lyden presented follow-up data of the 50 patients (53 limbs) in the "extreme lesion" subgroup, who had lesions >25cm long. Of these 50 patients, 84% were male, 30% had a history of diabetes, 26% a history of renal insufficiency, 90% a history of smoking and 30% a history of previous peripheral intervention. The mean lesion length in this subgroup was 33.8±5cm, 96% had total occlusions, and the majority had three run-off vessels (70%).

Technical success was 100% (delivery of the devices and to and removal from the identified area), procedural success was 98.1% (delivery and removal with the absence of in-hospital MAEs), and clinical success was 94% (≥1 grade of Rutherford class improvement at six months).

At 30 days, there were no reported deaths or major amputations of ipsilateral target limbs. There was one (2%) case of target vessel revascularisation, which was treated successfully with an additional Detour stent graft.

Lyden stressed that the key lesson taken from this experience was, "do not fear the profunda". The investigators found that landing level to, or slightly proximal to, the profunda/SFA bifurcation was optimal, and that this optimal placement could minimise edge stenosis.

In fact, when excluding failures caused by suboptimal positioning (n=7), primary patency improved to 88.9% (vs. 76.9%), primary-assisted patency improved to 91.1% (vs. 84.6%) and secondary patency improved to 95.6% (vs. 94.1%).

As for venous health impact, there were no deep vein thromboses in the bypass segment at six months, while VCSS (baseline 0.7±1.2 vs. six months 0.8±1.2, p=0.68) and Villalta (baseline 0.7±1.3 vs. six months 0.6±1.1, p=0.48) scores showed no significant difference between baseline and six-month follow-up.

At six months, 92% of patients saw an improvement ≥2 Rutherford classes compared to baseline. Ankle brachial index scores also improved significantly, from 0.64±0.17 at baseline to 0.92±0.14 at six months (p<0.0001).

"Overall, this subset of the DETOUR 1 trial showed promising safety and effectiveness for the Detour system in treating long-segment femoropopliteal lesions," Lyden told the audience. PQ Bypass is currently in discussion with the Food and Drug Administration for a US trial of the Detour system, with a view to begin enrolment in 2018.

Analysis of percutaneous large-bore arterial access closure shows fewer adverse outcomes and shorter hospital stay versus surgical cutdown

Percutaneous closure of large-bore arterial access sites using the Perclose ProGlide suture-mediated closure device (Abbott Vascular) is associated with significantly lower rates of blood transfusions, infections, mortality and length of hospital stay, compared with surgical cutdown in a real-world setting, according to new data presented at the Vascular Interventional Advances 2017 conference (VIVA; 11–14 September, Las Vegas, USA).

Based on these findings, Darren Schneider (New York, USA) told VIVA delegates, "Perclose should be considered for large-bore closure to minimise access site complications and resource use."

Access site closure for procedures requiring large-bore access is typically achieved using either surgical cutdown or percutaneous closure. In this case, Schneider was presenting data analysis of the percutaneous Perclose ProGlide device.

The retrospective study utilised IBM's Explorys data from IBM Watson Health, and included longitudinal data from 55 million US patients treated since 2012. The patients included underwent transcatheter aortic valve implantation (44.9%), endovascular aneurysm repair (38.6%), thoracic endovascular aneurysm repair (21.3%), or balloon aortic valvuloplasty (3.4%).

Schneider identified 757 Perclose patients and 757 cutdown patients with mostly similar baseline characteristics. Notable differences between the groups were seen in stroke comorbidity (7.7% cutdown vs. 5% Perclose, p<0.05), use of anticoagulants (17.8% cutdown vs. 44.9% Perclose, p<0.05) and use of MRSA antibiotics (27.3% cutdown vs. 11% Perclose, p<0.05).

Matched cohort results indicated that index hospitalisation blood transfusion was higher in the cutdown group (35.7%) than in the Perclose group (9.5%; p<0.001), as were haemorrhage (3% vs. 1.8%, p=0.13) and infection (22.2% vs. 15.6%, p=0.001). At 30 days, the differences were maintained, with blood transfusion rate of 35% vs. 10.7% for cutdown (p<0.001), haemorrhage rate of 3.7% vs. 1.7% (p=0.026), and infection rate of 31.2% vs. 21.6% (p<0.001).

Darren Schneider

Schneider reported that at index procedure, Perclose patients were 80% less likely to require a blood transfusion and 41% less likely to have an infection. At 30 days, Perclose patients were 79% less likely to require a blood transfusion, 43% less likely to have an infection, and 55% less likely to have a haemorrhage.

The mortality rate was lower for Perclose patients than cutdown patients (1.1% vs. 3%, p=0.006) at 30 days, as was length of hospital stay (5.4 vs. 9 days, p<0.001). "At 30 days," Schneider said, "Perclose patients were 70% less likely to die, while hospitalisation for Perclose patients was 43% shorter."

Schneider stressed that the trial was retrospective rather than randomised, that some clinical characteristics that may have impacted outcomes were unavailable in the database, that patients may have been misclassified due to incomplete/inconsistent medical records, and that direct causality cannot be ascertained.

Despite these limitations, Schneider told the audience that the data were encouraging. "Future analyses should focus on quantifying the cost-savings and patient benefit from avoiding these complications," he concluded.

ADVERTORIAL

Role of aspiration thrombectomy in the treatment of intraprocedural arterial thromboembolic complications and acute AV dialysis fistula thrombosis

By Simone and Chiara Comelli, Ospedale S Giovanni Bosco, Turin, Italy

We work in a robust, busy interventional vascular and neuro-Radiology department in the north Italian district hospital. Our practice is often focused on the management of acute ischaemic and haemorrhagic cases, involving both peripheral and neurological pathologies.Through work volume and case presentations, we have gained valuable experience in thromboaspiration over the last decade using Penumbra catheters and systems for the management of acute ischaemic stroke. With this experience in mind, we have shifted these ideas to the peripheral arterial system and onwards to venous pathology such as haemodialysis accesses failure, deep venous thrombosis (DVT) and its main complication, pulmonary embolism (PE).

With regards to acute venous and arterial thrombosis in the peripheral system, mechanical aspiration techniques have become our first choice as rescue method for acute and subacute (up to 7–10 days maximum) cases. We do for subacute cases consider antithrombotic pharmaceuticals such as r-tPA to facilitate the thromboaspiration manoeuvres in more aggressive or difficult thrombotic material. Our theory is to avoid, as much as possible, the risk of thromboembolic distal events in the arterial side. This, however, has changed with the introduction of continuous aspiration power with the **Indigo System** (Penumbra).

The Indigo separators help maintain patency within the catheter in challenging cases. Other mechanical thrombectomy devices/techniques may be used in conjunction with Indigo for chronic thrombotic debulking and vessel patency, in cases with old thrombus, such as chronic DVT cases.

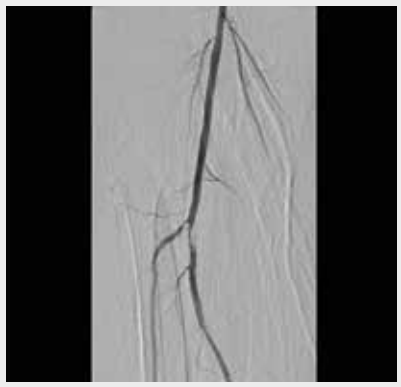
In cases of completely occluded or large diameter vascular segments, blood loss may be a question with aspiration technologies to many readers, however, in our experience with the **Indigo System** in large vessels and difficult cases, the largest amount of blood loss is less than 300–400ml, with no haemodynamic compromise noted in any of our patients intra- or post-procedurally. The following cases demonstrate the ability of aspiration thrombectomy in arterial and venous occlusions to extract thrombotic material and then identify the culprit lesion.

Case 1: Management of acute thromboembolic complication during SFA-popliteal recanalisation

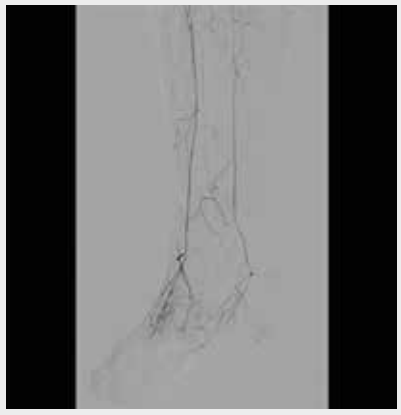
A 73-year-old male, known arteriopath, previously treated with bilateral iliac stenting, presented to our centre with a dystrophic lesion of the dorsal surface of the right foot. Following computed tomography angiography imaging, he was scheduled for recanalisation of chronically occluded right sided superficial femoral artery (SFA) P1 popliteal segment. The occlusion was approximately 15cm in length.

Systemic heparinisation of 2,500 IU sodic heparin was administered via a peripheral venous cannulation.

The angiography performed using the 6F 45cm-long introducer sheath (Cook Medical®) by left femoral retrograde contralateral access confirmed the right femoropopliteal chronic obstruction. The distal vascularisation was mainly sustained by both tibial arteries (anterior and posterior) with incomplete dorsal and plantar arcade filling.



Case 1 pre-procedure



Case 1 post-procedure

The occlusion was crossed successfully via an intraluminal approach using a 4F Navicross® catheter (Terumo®) and a straight tip 0.035” guidewire (Terumo). The occlusion was then treated with angioplasty using a 5mm and 6mm balloon catheter (FoxCross, Abbott Vascular®) reaching a sub-optimal patency. For this reason, and due to the fear of early or immediate reocclusion, we decided to reline the femoropopliteal segment using two Supera® stents (Abbott Vascular)—5x100mm and 5x150mm—in a telescopic fashion.

The angiogram images after stent placements demonstrated a good result along the treated segment. Unfortunately, as with many of these procedures, a thromboembolic material migrated at the origin of the tibioperoneal trunk protruding into the origin of anterior tibial artery. To manage this quickly with low risks of complication and further damage, we introduced the mechanical aspiration CAT6 catheter (**Indigo System**, Penumbra) and performed thromboaspiration with a Penumbra Pump MAX. Thromboaspiration was performed in under 15 minutes.

The final angiogram runs demonstrated complete patency of the bifurcation and the tibial vessels with no distal embolism or dissection. The blood aspirated through the system was less than 70ml.

Manual compression was used to close the percutaneous access site of the left common femoral artery. No post-procedural complications were observed. The last Doppler ultrasound four months after the procedure showed regular patency of femoropopliteal and tibial vessels. The patient is currently symptom-free.

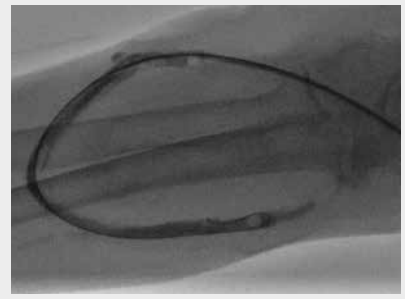
Case 2: Dialytic vascular access acute thrombosis

An 83-year-old female under anticoagulant therapy (warfarin) and international normalised ratio (INR) 3 with a six-year renal dialysis history and very poor venous access was admitted to our centre after an acute thrombosis of a mid-arm prosthetic arteriovenous loop (omero-basilic). This was identified following failure to dialyse successfully.

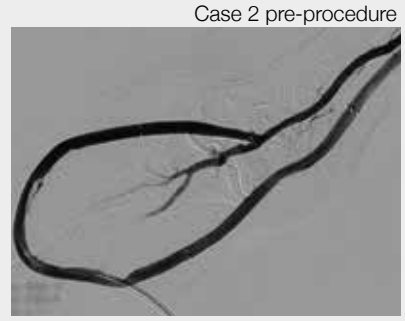
She presented with a systemic hypotension and pre-procedure ultrasound scanning showed an acute thrombosis (hypo-hyperechoic intraluminal material) of the prosthetic loop extending beyond the venous anastomosis on the basilic vein.

A first antegrade percutaneous approach was performed via a 4F sheath (St Jude Medical®) under ultrasound guidance, just after the arterial anastomosis to overcome the thrombosis and reach the venous side with the 0.035” Terumo guidewire. The venogram confirmed thrombosis inside the loop associated with a severe stenosis at the venous anastomosis and post-anastomosis region. Through an 8F sheath (St Jude Medical), we performed, in the first instance, an antegrade passage of mechanical aspiration catheter using the CAT8 TORQ catheter (**Indigo System**, Penumbra) connected to a Penumbra Pump MAX. The angulated tip allows circumferential aspiration in such cases. Another venogram was performed which demonstrated no evidence of other proximal or central venous stenosis.

Then we performed another retrograde puncture at the venous site of the loop reaching the omeral artery. The complete fistulography has shown regular patency of the omeral and its distal branches.



Case 2 pre-procedure



Case 2 post-procedure

Thrombus material was noted at the arterial side of the loop just past the arterial anastomosis.

The mix of acute and subacute to chronic clot found within the fistula initiated us to administer Heparin via the sheath to the venous segments (2,500 IU sodic heparin). We performed a couple of passes with CAT8 catheter antegrade and retrograde to reach adequate debulking of the loop.

After changing the 0.035“ wire for a 0.018” V18™ guidewire (Boston Scientific®) the severe stenosis was first corrected at the venous anastomotic region using a stent graft (Viabahn®, Gore®, 6x100mm) and then post-dilated with a 6mm balloon. The irregular arterial post-anastomotic region was treated using another stent-graft (Viabahn 6x50mm) and post-dilated with a 6mm balloon. With this approach we were able to cover the percutaneous antegrade access site giving good haemostasis.

The final fluoroscopy images demonstrated patency of the entire vascular circuit, with no outflow obstruction. The omeral artery and its branches were patent with no signs of distal embolism. Final puncture site haemostasis was achieved by manual compression. The patient recovered well and underwent a successful haemodialysis session the same evening.

EVAR reduces aneurysm-related mortality in very sick patients but does not reduce overall mortality

The very long-term follow-up data of the EVAR-2 randomised controlled trial were published in the November 2017 issue of the *Annals of Surgery* by Michael J Sweeting and colleagues, on behalf of the EVAR trial investigators. Roger Greenhalgh, Imperial College, London, UK, presented these data at CIRSE 2017 (16–20 September, Copenhagen, Denmark).

The EVAR-2 study, as reported in the *Annals of Surgery* paper, set out to compare long-term total and aneurysm-related mortality in physically frail patients with abdominal aortic aneurysm who were randomised to either early endovascular aneurysm repair (EVAR), or no-intervention. "EVAR does not increase overall life expectancy in patients ineligible for open repair, but can reduce aneurysm-related mortality," concluded the researchers.

"EVAR-2 remains the sole randomised trial to identify whether EVAR reduces mortality in patients physically ineligible for open repair," said Greenhalgh at CIRSE.

In the trial, between 1999 and 2004, the researchers enrolled 404 patients from 33 centres in the UK aged 60 years and over with abdominal aortic aneurysm greater than 5.5cm in diameter. These patients were randomised 1:1 to receive either EVAR (197) or no intervention (207). The investigators used a prescient traffic light system to determine patient fitness and eligibility for treatment.

The primary analysis compared total and aneurysm-related deaths in the groups until 30 June 2015 (mean, 12 years; maximum 14.1 years).

Roger Greenhalgh

The authors write: "Mean follow-up until death or censoring was 4.2 years. There were 187 deaths in the EVAR group and 194 in the no-intervention group. By 12 years of follow-up the estimated survival was 5.3% in the EVAR group and 8.5% in the no-intervention group; there was no significant difference in life expectancy between the groups (both 4.2 years; p=0.97). However, overall aneurysm-related mortality was significantly lower in the EVAR group (p=0.019). Patients surviving beyond eight years were younger, with higher body mass index, estimated glomerular filtration rate, and forced expiratory volume in one second".

"In other words, the EVAR stopped the aneurysm from rupture, but it did not alter the date of death," Greenhalgh told CIRSE delegates. He summarised the main points for the audience: there was a high 30-day operative mortality in the EVAR group of 9%; there were half the number of aneurysm-related deaths in the EVAR group over full follow-up (14% vs. 29%); but there was no overall survival benefit. "It was important to note the limited life expectancy of the patients, who all had high comorbidities. Seventeen per cent died of cardiovascular heart disease, cancer and respiratory disease. The condition of the patients initially is very important," Greenhalgh said.

He also alluded to the limitations of the data, the main ones being that many patients in the no intervention group crossed over at a later point to receive an EVAR. Greenhalgh also noted that the proportion of patients who are alive after eight years is small. Endovascular repair is an evolving technique and it could have different results in the future; EVAR practice that includes the devices of today and epidural anaesthesia, could yield a different trial result, he said. "There are newer devices but no evidence that they will themselves change outcomes," said Greenhalgh while commenting that the imaging and reinterventions of today might be better and that patient frailty may have prevented reintervention during the trial.

Vital to identify "factors for EVAR failure" and tailor surveillance strategies

At CIRSE 2017, Richard McWilliams, Royal Liverpool University Hospital, Liverpool, UK, examined whether new generation endografts were delivering on their promises. The discussion following his presentation focused on the importance of having a personalised, risk-adapted surveillance strategy that depended on identifying the subgroup of high-risk patients who would need the finest imaging.

McWilliams set out to identify the strengths and weaknesses of new devices for EVAR. He noted that the terms "third and fourth generation" when alluding to modern stent grafts were used loosely and were essentially "meaningless."

"It is worth considering why we adopt new technology. It is presumably because it addresses problems with existing/older technology; can do so in a manner that is not too expensive; and does not introduce too many new problems," McWilliams noted.

He referenced endografting data from the 15-year follow-up from the EVAR 1 trial that showed that EVAR's benefit of early reduction in the aneurysm-related mortality and total mortality was lost in the course of time due to secondary rupture and aneurysm-related causes of death. The trial also showed that there was a larger contribution from cancer-related deaths and a higher total mortality in the late follow-up for EVAR while, beyond eight years, open repair had a significantly lower mortality.

Speaking specifically about the Nellix graft (Endologix), which received the CE mark in 2013, McWilliams noted that the product had a good rationale. "It was addressing the persistent problems of endoleak, specifically type II endoleak. What were the expectations of success? Sac filling and sac anchoring were concepts upon which the expectation that the problems of migration and endoleak would be resolved. While many suggested that modern endografts did not need the same type of surveillance as older versions, we did not alter our surveillance strategy and continued our CT scanning. We published the first reports of migration of the endoprosthesis and also knew that with novel devices come new problems. We, therefore, had our eyes open for the unexpected, and saw new complications," he said. With longer follow-up physicians saw that "rather than being a buttressing barrier that would allow the stability of the endograft, the endobags and stents drifting through newly formed thrombus of variable consistency," said McWilliams. Then, physicians and the company reported complications and there were regulatory alerts, in response to which the manufacturers updated the instructions for use for the device. The modifications reduced the upper limit of neck diameter; redefined the neck; and introduced the concept of the aneurysm ratio.

McWilliams also presented on the Altura endograft system (Lombard Medical), which is another product significantly different from what physicians were used to over the years, he said. "Long-term data from new generation devices are not yet available. If we do want to adopt new technology, this should be based on evidence, rationale, team decisions, informing patients and hospital device committees. We need post-marketing surveillance and need to audit and publish our outcomes and report adverse events," he said.

When the speakers were asked by chairman Johannes Lammer, Vienna, Austria, about whether new generation devices are delivering their promise, Roger Greenhalgh, London, UK, made the point that the improvement in devices was only "part of the story" and that it was important to focus on the question: what are the factors that contribute to failure? "EVAR is here to stay; there is no going back to open repair. The way in which follow-up occurs, or not, after EVAR is crucial. The generation of graft is one aspect; what is equally pertinent is looking for a subset of patients who require more intensive follow-up. We cannot entirely rely upon manufacturers to make better devices; failures are also down to physician behaviour, including not ensuring optimal surveillance. We need to be able to spot the subset of patients who need less surveillance and have the finest imaging for those who are at high-risk of rupture, while also reducing exposure to radiation as much as possible," he said.

Richard McWilliams

Uptick in type III endoleaks causes US FDA communiqué

In late September, the US FDA, communicated to vascular and cardiothoracic surgeons, radiologists and cardiologists that it is evaluating recent information regarding type IIIa and IIIb endoleaks associated with the use of endovascular graft systems indicated for EVAR.

"Recent information from several sources, including FDA's Medical Device Reporting (MDR) system and Annual Clinical Updates to Physicians by the manufacturers, suggests an increase in the occurrence of type III endoleaks. This increase is compared to earlier clinical update reports in patients with various device models and implant duration lengths, including some patients who had previously stable repairs," the letter states.

"We are bringing this potential complication to your attention to remind and encourage you to report type IIIa and IIIb endoleak events to the manufacturer and the FDA. This may include reporting individual events as well as rates you may have experienced in your practice," the letter adds.

The FDA recommends that healthcare providers:

- Continue lifelong surveillance.
- Consider type III endoleaks in the differential diagnosis of patients presenting with symptoms of potential aneurysm expansion or rupture.
- Discuss with your patients all available treatment options to address type III endoleaks, including the risks and benefits of each, before deciding the best treatment approach.
- Report early or late device-related adverse events—including type IIIa and IIIb endoleaks—associated with the use of endovascular graft systems in EVAR; device-related adverse events that occur as a result of a secondary intervention to treat type III endoleaks.

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*Mwipatayi P et al. Durability of the balloon-expandable covered versus bare-metal stents in the covered versus balloon expandable stent trial (COBEST) for the treatment of aortoiliac occlusive disease. JVS 2016.

Atrium Advanta V12 is CE approved for restoring the patency of iliac and renal arteries. Renal approval is for 5-7mm sizes. Advanta V12 is not available in the U.S.

ESC publishes new guidelines on the diagnosis and treatment of peripheral arterial diseases

European Society of Cardiology (ESC) Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, developed in collaboration with the European Society for Vascular Surgery (ESVS), have been published in the *European Heart Journal*, *European Journal of Vascular and Endovascular Surgery*, and on the ESC website.

Peripheral arterial diseases—all arterial diseases except the coronary arteries and aorta—affect approximately 40 million Europeans, and increase the risk of stroke, disability, heart attack and death.

The new guidelines have been developed as a collaborative effort between cardiologists and vascular surgeons, with the Task Force led by Victor Aboyans (ESC chairperson, Limoges, France) and Jean-Baptiste Ricco (ESVS co-chairperson, Poitiers, France).

Aboyans said, "We now have a single European document on the management of patients with peripheral arterial diseases. Working together has enabled us to be comprehensive in our recommendations."

For the first time there is a single chapter devoted to the use of antithrombotic drugs in the new guidelines. The authors note that this is a "hot topic", and advice is given for each location of peripheral arterial disease regarding the use of antiplatelet and anticoagulant therapies.

Another new chapter is on the management of other cardiac conditions frequently encountered in patients with peripheral arterial diseases, including heart failure, atrial fibrillation, and valvular heart disease. Aboyans explains, "Patients with peripheral arterial diseases often have other cardiac conditions and while there is not much specific evidence on how to manage these we have produced recommendations, mostly based on expert opinion."

While there have been no new major trials on the management of asymptomatic carotid artery disease since the 2011 Guidelines, there have been new data on the long-term risk of stroke in patients with asymptomatic carotid stenosis. The Task Force now recommends revascularisation of asymptomatic carotid stenosis only in patients at high risk of stroke.

Aboyans said, "The previous guidelines recommended revascularisation for all patients with asymptomatic carotid stenosis, so this is an important change. Trials showing the benefits of revascularisation compared to best medical therapy alone were performed in the 1990s but stroke rates in all patients with asymptomatic carotid stenosis have decreased since then—regardless of the type of treatment—so the applicability of those trial results in the current management of these patients is more questionable."

In patients with renal artery disease, there is now a strong recommendation against systematic revascularisation of renal stenosis following the publication of several trials. The 2011 Guidelines stated that stenting could be considered in patients with renal stenosis due to atherosclerotic disease.

The chapter on mesenteric artery disease has been entirely revisited, and as Ricco explains, "We have updated this chapter with new data showing the interest of endovascular surgery in these often frail patients."

In lower extremity artery disease, Ricco emphasised the importance of the new "WIfI" classification that has been introduced for risk stratification of patients with chronic limb threatening ischaemia. The system takes into account the three main factors that contribute to the risk of limb amputation, which are wound (W), ischaemia (I), and foot infection (fI). The Guidelines are accompanied by a companion question and answer document which outlines how to manage patients with different presentations of peripheral arterial diseases. It is also published online in the *European Heart Journal*.

Serranator Alto serration balloon effective at 30 days in treating critical femoropopliteal lesions

Preliminary 30-day data from the PRELUDE trial investigating the use of the Serranator Alto percutaneous transluminal angioplasty (PTA) serration balloon catheter (Cagent Vascular) have shown 100% technical success and good effectiveness in moderate to severe calcification in the superficial femoral artery. The acute results show that the balloon can achieve low residual stenosis, and final six-month results are expected by the end of 2017.

Marianne Brodmann

Marianne Brodmann (Graz, Austria) presented the 30-day data at the Vascular Interventional Advances 2017 conference (VIVA; 11–14 September, Las Vegas, USA) on behalf of the PRELUDE investigators. She explained that the Serranator Alto balloon has four embedded serrated stainless steel strips, designed to create linear, interrupted lines of scoring along the endothelial surface as the balloon inflates. Responsive to the balloons energy, these serrations enable predictable and controlled lumen expansion as serrated material is more responsive to directed energy.

Discussing the data on behalf of the PRELUDE investigators during a VIVA press conference session, Peter Schneider (Honolulu, USA)—co-founder of Cagent Vascular—explained the concept behind the serrations. "What we have now are balloons that apply an equal amount of force in all directions. Nowhere in your life do you take that approach. You want to be more specific, and this serration approach allows the balloon to do that."

The PRELUDE study is a single-arm, prospective, multicentre, core-lab adjudicated feasibility study enrolling patients with superficial femoral or popliteal lesions. Follow-up is to be conducted at 30 days and six months. The primary objective is to evaluate the technical feasibility of the Serranator Alto in these patients, while the secondary objective is the optical coherence tomography (OCT) and intravascular ultrasound (IVUS) evaluation of the presence of serrations across the treated lesions in a 10-patient subset.

The primary safety endpoint is a composite of major adverse events and periprocedural death at 30 days post-procedure. The primary efficacy endpoint is the rate of successful delivery, inflation/deflation, and device retrieval with a final diameter stenosis <50% by visual assessment at the intended target site using only the device.

Patients with stenosis >70%, lesion length ≤10cm and reference vessel diameters of 4–6mm were included, and occlusions up to 6cm long were allowed. Twenty-five patients were enrolled at four centres. Moderate or severe calcification was present in 56% (n=14) of subjects, and 32% (n=8) had total occlusions.

The average pre-treatment stenosis was 88% and post-treatment was 23%. Only one stent (4%) was placed post-Serranator. No major adverse events or perioperative deaths were reported at 30 days. Serration effect was confirmed by the independent core lab in all OCT and IVUS images (n=10).

Brodmann explained that these preliminary data indicate that the Serranator Alto "is safe and effective in treating critical femoropopliteal lesions."

Three-year Eluvia results show long-term freedom from revascularisation

Boston Scientific announced the three-year results from the MAJESTIC trial for the Eluvia paclitaxel-eluting vascular stent system at the CIRSE annual meeting in Copenhagen, Denmark. The results were also recently published online in *CardioVascular and Interventional Radiology*.

In this study, long-term treatment durability was experienced among patients whose femoropopliteal arteries were treated with the Eluvia stent system.

The prospective, single-arm, multicentre clinical trial enrolled 57 patients with symptomatic lower limb ischaemia and lesions in the superficial femoral artery or proximal popliteal artery. Primary patency through two years was 83.5% with 91% of patients experiencing no or mild symptoms associated with claudication, or pain while walking. Updated primary patency data point of 83.5% at two years reflects adjudicated data as a result of additional patient follow-up at three years, the company states. Previously reported primary patency for MAJESTIC at two years was 78.2%. Results at three years demonstrated a sustained benefit of this therapy, with 85.3% of patients experiencing freedom from target lesion revascularisation (TLR). No stent fractures were identified, and no major target limb amputations occurred.

"Over the course of the MAJESTIC trial, the majority of the patients, including those with relatively challenging lesions, have remained largely symptom-free," said Stefan Müller-Hülsbeck, Vascular Center Diako Flensburg and head of the Department of Diagnostic and Interventional Radiology / Neuroradiology, Academic Hospitals Flensburg, Germany.

The Eluvia Stent System received CE mark in February 2016 and is an investigational device and not available for sale in the USA.

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Two- and four-year IN.PACT Admiral drug-coated balloon data indicate good mid- and long-term safety and efficacy

Medtronic has released data reinforcing the durability and safety of the IN.PACT Admiral drug-coated balloon (DCB) in patients with peripheral artery disease (PAD). The two-year, real-world results from the full clinical cohort of the IN.PACT Global Study and four-year results from the pivotal IN.PACT SFA Study were presented in two late-breaking clinical trial presentations at the Vascular Interventional Advances 2017 conference (VIVA; 11-14 September, Las Vegas, USA).

IN.PACT Global Study

Thomas Zeller (Universitaets-Herzzentrum, Freiburg-Bad Krozingen, Germany) presented the new, two-year results from the full clinical cohort of the IN.PACT Admiral DCB Global Study. The results are the first two-year, real-world, fully adjudicated DCB data to be presented in a scientific congress, which showed consistent performance in both safety and efficacy for IN.PACT Admiral DCB.

The data were calculated using Kaplan-Meier survival estimates and revealed a freedom from clinically-driven target lesion revascularisation (CD-TLR) rate of 83.3% in a real-world patient cohort with a mean lesion length of 12.09±9.54cm, 18% in-stent restenosis lesions, 35.5% occluded lesions and 39.9% diabetes subjects. Additional safety and effectiveness outcomes also included low rates of thrombosis (4.5%), occurrences of major target limb amputation (0.7%), and CD-TLR (16.9%) within two years.

"At two years, the IN.PACT Admiral DCB continues to confirm positive outcomes from the IN.PACT randomised trials, demonstrating efficacy, safety, and durability, despite the complexity of these lesions," said Zeller. "These results also highlight the clinical utility of the IN.PACT Admiral DCB as a primary therapy in treating patients with some of the most challenging PAD cases."

The IN.PACT Global Study has enrolled over 1,500 patients across 24 countries, including the 1,406 patients in the full clinical cohort presented at VIVA, to characterise the performance of the IN.PACT Admiral DCB in treating real-world patients with challenging and complex lesions. The study included adjudication of events by an independent clinical events committee.

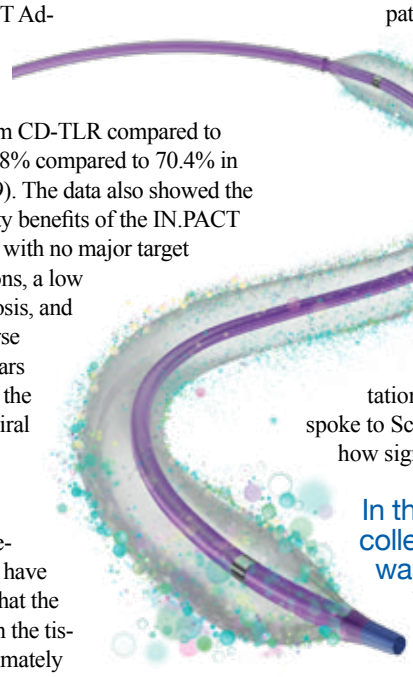
IN.PACT SFA Study

Peter Schneider (Honolulu, USA) presented the first, four-year data outcomes for a DCB, further demonstrating the safety and efficacy of IN.PACT Admiral DCB in patients with PAD. Of the patients who received a repeat procedure within four years, those in the IN.PACT Admiral DCB group showed that time to reintervention was approximately double that of those in the percutaneous transluminal angioplasty (PTA) group (average 739.2±384 days for IN.PACT Admiral DCB versus 302.9±213 days for PTA [p<0.001]).

Using Kaplan-Meier survival rate estimates, IN.PACT Admiral DCB continued to outperform in freedom from CD-TLR compared to PTA with a 76.8% compared to 70.4% in PTA (p=0.0399). The data also showed the long-term safety benefits of the IN.PACT Admiral DCB, with no major target limb amputations, a low rate of thrombosis, and no major adverse events from years three to four in the IN.PACT Admiral DCB group.

"With the IN.PACT Admiral DCB, preclinical studies have demonstrated that the drug remains in the tissue for approximately six months. Therefore, at four years, we would expect to see some catch-up effect and at least some late progression of atherosclerosis," said Schneider. "However, in the four-year data from IN.PACT SFA, we are still seeing sustained durability and clinical benefit. For patients suffering with this chronic condition, these findings are not only encouraging from a therapeutic perspective, but are also suggestive of improved quality of life, with patients requiring fewer reinterventions over time compared to PTA and leaving future treatment options open."

Peter Schneider



The IN.PACT SFA trial enrolled 331 patients at 57 sites across Europe and the USA who were randomised to treatment with either the IN.PACT Admiral DCB or PTA. The four-year data includes a total of 284 patients (184 DCB and 103 PTA).

Following the presentation of the data, *Vascular News* spoke to Schneider to understand just how significant these results are.

In this trial you did not collect patency data – why was this?

We collected patency data through three years. This was based on a study design from 2009 and 2010. The three-year study results were presented last year at VIVA and are currently in publication. After three years, we rely on clinically derived endpoints, such as CD-TLR to assess the patients' progress.

Do you have any insights into why PTA catch-up was less than you expected?

The results for the PTA group in this study were excellent. There are several potential reasons for this. Angioplasty technique in the study was meticulous and attempted to avoid dissection and avoid stents. Over the long term, there is likely a disadvantage to the presence of a stent and the potential for intimal hyperplasia and in-stent restenosis. Patients who failed pre-dilatation were screen failures and were not included. Had they been included, the angioplasty group may have fared worse. Since the randomisation was two DCB to one PTA, the PTA group was quite small at four years and this becomes statistically less valid. Nevertheless, if you look across studies, the results in the PTA group in IN.PACT were excellent. Despite this, freedom from CD-TLR four years after DCB was better than after PTA. If this result were compared to contemporarily available PTA data, the comparative results of the two treatments would be even more divergent.

Do you expect the PTA group to catch-up to the DCB group at five-year follow-up?

The DCB group had some fallout between three and four years, as would be expected for virtually all treatments we can offer to PAD patients. The PTA group results were flat between three and four years. This is extremely unusual after PTA, or after any treatment for that matter. It may have to do with sample size. Nevertheless, if it remains unchanged, the PTA group may "catch up" to the PTA group. Only time and data collection will tell us. However, it is worth expanding the view to include other multi-year post-PTA data and clinical experience. When you look at it in that context, the 43 patients remaining in the PTA group at this point should not be given undue weight in how we understand this issue.

News in brief

CryoLife announces definitive agreement to acquire Jotec

CryoLife has entered into a definitive agreement to acquire Jotec AG. A press release states that the combination of CryoLife and Jotec will create a company "with a broad and highly competitive product portfolio focused on aortic surgery, and will position CryoLife to compete strongly in the important and growing endovascular surgical markets."

Pat Mackin, chairman, president, and chief executive officer of CryoLife, said, "We believe this acquisition will enable CryoLife to deliver sustained, high single-digit revenue growth, while also diversifying our revenues into a significantly larger addressable market. Jotec has a technologically differentiated product portfolio addressing the US$2 billion global market for stent grafts used in endovascular and open repair of aortic diseases."

"Their advanced product portfolio has allowed them to achieve a 17% revenue CAGR over the past five years, significantly outpacing the growth in the overall European market. We expect the acquired portfolio to continue to post double-digit growth outside of the USA for at least the next five years. In addition, the acquisition will leverage our global infrastructure and accelerate our ability to go direct in Europe, and will foster considerable cross-selling opportunities between the CryoLife and Jotec product portfolios. The transaction will also drive gross margin expansion and accelerate our trajectory towards 20% or higher operating margins. We believe this will position CryoLife to deliver growth in non-GAAP EPS at a CAGR of at least 20% over the next five years."

Mackin added, "We also expect the Jotec new product pipeline and R&D capabilities to drive longer-term growth beyond the five-year horizon, particularly as their most innovative products enter the US market. We plan to utilise CryoLife's clinical and regulatory expertise to gain FDA approval for these products, which we believe will allow for entry into the US market."

Thomas Bogenschütz, CEO of Jotec, commented, "CryoLife is ideally positioned to accelerate adoption of our products through its highly complementary and global cardiac and vascular surgery business. We are looking forward to working with CryoLife's team to drive growth of our existing business, expand into new geographies, and accelerate our R&D initiatives in key markets such as the USA."

Jotec generated revenue of approximately €41 million in 2016, representing compound annual growth of approximately 17% over the preceding five years. Jotec generated revenues of €43 million, or approximately $51 million at current currency exchange rates, for the twelve months ended 30 June, 2017.

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Extended follow-up of OVER trial "favours endovascular aneurysm repair"

According to Frank Lederle (Minneapolis Veterans Affairs (VA) Medical Center, Minneapolis, USA), results from the extended follow-up of the OVER (Open versus endovascular repair) trial favour endovascular aneurysm repair (EVAR) compared with open repair. However, he noted that there were no significant differences in all-cause mortality between EVAR and open repair.

Speaking at the 2017 meeting of the European Society for Vascular Surgery (ESVS, 19–22 September, Lyon, France), Lederle said that the OVER trial was "officially completed in 2011 and published in The New England Journal of Medicine in 2012". However, he added that an extended follow-up of the study was approved in 2010. "This is the first time the clinical results subsequent to that paper have been presented anywhere and this is the only update that will be done," he told delegates at ESVS.

In OVER, 881 patients (99.3% male; 87% white; and mean age 70 years) were randomised to undergo EVAR with a US FDA-approved EVAR device. According to Lederle, 39% of the EVAR patients received a Zenith EVAR device (Cook Medical), 37% received an Excluder (Gore), 21% received an Aneurx (Medtronic), and 3% received a Guidant device (Endologix). "As per our previous reports (before 2010/2011), there was a total of 292 deaths—146 in each group," he commented. The overall conclusion of the study was that EVAR and open repair resulted in similar long-term survival (up to nine years).

For this extended follow-up, Lederle and colleagues reviewed data from US databases. They identified study patients who died through to 2016, causes of death through to 2014, and secondary therapeutic procedures through to 2015. The investigators found that by 2016, 270 EVAR patients had died compared with 290 open patients (p=0.1765). Calling this finding "an advantage for EVAR", Lederle noted there were now "nearly double the number of primary outcomes" (560 by 2016 vs. 292 before 2010/11) and that "now, two thirds of our cohort have died".

He commented: "Looking at the primary outcome of all-cause mortality, at eight years of follow-up, we had shown that the perioperative advantage of EVAR continued for several years, was significant for three of them, visible on a graph for five years, and that the curves came together as has been seen in the other trials. But, now, we have follow-up at 14 years and, again, the curves separate and this time favours EVAR once again."

Frank Lederle

Although observing that this separation between EVAR and open repair was "was not statistically significant", Lederle called it "a substantial finding". He noted that by 10 years, he and his colleagues had data for 367 patients—"that is more patients than were initially randomised in the DREAM (Dutch randomized endovascular aneurysm repair) trial".

In terms of causes of death in the extended follow-up period, the investigators found two more aneurysm-related deaths (one in each group). Of these, the EVAR death was recorded as aortic aneurysm without rupture, Lederle reported, "but the cause was unknown; it was either rupture or sudden cardiac death". He added that the death of the open repair patient was "clearly rupture of a thoracic aortic aneurysm".

More secondary procedure occurred in the EVAR group during the extended follow-up than in the open repair group, but this difference was not significant: 38 new procedures in 29 patients the EVAR group vs. nine new procedures in the nine patients in the open repair group. Lederle commented: "Interestingly when we looked at patients who had either died or had a procedure, the numbers were equal (317 vs. 316; p=0.76). The excess procedures tended to occur in patients who later died."

He concluded: "There was no difference in the primary outcome of all-cause mortality but, unlike EVAR 1, late trend favours the EVAR group. Aneurysm rupture after repair was uncommon but nearly all occurred in the EVAR group."

According to the 15-year follow-up of EVAR 1, EVAR has an early survival benefit but inferior late survival compared with open repair. The EVAR 1 trial investigators concluded that this needed to be addressed by lifelong surveillance of EVAR and re-intervention if necessary.

Five-year ENGAGE data demonstrate comparable EVAR outcomes in male and female patients

Five-year data from the ENGAGE global registry indicate that endovascular aneurysm repair (EVAR) outcomes are comparable between male and female patients when using the Endurant II stent graft (Medtronic).

The five-year ENGAGE global registry data were presented for the first time by Marc Schermerhorn, (Beth Israel Deaconess Medical Center, Boston, USA) in a late-breaking clinical trial at the Vascular Interventional Advances 2017 conference (VIVA; 11–14 September, Las Vegas, USA).

Schermerhorn told the VIVA audience that women have historically demonstrated worse EVAR outcomes than men due to differences between the female and male anatomies, including shorter, more angulated aortic necks, smaller aneurysms, and smaller iliac vessels. Female patients also have historically demonstrated higher rates of mortality, access complications, and endoleaks compared to men.

"It is well-known in the clinical community that women have not benefitted to the same extent as men when receiving an EVAR procedure, and in turn, have become a greatly underserved patient population," said Schermerhorn. "Endurant is now the only stent graft system to close the outcomes gap between men and women at 30 days, one year, and five years, which sets a new benchmark for EVAR device performance and has the potential to change the treatment paradigm for female patients."

The five-year gender subset analysis of the ENGAGE global registry included 1,263 patients (133 female and 1,130 male). The study population was comprised of females with an average age of 75.7 years with smaller diameter proximal necks and narrower access vessels. Approximately 16.5% of females compared to 11.5% of males had proximal neck lengths <15mm and 19.7% of females compared to 9% males had infrarenal neck angles of >60 degrees. The data underscore previous findings between men and women at 30 days and one year, which demonstrated consistent efficacy and safety.

Marc Schermerhorn

The five-year data demonstrated a successful delivery and deployment rate of 99.2% in the female cohort compared to 99.5% in the male cohort (p=0.746). The study also showed consistency between genders, with:

- A freedom from aneurysm-related mortalities (ARM) in females of 100% compared to 97.5% in males (p=0.0881);
- Type Ia endoleaks were observed in 3.8% of females compared to 1.3% of males (p=0.197) at five years;
- A freedom from secondary procedures in females of 85.6% compared to 84.1% freedom from secondary procedures in males (p=0.5150);
- Aneurysm sac stability or decrease was observed in 89.6% of females compared to 89.4% of males at five years;
- A freedom from rupture rate in females of 100% compared to 98.4% in males (p=0.2263).

ENGAGE is underway at 79 sites in 30 countries and will have clinical follow up out to 10 years. The goal of ENGAGE is to gather evidence in a real-world patient population, including patients with challenging anatomy who have historically been difficult to treat, and are associated with limited eligibility for endovascular repair and higher rates of secondary interventions.

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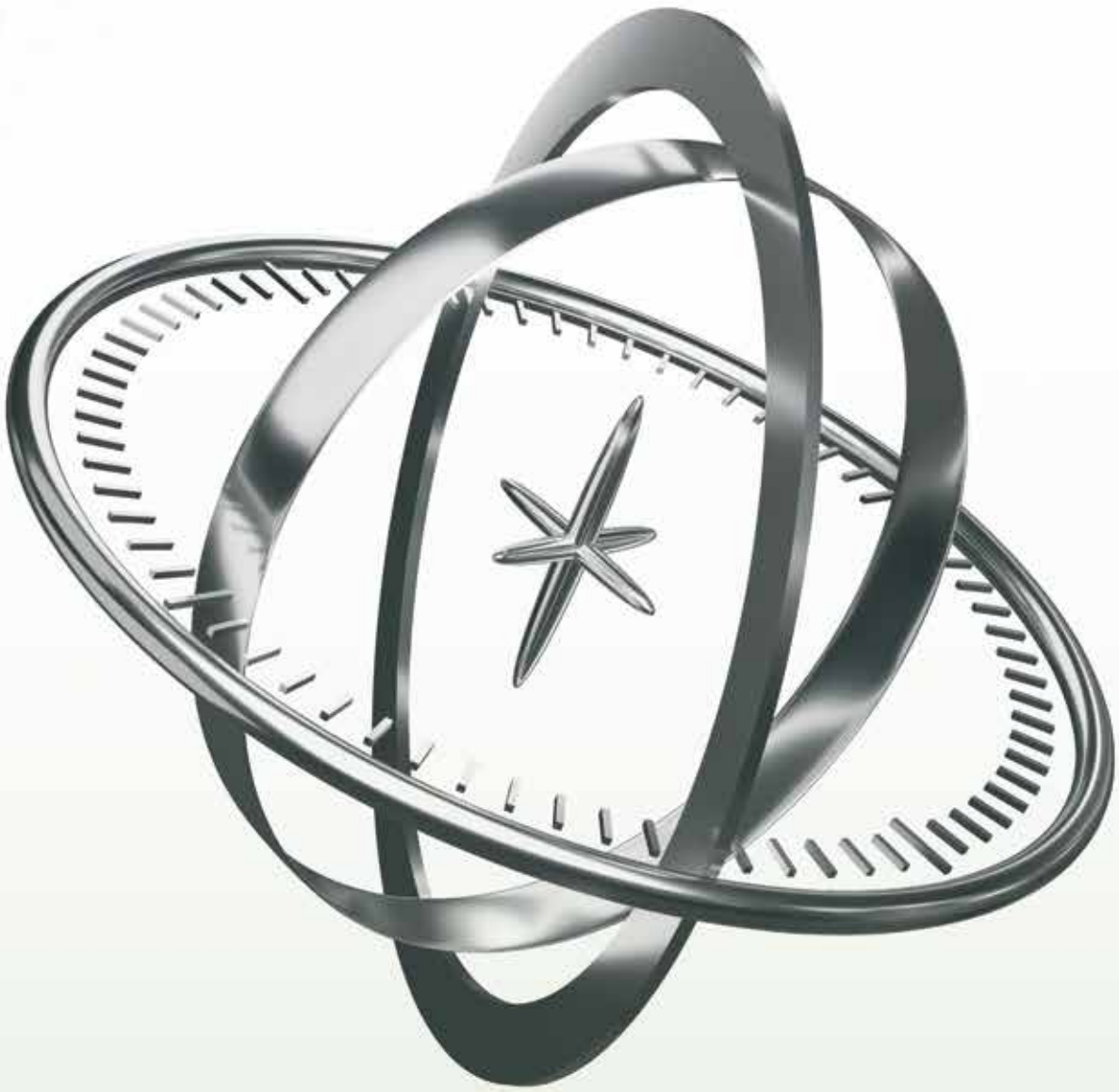

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Encouraging 100% primary patency and improved quality-of-life scores at six months for SurVeil DCB

Data from the Surmodics PREVEIL early feasibility study of the company's SurVeil drug-coated balloon (DCB) was shared in a late-breaking clinical trial presentation at the Vascular Interventional Advances meeting (VIVA; 11-14 September, Las Vegas, USA).

PREVEIL is a prospective, US, multicentre, single-arm trial designed to assess the safety and feasibility of the SurVeil DCB in the treatment of subjects with symptomatic peripheral artery disease due to de novo lesions of the femoral and popliteal arteries.

Gary Ansel (OhioHealth, Columbus, Ohio) presented six-month results from 13 patients (Rutherford class 2 to 4) at three clinical sites who were treated with the SurVeil DCB. The average treated lesion length was 56mm. The researchers assessed primary patency and late lumen loss through six months, plasma paclitaxel levels, and changes in Rutherford classification, resting ankle brachial index/toe brachial index (ABI/TBI), six-minute walk test, and walking impairment questionnaire (WIQ) at one, six, 12, 24 and 36 months. The key secondary safety endpoints included freedom from major vascular complications, evidence of paclitaxel toxicity, or thrombolysis in myocardial infarction.

Data from the study show that acute success measures of safety were achieved in 100% of patients. Results also showed primary patency of 100% and mean late lumen loss of 0.27±0.54mm at six months. Significant improvement in Rutherford classification, ABI/TBI, six-minute walk test, and WIQ were seen at 30 days and six months. The median paclitaxel plasma concentration peaked immediately post-procedure (Cmax 1.07ng/mL) and was undetectable at 30 days. Secondary technical, device, and procedure success criteria were achieved.

"We are encouraged by the early patient data using the Surmodics SurVeil DCB platform and are excited to continue clinical evaluation of the product in the US pivotal trial," said Ansel, who is a principal investigator in both the PREVEIL trial and the SurVeil DCB pivotal trial, TRANSCEND.

In July, Surmodics received an investigational device exemption (IDE) from the US Food and Drug Administration (FDA) to initiate a pivotal clinical trial of the SurVeil DCB. The randomised trial, TRANSCEND, will evaluate the SurVeil DCB for treatment for peripheral arterial disease in the upper leg in a head-to-head comparison with Medtronic's IN.PACT Admiral DCB, according to a press release from Surmodics, which expects to initiate enrolment in the TRANSCEND clinical trial in the fourth quarter of 2017.

Two-year efficacy of Stellarex 0.035" low-dose drug-coated balloon demonstrated

Philips has announced the two-year results from the ILLUMENATE European randomised clinical trial (EU RCT) demonstrating the efficacy of the Philips Spectranetics' Stellarex 0.035" drug-coated balloon (DCB) for peripheral artery disease (PAD) in comparison to uncoated balloon angioplasty.

Marianne Brodmann, of the Medical University of Graz in Austria, presented the data as a late-breaking trial at the Vascular Interventional Advances annual conference (VIVA; 11–14 September, Las Vegas, USA).

The ILLUMENATE EU RCT, which is part of a series of five trials evaluating the safety and efficacy of Stellarex for superficial femoral artery and popliteal disease, includes 328 PAD patients from 18 centres across Germany and Austria and compares the Stellarex DCB to an uncoated angioplasty balloon.

The results show that at 24 months, 75.9% of patients treated with Stellarex maintained blood flow through the treated segment of the diseased artery, assessed through blinded core-lab adjudicated patency. Only 61% of patients treated with an uncoated balloon still maintained blood flow at 24 months. The data shows that Stellarex demonstrates higher efficacy and patency results, and longer treatment durability compared to an uncoated balloon, which is the current standard of care in the USA.

"The Stellarex DCB produced durable results in this rigorous trial, validating earlier findings among the ILLUMENATE trial series," stated Brodmann. "These consistent, top-tier outcomes are achieved with a low-dose balloon. Stellarex is the first low-dose DCB to demonstrate a significant treatment effect at two years."

The ILLUMENATE EU RCT has independent evaluation including supervision by a clinical events committee, a data safety and monitoring board, and assessment by angiographic and duplex ultrasound core laboratories. Philips Spectranetics fully funded the ILLUMENATE EU RCT as part of the ILLUMENATE series of five trials to evaluate the benefits of Stellarex 0.035" for various patient groups in comparison to an uncoated percutaneous transluminal angioplasty (PTA) balloon, which is the current endovascular standard of care.

Stellarex

Luminor DCB shows high clinical effectiveness in six-month EffPAC trial data

The six-month results from the full clinical cohort of the EffPAC randomised study were presented in the drug-coated balloon (DCB) abstracts session at the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) 2017 conference in Copenhagen, Denmark. The data demonstrate the efficacy of iVascular's Luminor DCB in patients with peripheral arterial disease (PAD).

EffPAC (Effectiveness of paclitaxel-coated Luminor balloon catheter vs. uncoated balloon catheter in the arteria femoralis superficialis) enrolled 171 patients at 11 German centres who were randomised to treatment with either the Luminor DCB or percutaneous transluminal angioplasty (PTA). The six-month data include a total of 153 patients (77 DCB and 76 PTA).

According to iVascular, Luminor is a paclitaxel-coated balloon with a proprietary coating, using unique nanotechnology for minimised drug loss during navigation and enhanced delivery to the artery wall. A full range is available with 0.014", 0.018" and 0.035" guidewire compatibility, providing ultra-low profile and fast deflation time.

Ulf Teichgräber, director of the Department of Radiology of the University Hospital Jena, Germany, presented the new, primary endpoint late lumen loss and the clinical six-month results from the full cohort of the EffPAC study demonstrating the effectiveness of Luminor DCB vs. PTA in the superficial femoral artery.

The study met its primary endpoint (late lumen loss) and secondary endpoints (freedom from target lesion revascularisation; patency; and change of ankle brachial index, Rutherford stage and quality of life with high statistical significance). Primary endpoint revealed a late lumen loss (LLL) of 0.14mm in the DCB group vs 1.06mm in the PTA group ($p<0.001$), while target lesion revascularisation (TLR) was 1.3% (DCB) vs 17.1% (PTA).

Rutherford stages were improved overall for 85.2% patients (DCB) vs. 75% (PTA) ($p=0.021$), and by three stages for 44.6% patients (DCB) vs. 27.8% (PTA). There were no amputations, or product-related adverse events in the DCB group.

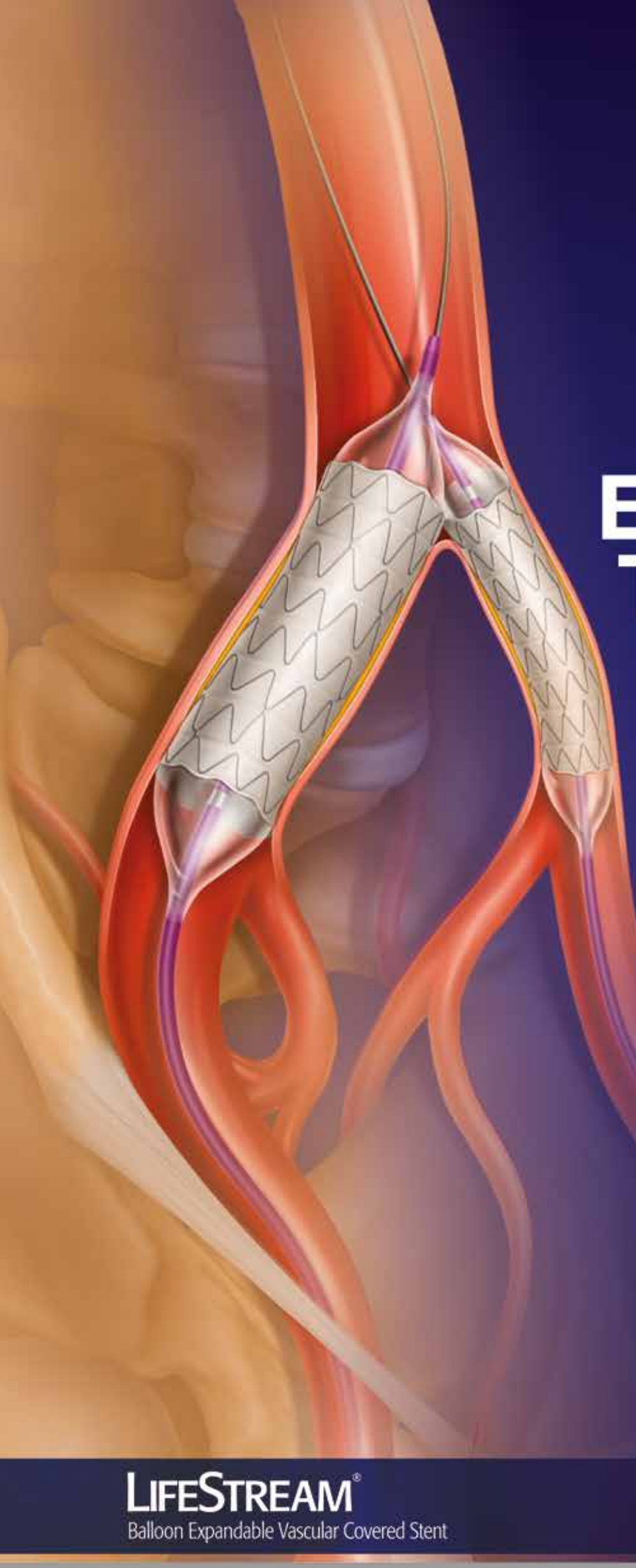
iVascular Luminor DCB

A comparison with other published data from randomised controlled trials involving DCBs, underlined that Luminor DCB shows higher efficacy than most other available DCBs. In a press release from iVascular, Teichgräber said: "These incomparable outcomes are the result of the innovative coating technology of Luminor DCB, which is shown not only in the patency, LLL and TLR data, but also in significant improvement of patients' clinical status".

On 21 September 21 iVascular announced that the Luminor 14m has received the Canadian Medical Device License (MDL). Luminor DCB received the CE mark in 2013 to treat superficial femoral, popliteal and infrapopliteal arteries and is available in more than 50 countries.

TINTIN trial

iVascular has announced the initiation of the TINTIN study, evaluating the combined therapy of Luminor drug-coated balloon (DCB) and iVolution self-expandable stent. The TINTIN study is prospective, investigator-initiated, non-randomised, multicentre trial, investigating the 12-month safety and efficacy of combined Luminor DCB and iVolution self-expandable stent in TASC C and D femoropopliteal atherosclerotic lesions.



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Particulate embolisation after femoral artery treatment with drug-coated balloons

ALOKE V FINN

COMMENT & ANALYSIS

Drug-eluting technologies, such as balloons coated with paclitaxel (DCB) are now the gold standard treatment for patients presenting with symptomatic peripheral artery disease (PAD) in the femoropopliteal region. DCBs have shown better clinical outcomes against uncoated balloons (PTA) for the treatment of femoropopliteal disease in large multicentre trials.[1-3] After the introduction of the first DCB (Lutonix's 0.035 over-the-wire DCB) there have been several entrants into the market. However, multiple clinical and pre-clinical studies have illustrated there are differences in performance and safety between the different products.[4]

DCBs are unlike drug-eluting stents (DES) which are routinely used for the treatment of coronary artery disease and rely on drug delivery from polymers to deliver the drug over 60–90 days. For the most part, DES effectively deliver the drug to the target arterial wall site while minimising its delivery to other non-target beds. DCBs, on the other hand, rely on drug delivery to the arterial wall site during the inflation time of the balloon (generally 90 seconds). During balloon inflation the excipient coating delivers crystalline paclitaxel, but more importantly facilitates the persistence of the drug at the site of the target tissue where it is needed to help prevent restenosis. However, it has been reported that the excipient and drug may embolise to non-target organs during the process of inflation. The potential consequences of these emboli remain uncertain, but it is logical to believe that this is an unwanted consequence because of the known tissue damaging effects of paclitaxel. Case reports have documented the occurrence of pannicilitus occuring weeks after use of the IN.PACT Admiral DCB (Medtronic).[5]

The most commonly-used drug for DCB is paclitaxel, a cytotoxic drug which has lipophilic properties, allowing passive absorption through cell membranes and sustained drug effect at the target site. The various DCB technologies differ in their design with regards to excipient coatings and drug form (amorphous vs. crystalline, including the size of the crytals). Drug delivery to the luminal surface is facilitated by different carrier excipients such as iopromide, urea, or polysorbate/sorbitol. Each DCB technology should be evaluated separately. There are now three US Food and Drug Administration (FDA)-approved DCBs:

1 The Lutonix 035 DCB is a low-dose (2mg/mm2) paclitaxel-coated balloon with a polysorbate/sorbitol carrier;

2 The IN.PACT Admiral DCB is loaded with a higher concentration of paclitaxel (3.5mg/mm2) and uses a urea-based excipient;

3 The Stellarex DCB (Spectranetics) is a low-dose (2mg/mm2) paclitaxel-coated balloon with a polyethylene glycol carrier.

The Ranger DCB (Boston Scientific) also contains low-dose (2mg/mm2) paclitaxel with a acetyl-tributyl citrate 2 carrier and is undergoing human trials for FDA approval.

These design features can produce differences in effective drug delivery to target tissues and to non-target tissues. Of course the ideal DCB technology should effectively deliver drug to the target site (eg. superficial femoral artery) while minimising occurrence of downstream emboli. Such differences in DCB technology are difficult to detect in the clinic where patients involved in clinical trials are highly selected and where the clinical tests used to assess patient outcome are unable to discern whether such emboli have occurred. The porcine preclinical model allows for histologic examination of treated femoral arteries and associated downstream non-target territories to determine the local tissue reaction in the treated artery wall and embolic safety characteristics.

In a previously-published study, the Lutonix 035 and the IN.PACT Admiral were tested and compared for target vessel changes and downstream embolic events. Femoral artery target tissue effects such as medial proteoglycan score and smooth muscle cell loss score were statistically significantly greater in the IN.PACT DCB at 90 days follow-up after overlapping balloon (3x dose) inflations, and, moreover, were accompanied by more downstream embolic debris and higher paclitaxel levels in downstream tissues.[6] More recently, I presented (at VIVA 2017, 11–14 September, Las Vegas, USA) the results of another head-to-head preclinical study examining IN.PACT, Stellarex, and Ranger at triple doses in the same model at 28 days. For all DCBs tested, similar drug vasculature effect was seen at the target treatment (ie. superficial femoral artery) site. However, the percentage of sections with downstream vascular changes in arterioles were highest for IN.PACT, followed by Stellarex and least in Ranger. Embolic crystalline material was also observed in all cohorts and followed a similar trend. Drug analysis however, showed similar paclitaxel concentrations in non-target coronary band tissue but higher levels in downstream skeletal muscle for IN.PACT versus the other two DCBs.

All DCBs tested exhibited downstream effects of paclitaxel drug and/or downstream emboli though differences between different DCBs were seen. The findings of embolic debris from DCB coatings is of potential importance and may be further compounded in patients with claudication and more complex critical limb ischemia with limited flow reserve. Further work is needed to better understand the potential significance of these findings for patients.

Aloke V Finn is the medical director at CVPath Institute, Gaithersburg, and associate professor of Medicine at the University of Maryland School of Medicine, Baltimore, USA

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News in brief

FDA gives Endologix IDE approval for EVAS2 study

Endologix has received Investigational Device Exemption (IDE) approval from the US Food and Drug Administration (FDA) to commence a confirmatory clinical study (EVAS2) to evaluate the safety and effectiveness of the Nellix endovascular aneurysm sealing system (EVAS) for the treatment of infrarenal abdominal aortic aneurysms.

The EVAS2 multicentre safety and effectiveness confirmatory study will prospectively evaluate refined Indications for Use (IFU) and the Nellix Gen2 EVAS system. Endologix recently received CE mark approval for new IFU. The study is approved to enrol up to 90 primary patients, with one-year follow-up data required for the pre-market approval application (PMA).

The Nellix EVAS system is an endovascular abdominal aortic aneurysm (AAA) therapy designed to seal the entire aneurysm. Nellix is the first and only EVAS product developed as an alternative treatment approach to traditional EVAR devices.

John McDermott, chief executive officer of Endologix, says, "We are pleased to receive IDE approval from the FDA to begin this confirmatory study, and look forward to collaborating with the investigators to achieve the goal of commencing enrolment by the end of this year. Based on the anticipated enrolment timeline, one-year follow up period, and regulatory review process, we continue to estimate PMA approval in 2020."

Two-year results of the EVAS FORWARD IDE trial demonstrated positive data earlier this year. Presented at the annual meeting of the Society of Vascular Surgery (SVS; 31 May–3 June, San Diego, USA), the study revealed a freedom from all endoleaks in 94% of cases.

First patient enrolled in Bolton Medical's RelayPro FDA trial

The first patient has been enrolled in Bolton Medical's RelayPro US Food and Drug Administration (FDA) Phase II clinical trial.

This study will assess the safety and efficacy of RelayPro to treat Type B dissections.

Christian Shults, cardiothoracic surgeon and Tareq Massimi, vascular surgeon, Washington Hospital Center, Washington DC, USA performed the procedure. The trial National Principal Investigator is Edward Woo, chief of Vascular Surgery, MedStar Washington Hospital, Washington DC, USA.

"The patient's anatomy and disease state made the case especially challenging. For this case I selected the RelayPro's non-bare stent configuration because of the fully covered proximal end. RelayPro performed ideally and the case went very well. We were able to nail the targeted proximal and distal landing zones, which is key in these cases," says Shults. "It was a very challenging case, but control and accuracy of RelayPro was just right for it," says Tareq Massimi.

Bolton is part of the Terumo Corporation. Terumo announced the acquisition at the start of this year.

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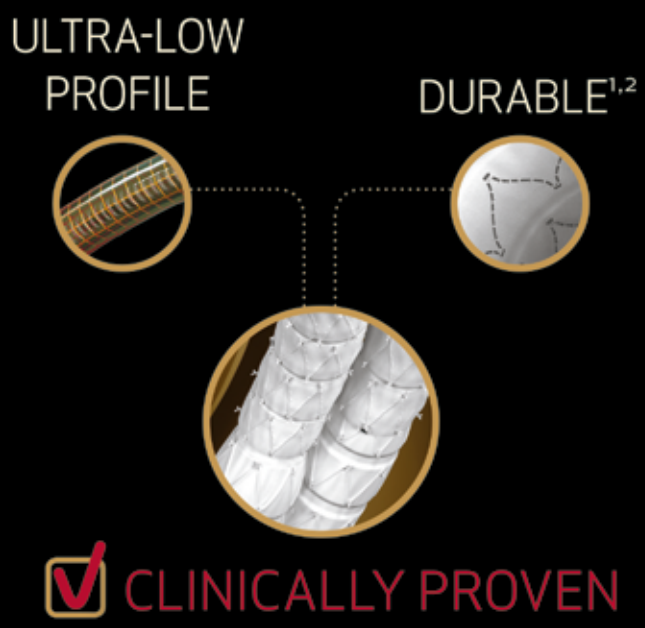

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LOCOMOTIVE trial achieves six-month patency of 90.7% for focal stenting in long femoropopliteal lesions

Data from the LOCOMOTIVE trial—a trial investigating the VascuFlex Multi-LOC multiple stent delivery system (MSDS; B Braun)—revealed that the strategy was safe and effective for focal stenting in long femoropopliteal lesions. The system achieved primary patency of 90.7% (n=68/75) and a 5.3% (n=4/75) all-cause target lesion revascularisation (TLR) rate at six months. The data were published in *VASA* (Amendt K et al. *VASA* 2017 31:1–10).

LOCOMOTIVE is studying the MSDS strategy in de novo and restenotic lesions, with the exception of in-stent restenosis (ISR) or restenosis following drug-coated balloon (DCB) angioplasty.

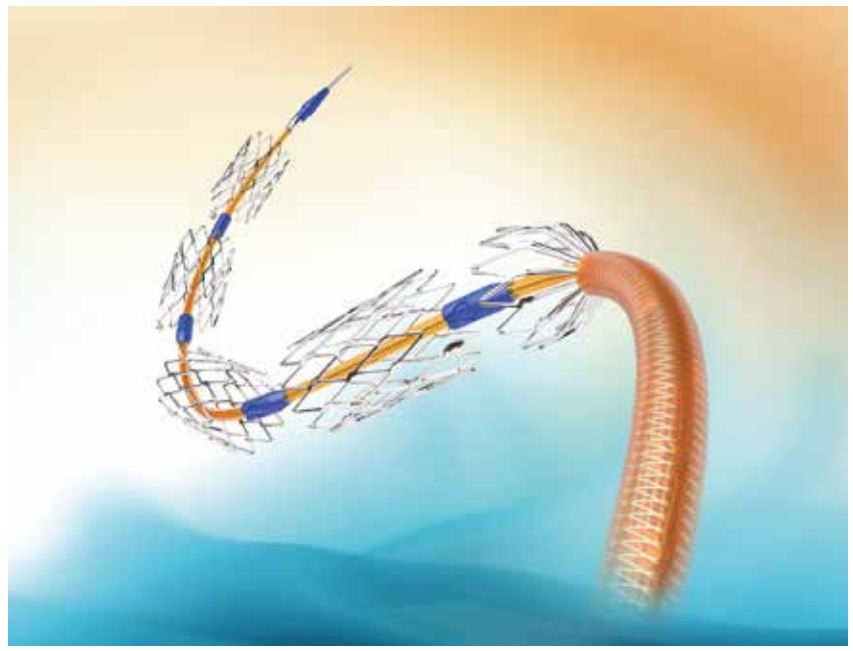
MSDS was indicated to treat flow limiting dissections or significant recoil (persisting stenosis >30%) after conventional balloon angioplasty and/or DCB dilatations in the superficial femoral artery and/or the popliteal segments (P1–P3).

The first-in-man LOCOMOTIVE study (ClinicalTrials.gov Identifier: NCT02531230) included 75 patients (mean age 72.9±9.2 years) in several German centres. The primary endpoint was defined as the all-cause TLR at six months. Femoropopliteal lesions were prepared with uncoated and/or paclitaxel-coated peripheral balloon catheters. When flow limiting dissections, elastic recoil or recoil due to calcification required stenting, up to six short stents per delivery device—each 13 mm in length—were implanted. Sonographic follow-ups and clinical assessments were scheduled at six months post-procedure.

The majority of the 176 individually-treated lesions were in the superficial femoral artery (76.2%, n=134/176) while the rate of TASC C/D lesions was 51.1% (n=90/176). The total lesion length was 14.5±9cm with reference vessel diameters of 5.6±0.7mm. Overall, 47±18% of lesion lengths could be saved with stenting. At six months, the primary patency rate was 90.7% (n=68/75) and the all-cause TLR rate was at 5.3% (n=4/75) in the overall cohort.

"The first clinical experience at six months suggests that the MSDS strategy was safe and effective in patients undergoing femoropopliteal revascularisations with TLR rates in critical and non-critical limb ischaemia patients of between 5% and 6% at six months," write the authors, led by Klaus Amendt (Mannheim, Germany). "Moreover, the overall primary patency at six months was over 90% in morphologically challenging lesions and the procedural success rate to release the individual stent segments was 100%. Overall, almost half of the lesion lengths could be saved from stenting as compared to the full metal jacket strategy."

The LOCOMOTIVE EXTENDED (ClinicalTrials.gov Identifier: NCT02900274) trial will confirm these early promising results in a larger patient cohort (>200 patients) in Europe and Asia.



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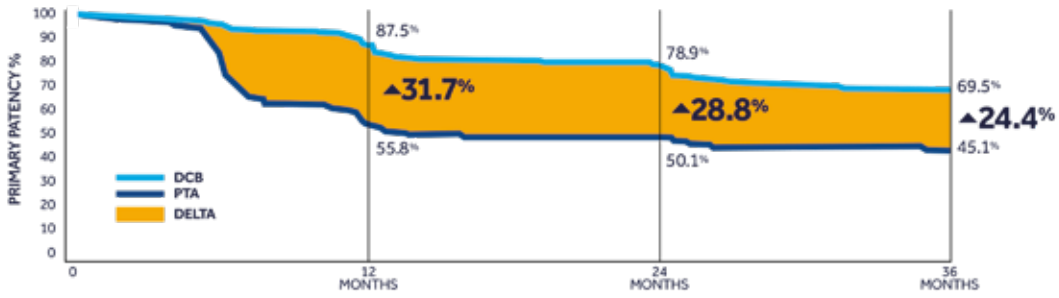
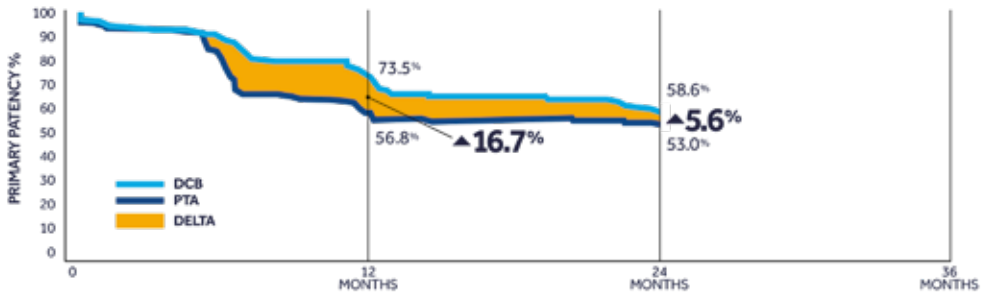
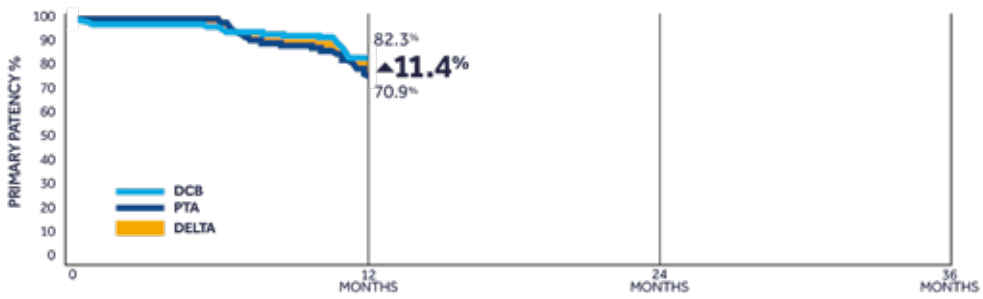


Lutonix™ DCB[2]



Stellarex™ DCB[3]



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1 Medtronic Data: 1-year Outcomes: IN.PACT Admiral IFU M052624T001 Rev. 1F. 2-year Outcomes: Laird et al. JACC. VOL .66, NO.21, 2015. 3-year: Krishnan, P. VIVA, 2016. Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR, ≤2.4 Primary Efficacy reported on Kaplan-Meier survival analysis.

2 Bard Data: LEVANT 2 Trial. SVS 2015: Primary patency is defined as the absence of target lesion restenosis defined by PSVR of ≥2.5 and target lesion revascularization. Primary Efficacy reported on Kaplan-Meier Survival Analysis, not pre-specified.

3 Spectranetics Data: ILLUMENATE Pivotal Trial, TCT 2016: Primary patency defined as freedom from target lesion restenosis (determined by duplex ultrasound PSVR ≤2.5) and freedom from clinically-driven TLR at 12 months.

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Profile

Stéphan Haulon

Growing up in Kenya, Stéphan Haulon's early experience of the medical profession came in the form of the "flying doctors", who piloted small planes to remote areas to care for patients. Combined with his post-medical school experience providing humanitarian relief in post-genocide Rwanda, Haulon's introduction to a medical career was anything but routine. Haulon spoke to *Vascular News* about how his training—including a particularly formative period at Cleveland Clinic with Roy Greenberg—provided the foundation of a career built alongside cutting-edge technology, patient-specific treatment, and "thinking outside of the box".

Why did you decide you wanted a career in medicine, and why in particular did you choose to enter the vascular field?

I was raised in Nairobi, Kenya, in Eastern Africa. I was very impressed by the "flying doctors" working there; they would fly and land their small planes anywhere to take care of sick people alone, or to transfer them to city hospitals. These were my heroes as a child. I always wanted to become one of them. When I graduated from medical school, and just before starting my vascular training, I had the opportunity to go back to Africa with "Médecins du Monde", a French humanitarian volunteer organisation, with whom I spent a month in Kigali, Rwanda, just after the 1994 summer genocide. This is really why I decided to be a doctor, and if my work is now far from humanitarian practice, I will be involved with it again at the end of my career.

When I was a general surgery resident, I started with an OB-GYN rotation and then moved to vascular surgery. The various approaches, from the neck to the lower limbs, including the chest and the abdomen, were of great interest as a young surgeon. The ability to collaborate with other surgical specialties, such as urology, cardiothoracic surgery, etc. was very stimulating and I learned a lot from these multidisciplinary approaches. Ultimately, during my second rotation in vascular surgery, I was exposed to initial experiences with endovascular aneurysm repair (EVAR).

The head of vascular and cardiothoracic surgery at that time, Pr Czelas Stankowiak, was a pioneer and a visionary, and performed the first EVAR procedure in Lille in 1996. I was instantly enthusiastic about this revolutionary approach, despite most of my young and also experienced colleagues considering this procedure a "non-surgical approach" with no future. During the rest of my residency, I learned a lot from my interventional radiology colleagues (another winning multidisciplinary collaboration).

Finally, vascular patients are mostly polyatheromatous patients, who require a global treatment strategy and not only a surgical repair. Early and long-term outcomes are highly dependent on that multidisciplinary medical and surgical path of care, involving vascular medicine and cardiology. All these collaborations, and the infancy of a breaking technology, made my choice to enter vascular surgery obvious. I have never regretted it! I was far from visualising what was going to happen next…

Who have been your most important career mentors and what wisdom did they impart?

My mentor and best friend was Roy K Greenberg. On top of teaching me everything I know about complex aortic endovascular repairs, he taught me to "think outside of the box!" and to understand the physics and haemodynamics of the aorta, and how to build an aortic and a research programme. From this transatlantic training experience, funded by the European Society for Vascular Surgery (ESVS) and Society for Vascular Surgery (SVS) Marco Polo Grant, I realised that those currently in training should be prepared to engage in global training and that trainers should be prepared to provide it. Roy was an unbelievably talented endovascular practitioner, a gifted inventor and developer, caring for his patients, meticulous in his documentation, hard-working and humble, a great team leader and teacher, an inspirational speaker, and had the ability to look at a problem differently than others. He was, above all, a fantastic friend; to harmonise with someone at work is a joy, to harmonise at work and play is something very special.

He has trained many other leaders in the field, all close friends, including Tara Mastracci, Gustavo Oderich, Tim Resch, and Andy Schanzer, who also consider Roy a model mentor.

Although they were not my mentors per definition, I was fortunate to meet and spend time with other pioneers in the field who were also eager to share their experience and enthusiasm: David Hartley, Michael Laurence Brown, and John Anderson from down under; and Krassi Ivancev and Tim Chuter from Malmö and San Francisco.

My open surgery mentor was Mohamad Koussa, a remarkable open cardiovascular surgeon; in addition to teaching me open surgery, he was a great supporter in the development of my endovascular thoracoabdominal and arch practice.

I also want to acknowledge those who helped me with my local, national and international academic career: Professors Branchereau, Ricco, Prat and Warembourg.

What has been the biggest development(s) in vascular medicine during the course of your career?

The endovascular revolution started when I was a resident. Since then, vascular surgery has been collaborating with endograft and imaging companies to push the boundaries of this minimally invasive approach that was first proposed to patients who were not candidates for an open repair, and, once evaluated, to a larger range of patients. We are now treating arch and thoracoabdominal aneurysms and dissections without the need for a sternotomy or a thoracophrenolombotomy approach. There are still a lot of developments required to simplify these very challenging procedures and to improve early and late outcomes, but we have to acknowledge the immense impact that the endovascular era has had on our practice. I want to make it crystal clear that I am not promoting the endovascular over the open repair approach; the modern vascular surgeon must be trained and an expert with both techniques, they will prefer one or the other, or perform both at the same time, depending on the location of the vascular disease and the patient's physiology. That is what makes the vascular surgeon unique; no one else has such comprehensive skills.

What is the most interesting paper or presentation that you have seen recently?

I am currently very impressed by all the developments in augmented reality and artificial intelligence. This will be the upcoming revolution, after the endovascular one. We are currently underestimating the impact that this will have on our daily practice. There are so many resources and so much brainpower dedicated to the development of these new tools that we will soon enter a new cycle: be prepared!

Three-dimensional (3D) printing will also have an impact in our field, for simulation and training. In the near future, 3D printers will almost instantly build devices tailored to the patient's anatomy; we are thus rapidly moving towards personalised medicine.

What are your current research interests?

I am focusing on imaging applications that will reduce exposure to radiation, having in mind that our young colleagues will perform 80% of their practice exposed to X-rays. I am developing a new generation of branched and fenestrated endografts, and dedicated bridging stents. I have learned so much from working with engineers from the imaging and endovascular device companies, and in the biomaterial lab. Again, the multidisciplinary approach is key for success.

When choosing between off-the-shelf, custom-made and chimney endografts for complex EVAR procedures, how do you decide which approach to take?

My preferred option to treat a complex aneurysm is a custom-made endograft. I believe that an endograft specifically tailored to the patient's anatomy will have the best long-term outcome, and this is really what matters. Most techniques report favourable early or mid-term outcomes, but what we are really aiming for is long-

term outcomes, after five-year follow-up. In acute cases, in patients not candidate for an open repair, we currently have no other option than to implant an off-the-shelf endograft, the only available being the t-branch (Cook Medical). I consider chimneys only as bailout procedures, but I have to acknowledge that I have a bias; I have been "spoiled", ever since I have finished my training in 2003, as I have always had access to custom-made devices. This is, unfortunately, not the case for most of my colleagues.

Do you think that we will ever be able to move to an endovascular-first approach to ascending aorta/arch repair?

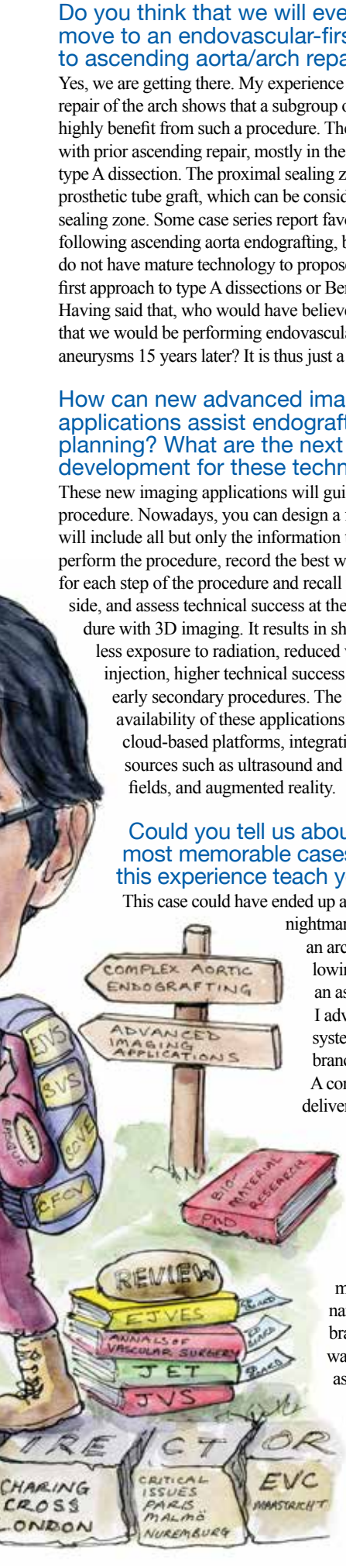
Yes, we are getting there. My experience with endovascular repair of the arch shows that a subgroup of patients may highly benefit from such a procedure. These are the patients with prior ascending repair, mostly in the setting of an acute type A dissection. The proximal sealing zone is then in a prosthetic tube graft, which can be considered as an ideal sealing zone. Some case series report favourable outcomes following ascending aorta endografting, but we currently do not have mature technology to propose an endovascular-first approach to type A dissections or Bentall procedures. Having said that, who would have believed in the mid-90s that we would be performing endovascular repairs of arch aneurysms 15 years later? It is thus just a matter of time.

How can new advanced imaging applications assist endograft implantation planning? What are the next steps in development for these technologies?

These new imaging applications will guide you through the procedure. Nowadays, you can design a fusion mask that will include all but only the information that is required to perform the procedure, record the best working positions for each step of the procedure and recall them from table side, and assess technical success at the end of the procedure with 3D imaging. It results in shorter procedures, less exposure to radiation, reduced volume of contrast injection, higher technical success rates and fewer early secondary procedures. The next steps are the availability of these applications for everyone on cloud-based platforms, integration of non-X-ray sources such as ultrasound and electromagnetic fields, and augmented reality.

Could you tell us about one of your most memorable cases? What did this experience teach you?

This case could have ended up as my worst nightmare. In a patient with an arch aneurysm, following implantation of an ascending endograft, I advanced the delivery system of an arch branched endograft. A conflict between the delivery system and the ascending endograft resulted in forward migration towards the aortic valve of the ascending endograft, and immediate haemodynamic instability. The branched component was rapidly deployed as planned to remove the delivery system from the aortic valve and provide supra aortic trunk perfusion. Aortography showed (fortunately) that the coronary arteries were patent but severe aortic regurgitation was present. The strut of the proximal bare metal stent of the ascending endograft was obstructing the aortic valve, and this was confirmed by transoesophageal echocardiography which showed no movement of the left coronary cusp. An emergency transcatheter aortic valve replacement procedure was performed resulting in immediate haemodynamic improvement. Because this case had been discussed and planned during our weekly aortic multidisciplinary meeting involving anaesthesiology, cardiology and cardiac surgical colleagues, everyone was already informed and concerned about that case, and thus rapidly efficient in treating this life-threatening complication. Alone, I would not have been able to fix it. It is mandatory to have a team approach and to seek other colleagues' expertise.



What are some of the proudest moments in your career?

I am very proud when young colleagues that I have trained get an academic appointment. Recently I was very honoured and privileged to be elected ESVS president for 2019–2020. The European Society is very active, includes all countries throughout Europe, and non-European councillors are now joining (India) in conjunction very strong links to some large non-European communities that are created. I am very proud to be part of this vision of a society open to others, having so many concerns on how politicians around the world are working in the opposite direction.

My proudest moment was when I was asked to give the first Roy Greenberg Distinguished Lecture at the 2013 SVS Annual Meeting in San Francisco, under the presidency of Peter Gloviczki. This was a very particular event, because Roy, my mentor, had chosen me for that lecture, which has a very special significance. In addition, he was not able to attend the Annual Meeting, but I knew he was listening to my lecture. It was for me a great opportunity to share my experience from training with a pioneer, the phenomenon Roy K Greenberg!

What three questions in vascular medicine still need to be answered?

1. Which acute type B dissections require aortic endografting in addition to best medical treatment?
2. When should surgery be performed in asymptomatic carotid stenosis?
3. What is the best endovascular approach to peripheral artery occlusive disease?

In addition:

4. How can we make newly-approved technology available for everyone?
5. How can we perform endovascular repairs without being exposed to radiation?

What advice would you give to young vascular surgeons starting out in their careers?

That they should be prepared to engage in global training; it is of paramount importance to be exposed to many different approaches to treat vascular patients. Training has to include both open and endovascular techniques; this is what makes our specialty so special. And never forget the advice that I got from my mentor: think outside of the box! It is not because one technique has been performed for decades that it is the ultimate technique to treat the disease. Learn from the other specialties and stay tuned to new technology. Finally, be obsessed about radiation protection.

What are some of your hobbies and interests outside of medicine?

The Alps! I spend most of my free time over there, hiking and mountaineering during summer, and downhill and country skiing during winter. I enjoy travelling around the planet with my family, visiting new cities, museums (especially contemporary art), and meeting people. Another is rugby—I used to play and now I watch it! I am originally from the Basque country, in the south west of France, where rugby is a religion! Finally, like any Frenchman, I enjoy good food and wine.

Fact File

Current roles

Professor of Vascular Surgery, Chairman of Aortic and Vascular Surgery, Hôpital Marie Lannelongue, Université Paris Sud, Le Plessis Robinson, France

Undergraduate and postgraduate education

2003	European Board of Vascular Surgery
2002	PhD in Biomaterials, Lille 2 University, Lille, France
2001	Board Certification in Vascular surgery (France)
2000	Board Certification in General surgery (France)
1999	Medical Thesis, Lille 2 University, Lille, France
1997	Master of Science degree in Biomaterials, Paris 13 University, Paris, France
1988–1994	Medical School, University Hospital Broussais, Paris 6 University, Paris, France

Postgraduate appointments

2018	Professor of Vascular Surgery, Paris Sud University, Paris, France
2017	Consultant Vascular Surgeon, Hôpital Marie Lannelongue, Paris, France
2008	Consultant Vascular Surgeon, King's College Hospital, London, UK
2006	Professor of Vascular Surgery, Lille University Hospital, Lille, France
2003	Consultant Vascular Surgeon, Lille University Hospital, Lille France
2002–2003	Vascular Surgery Research Fellow, The Cleveland Clinic Foundation, Cleveland, USA, under the supervision of Roy K. Greenberg
2000–2002	Vascular Surgery Clinical Fellow, Department of Vascular Surgery, Lille University Hospital, Lille, France
1994–2000	General and Vascular Surgery Resident, Lille University Hospital, Lille, France

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Data from multiple studies support concept of low metal burden therapies in the superficial femoral artery

Physicians demonstrated that reducing metal burden in superficial femoral artery (SFA) therapy could effectively reduce restenosis rates, according to results from various Biotronik studies presented at the 2017 Cardiovascular and Interventional Radiological Society of Europe meeting (CIRSE; 16-20 September, Copenhagen, Denmark).

In-stent restenosis remains one of the most challenging aspects of SFA treatment. Reducing the stent (metal) load may lead to reduced restenosis rates. During a well-attended session on reducing metal burden chaired by Jos van den Berg, Ospedale Regionale di Lugano, Switzerland, discussions centred on clinical options to treat SFA lesions with reduced or no metal burden. The symposium included a presentation of clinical results from an extensive drug-coated balloon (DCB) only registry as well as studies focusing on the combined use of DCB and a low chronic outward force (COF) stent. The session also covered the clinical impact of COF in nitinol stents.

Martin Funovics, Medical University of Vienna, Austria, presented results from preclinical data on the use of low COF vs. high COF stents. This was further supported by the interim results of the BIOFLEX COF randomised controlled trial (RCT), which established that lower COF results in lower restenosis rates for the first time ever in a dedicated RCT. This could be pivotal in changing the way that physicians plan treatment of SFA disease when implanting self-expanding stents. The innovative methodology of evaluating efficacy using "normalised, cumulative per cent restenosis" offers an accurate way to systematically assess restenosis with a higher sensitivity and specificity than the traditional Doppler ultrasound method for the first time.

The all-comers stenting registry BIOFLEX PEACE, which investigated the Pulsar-18 stent, was presented by Claus Nolte-Ernsting, Muelheim, Germany, on behalf of Michael Lichtenberg, Klinikum Arnsberg, Germany. The registry demonstrated that in a real-world setting, physicians are aware of the higher COF/higher restenosis link. This is a shift from the established 1-2mm that has been followed in the last decade. Reducing stent oversizing is a simple method to reduce the COF of the implanted stent. A primary patency rate of 86.2% and an fTLR rate of 97.1% despite a lesion length of 11.6cm appear to indicate improved outcomes.

Gunnar Tepe, Institute of Radiology, Rosenheim, Germany presented results from the long-awaited Passeo-18 Lux all-comers registry BIOLUX P-III, which enrolled over 700 patients with SFA lesions. A primary patency rate of 84.9% and fTLR rate of 94.5% clearly indicate the success of the Passeo-18 Lux. Despite the high moderate/severe calcification rates of 41.7% in lesions with an average length of 9.4cm, the bailout stenting rate was only 20%.

BIOLUX 4EVER, a novel study designed to challenge the need for an SFA drug-eluting stent (DES), looked into the use of full-lesion coverage with a DCB followed by a bare metal stent (BMS). Presented by Koen Deloose, AZ Sint-Blasius Hospital, Dendermonde, Belgium, the Passeo-18 Lux and Pulsar-18 study devices generated a primary patency rate of 89.9% at 12 months in average lesion lengths of 8.3cm. At the 24-month follow-up, primary patency was numerically higher with the DCB and BMS than with the DES. Although these were the interim results from 85 of 120 patients, the primary patency of 84.1% reported compares favourably to reported DES results of 78.2% and 74.8%.

Exploring how to translate all the presented data into clinical practice, Ralf Langhoff, Sankt-Gertrauden Krankenhaus, Berlin, Germany, shared a treatment strategy algorithm based on clinically available evidence on the Passeo-18 Lux DCB, the Pulsar-18 BMS and the combined use of both. Starting treatment with the Passeo-18 Lux, the physician can decide whether the lesion also needs to be stented based on the response to the DCB. To test this algorithm, he further proposed an outline for a trial.

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Nov 17 | Issue 76

The APPROACH concept for identifying factors influencing therapeutic decision-making of complex pararenal aortic pathologies

KONSTANTINOS P DONAS

COMMENT & ANALYSIS

The choice of treatment for patients with complex aortic pathologies with involvement of one or more aortic side branches is challenging. In this article, Konstantinos P Donas, Giovanni F Torsello, and Giovanni B Torsello explain how they use the APPROACH concept to assist their decision making in complex pararenal aortic pathologies.

The choice of treatment for patients with complex aortic pathologies with involvement of one or more aortic side branches is challenging. The criteria to select the best treatment option for these patients are multifaceted. Factors related to the patient, the operator, the institution, and costs—but also other morphological parameters—can potentially influence the selection of the most suitable therapeutic modality. Unfortunately, there has been no focus on decision-making in the selection of the technique employed. Consequently, the published evidence does not reflect, *per se*, the clinical reality. The APPROACH concept encompasses eight criteria that influence decision-making regarding the treatment of patients with complex pararenal aortic pathologies: aortic pathology, patient´s clinical profile, proven literature evidence, renovisceral morphology, operator preference and skills, access issues, costs, and hostile neck features.

In this article, I will focus on renovisceral morphology, access issues, and hostile neck, in order to demonstrate the concept behind APPROACH.

Renovisceral morphology

The importance of the renal artery morphology is reflected by the orientation, the presence of severe stenosis of the involved renal arteries but also from the distance to the orifice of the superior mesenteric artery. This can be a key decision-making factor when considering fenestrated stent-grafts or chimney endovascular aneurysm repair (EVAR). Downward-oriented vessels simplify cannulation from the upper extremity, while an upward-going renal is better approached from the transfemoral access (Figure 1).

Access issues

This criterion includes the morphology of the iliac vessels as well as of the supra-aortic arteries. The anatomy of these vessels in terms of kinking and elongation and the presence of occlusion or high-grade stenosis, thrombotic material, or excessive calcification significantly impact the use of devices with lower crossing profiles and improved trackability. Figure 2 shows a challenging case with hostile iliac arteries.

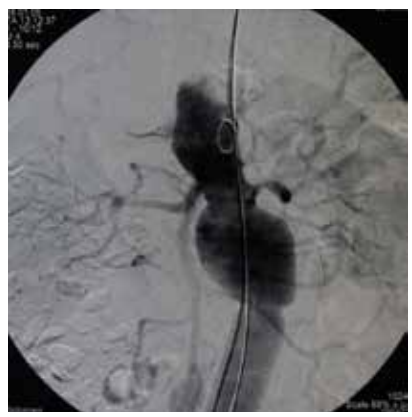

Figure 1

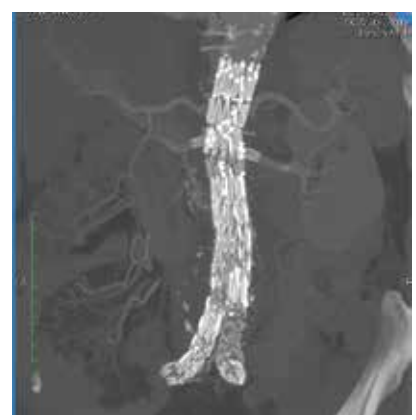

Figure 3b

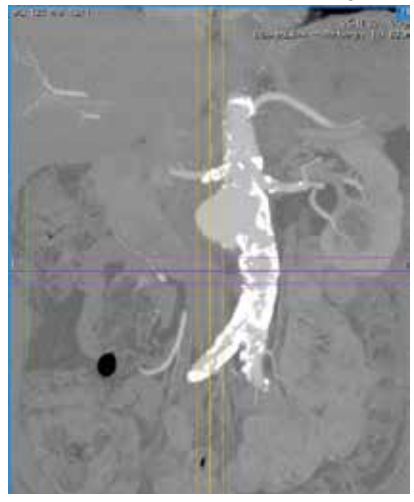

Figure 2

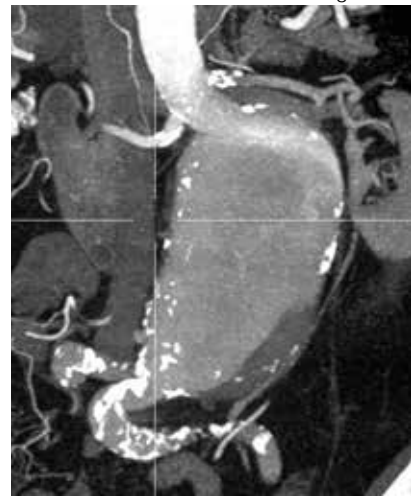

Figure 4a

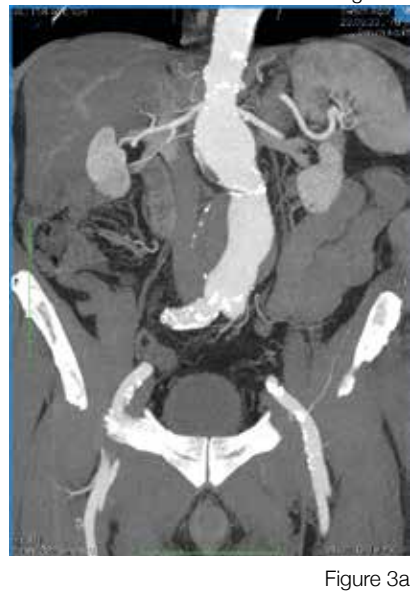

Figure 3a

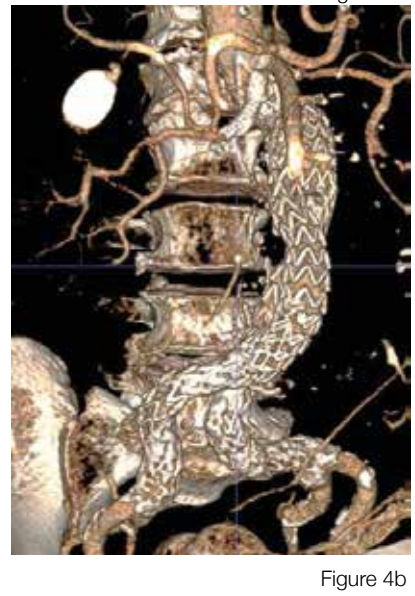

Figure 4b

Hostile neck

The shape of the neck of complex aortic aneurysms plays a substantial role in the selection of a treatment modality. In case of straight anatomy use of a fenestrated endograft (Figures 3a and 3b) seems to be preferable compared to a more kinked neck anatomy which needs a flexible endograft as in cases of additional placement of chimney grafts in the involved target vessels (Figures 4a and 4b).

The main goals of the APPROACH concept are:

- Improvement of our understanding of the reasons influencing the selection of treatment for complex pararenal aortic pathologies.
- Creation of a score system (the Approach Concept Score (ACS) system) including the most important decision-making factors and treatment options. This will allow a tailored approach for each physician to each case based on his clinical reality.
- Conduction of studies and representative treatment algorithms reflecting clinical reality in demanding pathological entities with several treatment options.

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Atherectomy lesion preparation enhances paclitaxel distribution in calcified peripheral arteries

CBSET, a not-for-profit preclinical research institute dedicated to translational research, education, and advancement of medical technologies, has announced that its scientists have published data and analyses that provide insights into the barrier effects of calcified plaque on drug delivery and the treatment success of adjunctive lesion preparation therapy.

"This preclinical demonstration of the hindrance of drug distribution by calcified tissue and improved drug delivery after modification of calcified atherosclerotic plaque could have significant clinical implications," said Michael Jaff, president, Newton-Wellesley Hospital, and professor of Medicine, Harvard Medical School, Boston, USA.

These data demonstrate enhanced paclitaxel distribution in calcified human arteries after lesion treatment using the Diamondback 360 orbital atherectomy system in a cadaver model with simulated flow and are published in the online *Journal of Controlled Release*.

"These data suggest that clinical association of diminished efficacy of anti-restenotic drugs in severely calcified arteries is at least partly due to limitations in drug absorption," Jaff continued.

"The data are exciting in that they suggest that subtle modification to the plaque surface can have profound effects on drug penetration. Massive debulking may be a relic of the past, and a more muted approach may extend endovascular intervention for PAD treatment into vessels even below the knee," said Elazer Edelman, Chairman and co-founder of CBSET, and senior author of the paper. "This paradigm shift, which relies on quantitative studies, creates an opportunity for the medical device industry to optimise drug delivery therapies to complex lesions."

"CBSET is committed to the development of novel experimental and computational models for defining the barrier effects of tissue components on drugs of interest and evaluating novel endovascular therapies," explained Rami Tzafriri, Director of Research and Innovation at CBSET and first author of the paper. "Quantification of the barrier effects of calcified plaque through computational modelling of arterial drug distribution experiments provides a framework by which to evaluate and optimize a range of emerging drug delivery and lesion preparation therapies for peripheral artery disease."

Successful results for Aortica's AortaFit FEVAR planning software

Benjamin Starnes, chief of Vascular Surgery at the University of Washington (Seattle, USA), has reported successful results for the first 30 patients undergoing fenestrated endovascular aneurysm repair (FEVAR) planned and performed using Aortica's AortaFit automated case planning software.

The cases are part of Starnes' US Food and Drug Administration (FDA)-approved physician-sponsored investigational device exemption (IDE) study.

Complexity can arise when branch arteries are too close to the origin of the aneurysm and complicate or preclude safely deploying a standard endograft. In a FEVAR procedure, fenestrations are carefully created on the endograft to line up with branch arteries that supply blood to vital organs.

Both the planning of where to place the fenestrations and the delivery of the fenestrated endograft can be highly complex and time-consuming, significantly limiting adoption.

Starnes' IDE study is evaluating technologies and methods to dramatically simplify both the case planning and the delivery of FEVAR endografts.

Since 2016, Aortica's AortaFit planning software has been a part of this study. Results from these first 30 patients using the software were presented at the Western Vascular Society meeting (23–26 September; Blaine, USA).

"I have now used Aortica's AortaFit successfully in 30 patients overall, using standard endografts from three of the major manufacturers—Bolton, Cook and Medtronic," stated Starnes. "The software digitises a patient's computed tomography scan and utilises an algorithm to account for the effect of the implant on the geometry of the anatomy to create an exact replica of each patient's aortic anatomy as it would look with the introduction of the implant.

"The entire process takes just a few minutes to create an accurate multi-vessel fenestrated graft plan. This compares to the hours it takes to plan cases using manual planning and today's existing technology. Because the graft plan is so precise, the software also simplifies the process of aligning and placing the endograft in the patient," Starnes continued.

"The results in these first 30 patients are highly favourable with low morbidity and mortality. Graft implantation was successful in 100% of patients (30/30), with 97% of branch arteries preserved at index (84/87). The three branch arteries not cannulated were due to complications not related to the graft plan. There have been no type 1a or type 3 endoleaks through 30 days. Two deaths were reported, but both were unrelated to AAA disease."

William Quinones-Baldrich, professor of surgery at UCLA (Los Angeles, USA) commenting on the results stated, "This is the future. Everyone at this conference should remember you saw this here today."

DGG secures reimbursement for abdominal aortic aneurysm screening by family practitioners

After years of lobbying, the Deutsche Gesellschaft für Gefaesschirurgie (DGG) has secured health insurance reimbursement for abdominal aortic aneurysm screening conducted by family practitioners.

A DGG press release explains that aorta diameter expansion is present in approximately 10% of the male population older than 65 years. Normally between 1.5 and 2cm, a life-threatening rupture becomes a risk at 5cm. Once diameter reaches 7cm, the rate of six-month mortality from rupture is approximately 90%.

Once rupture occurs, only approximately 20% of patients survive long enough to make it to a hospital, of which half survive with emergency operations. Pre-rupture in the non-symptomatic stage, once the aneurysm discovered and operated upon, the mortality rate is just 2%. Hospitals performing these operations must be specified by the German Joint Federal Committee.

Such a difference in mortality rates has led the DGG to advocate screening programmes for aneurysms, examples of which have already been implemented in Denmark, the UK and the USA, showing encouraging results.

The DGG says that it has been providing targeted input towards this goal for more than 10 years through a variety of articles, an annual "screening day", and support of other prominent voices.

The screening procedure itself can be carried out in a few minutes, and is easy to learn, producing almost 100% accurate results. It is now being introduced to the patient representatives in the GBA, through which financing by health insurance companies is possible.

In light of the decision to allow reimbursement for abdominal aortic aneurysm screening conducted by family practitioners, the DGG is asking men aged between 65 and 80 years to consider taking the precaution to be screened.

Questions still remain as to which doctors will carry out the screening ultrasound examinations and whether or not they will have to certify further. A DGG press release also says that it remains to be seen whether a screening programme of this kind can be carried out by an obligatory scientific register and thus the effectiveness in Germany will need to be examined.

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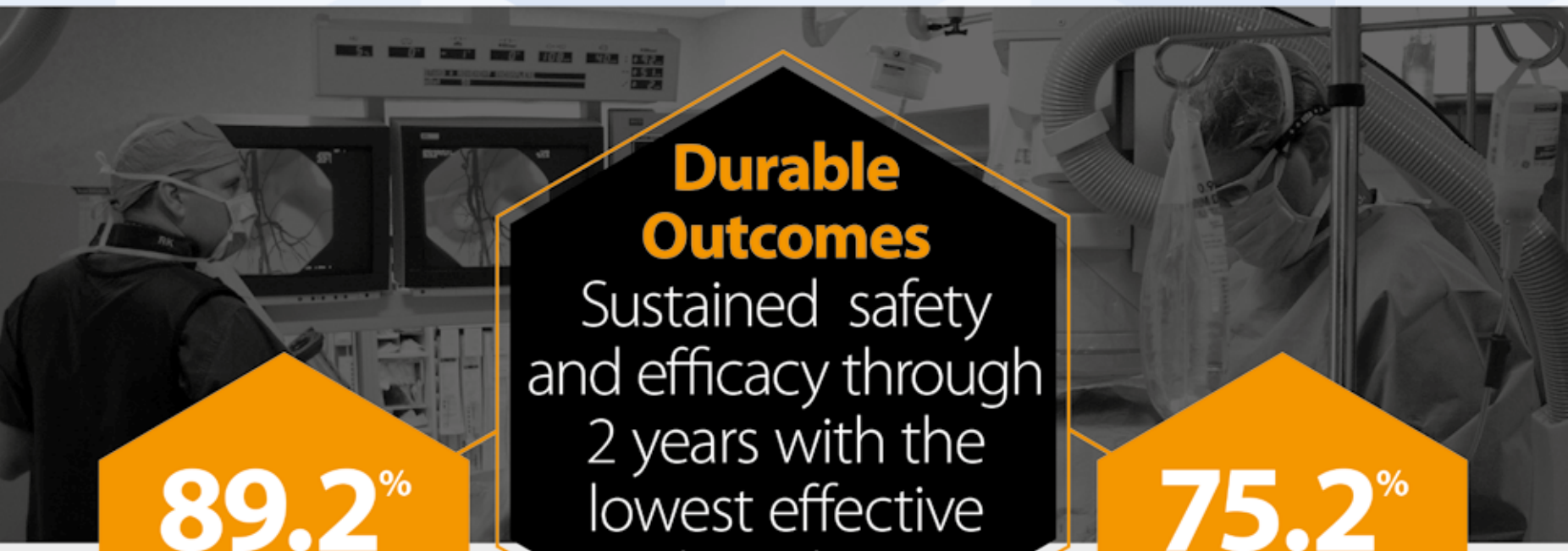

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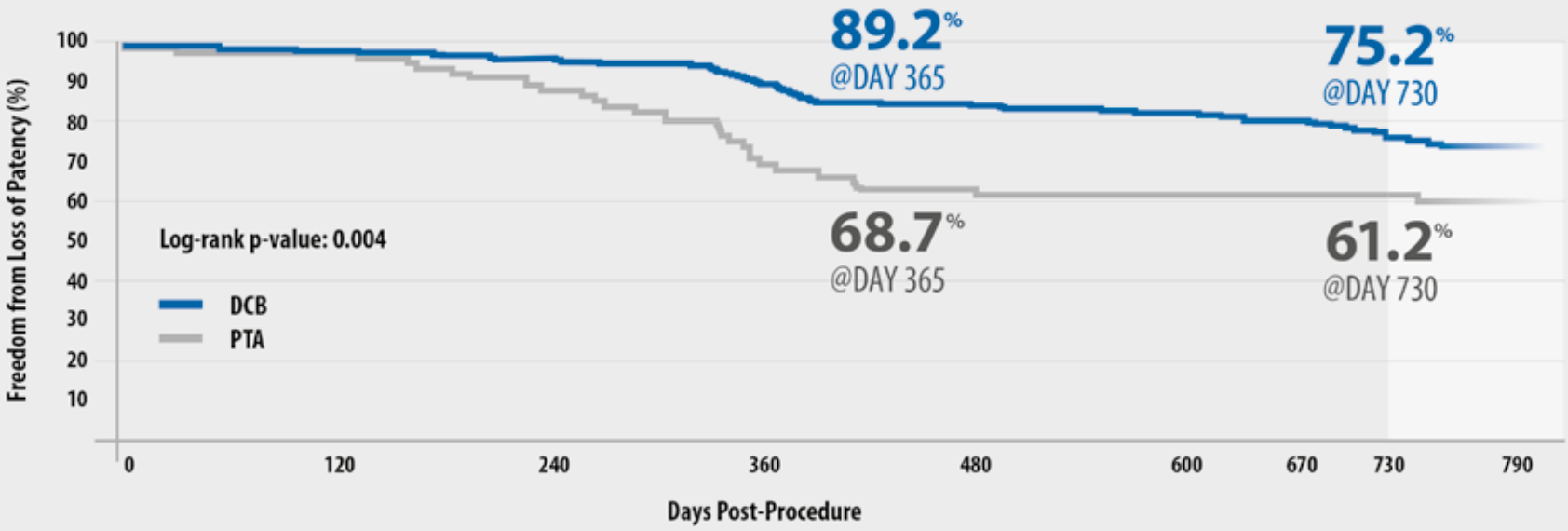

*0.82 mm **2µg/mm²

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Nov 17 | Issue 76

Hyperspectral imaging for assessing regional foot perfusion

BAUER E SUMPIO

COMMENT & ANALYSIS

There has been significant progress in limb salvage in patients with peripheral artery disease (PAD) and critical limb ischaemia (CLI) over the past two decades. These advancements have been promoted by the increased knowledge and understanding of the disease processes as well as the refinement in the interventions and enhanced patient care after revascularisation. Writing for *Vascular News*, Bauer E Sumpio explains a new tool for assessing foot perfusion—hyperspectral imaging—and explains how it adds to the vascular specialists' armamentarium.

Invasive and/or non-invasive angiography remains the gold standard for visualising the atherosclerotic lesions but newer technology is now emerging as vascular specialists shift their focus from a macro limb perspective to a more regional foot perspective. Among the current and emerging regional perfusion imaging modalities is hyperspectral imaging (HSI) using visible light which may help delineate regional foot perfusion for guiding directed revascularisation therapy of PAD/CLI.

The most important factor for determining the healing potential of a pedal wound is the degree of perfusion to the affected foot segment. The classic pathway for assessment involves history taking, physical examination, and review of both physiological markers and anatomical imaging obtained through non-invasive imaging.[1] However, due to the persistent rate of limb loss despite revascularisation via the "best vessel" approach, there has been increasing interest in performing targeted reperfusion interventions to improve rates of limb salvage and decrease rates of secondary complications. The angiosome concept, was introduced by Taylor and Palmer more than 25 years ago, and extended to the foot by Attinger.[2,3] Since then there have been various studies comparing outcomes for both open bypass and endovascular interventions using angiosome-based revascularisation (direct) versus non-angiosome-based revascularisation (indirect).[4] With the growing interests in targeted revascularisation for regional areas of lower limb ischaemia, new modalities are now evaluating micro-perfusion in the lower extremity guided by the angiosome model.

Hyperspectral imaging

HSI utilises scanning spectroscopy to construct spatial maps for tissue oxygenation using wavelengths (between 500–700 nanometres [nm]) of visual light (Figure 1). These wavelengths penetrate to 1–4mm below the skin to the subpapillary plexus. The subcutaneous arteries form a network in the subpapillary plexus and supply the skin with blood. By combining digital imaging with conventional spectroscopy, targeted wavelengths for the absorption profile for oxyhaemoglobin and deoxyhaemoglobin can be identified and measured.

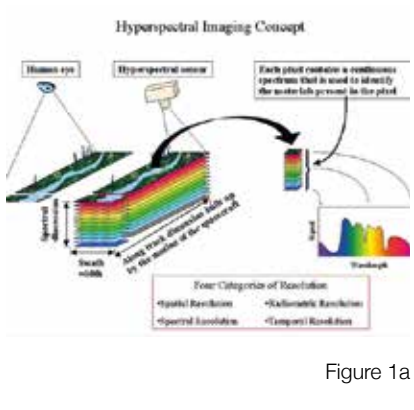

Figure 1a

Chin *et al*[5] reported differences in the tissue oxygenation of patients with PAD along angiosome regions of the foot. They identified significant differences in deoxyhaemoglobin at the plantar angiosomes, which encompasses the plantar metatarsal, plantar arch, and plantar heel. The level of deoxyhaemoglobin in these angiosomes was found to be decreased in patients with PAD compared to non-PAD patients. Nuovong *et al*[6] performed a prospective study, demonstrating that HSI is predictive of ulcer healing in diabetic patients with foot ulcers. They reported higher oxyhaemoglobin levels in the 85% of diabetic foot ulcers that healed vs. the 64% that did not heal. They concluded that HSI offers high sensitivity (86%) and specificity (88%) in determining healing potential.

Because the prognosis of ischaemic vascular disease is directly related to the functional perfusion level, rather than merely a vascular structure, functional perfusion imaging is superior to structural vascular imaging in guiding targeted therapy via the angiosome model (Figure 2). Compared to ankle brachial index (ABI) and pulmonary vascular pressure, HSI can deliver a finer assessment of perfusion in specific anatomic areas. This is accomplished through its anatomic oxygenation maps in contrast to the gross oxygenation used in ABIs. Its non-invasive nature is a major asset, as no patient contact is necessary to image the target area. The use of visual wavelengths of light can further protect patients from exposure to ionising radiation.

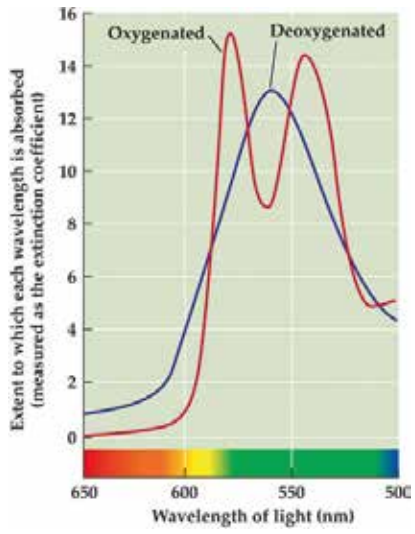

Figure 1b

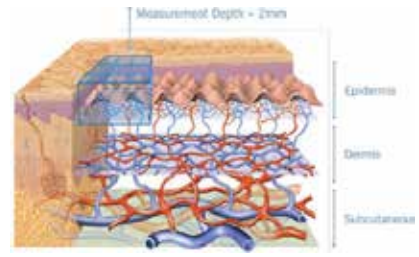

Figure 1c

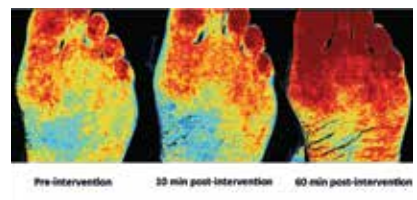

Figure 2

Anatomic maps can be rendered with other modalities, however, HSI avoids the use of intravenous contrast agents, which often require more highly-trained personnel, elaborate examination areas, and supply storage facilities.

HSI may still remain vulnerable to weaknesses faced by other skin perfusion detectors such as TcPO2 and LDF. Inflammatory reactions, such as those induced by infection, could cloud the interpretation of measurements in with local hyperaemia exists. Target area positioning will also need to be standardised as the study by Chin *et al*[5] suggested detectable changes to the veno-arteriolar reflex with ischaemia. Nonetheless, the study by Nuovong *et al*[6] does demonstrate the feasibility of HSI to identify changes in skin microcirculation in diabetic patients. Furthermore, a recent prospective non-randomised single-centre controlled trial performed by Chiang *et al* on 294 patients demonstrated the reliability of HSI to TcPO2, ABI, skin temperature, and severity of PAD with good correlation and low inter-operator and intra-operator variability.[7] The authors conclude that HSI may be useful as a screening tool in early-stage PAD. In addition, HSI has demonstrated an ability to show real-time perfusion of the angiosome for preoperative planning. This technology can potentially evaluate the level of reperfusion after an intervention to monitor success or failure after index procedure.

With the knowledge that the prognosis of PAD and CLI is closely correlated to the functional perfusion level of the affected extremity rather than the macro-vascular structure, regional foot perfusion imaging may predict wound healing success in addition to becoming a dependable surveillance tool. The clinical evaluation of the angiosome model will only be truly realised if a proper imaging system is in place that is non-invasive, fast, and safe and can easily delineate wound topography to guide directed revascularisation therapy. With increasing interest and continued refinement in our understanding of PAD/CLI, the field of vascular surgery moves towards achieving a significant reduction in persistent ulceration and a decreasing the rate of complications after revascularisation for our patients. To accomplish this we must be willing to adopt new paradigms and techniques in the treatment of this complex disease process. The implementation of these newer modalities as part of our routine clinical evaluation appears increasingly closer as each individual technology is optimised and we understand how to better utilise them effectively in conjunction with clinical judgment.

The adaption of the angiosome model as well as utilising perfusion-based imaging studies allows the vascular specialists to refine their understanding of the disease process in CLI while enhancing therapeutic modalities, clinical decision-making, and improving outcomes after revascularisation interventions.

Bauer E Sumpio is a Professor of Surgery, Radiology and Medicine, Yale University School of Medicine, New Haven, USA. He is on the Scientific Advisory Board of HyperMed Imaging, Inc

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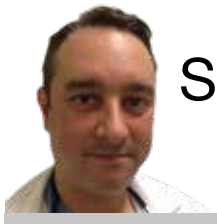
Beyond standard angiography—quantification of perfusion following peripheral endovascular procedures



STAVROS SPILIOPOULOS
KONSTANTINOS KATSANOS

COMMENT & ANALYSIS

Modern medicine requires objective measurable scientific outcomes. New methods of quantification will most likely forestall phrases like "looks ok", or "should be enough" from everyday clinical practice, particularly in the endovascular treatment of peripheral arterial disease, write Stavros Spiliopoulos and Konstantinos Katsanos.

Despite the fact that numerous novel, sophisticated, devices have been introduced in everyday clinical practice in order to improve outcomes of endovascular procedures for the management peripheral arterial disease, the functional evaluation of these outcomes is still based on the same tests used over many decades, such as the final angiographic result, pressure measurements across the treated lesion and ankle-brachial index (ABI). However, these methods can only indirectly assess the primary outcome of revascularisation, which is tissue perfusion, while an objective quantification of limb perfusion is currently not possible. Modern medicine requires an objectively measurable procedural outcome of limb perfusion for the assessment of endovascular procedures. Cardiologists have been investigating various modalities for the determination of functional parameters during coronary angioplasty such as fractional flow reserve (FFR) for assessment of lesion severity, TIMI myocardial perfusion grade and coronary flow reserve for evaluation of tissue perfusion and coronary microcirculation.[1,2]

The first endeavour to noninvasively evaluate limb perfusion following revascularisation was made using laser Doppler skin perfusion pressure (SPP) measurements and transcutaneous oxygen ($TCPO_2$) monitoring. SPP measurements of the capillary opening pressure following slow release of the pressure occlusion cuff provide an indirect estimation of the microcirculatory flow status to predict wound healing. $TCPO_2$ measures oxygen concentration of subcutaneous tissue 1–2mm in depth and can, therefore, provide direct information about the endpoint of limb perfusion, which is tissue oxygenation. SPP values above 40mmHg and $TCPO_2$ values above 30mmHg have been correlated with improved wound healing rates. Implantable O_2 microsensors are another option for the evaluation of post-angioplasty limb perfusion currently under investigation. More recently, microwave radiometry technology has been used for the thermographic evaluation of the deeper tissue layers of ischaemic feet and the researchers have found that critical limb ischaemia patients with tissue loss demonstrated lower mean temperature values compared to non-ischaemic patients.[3] This thermometric technology is currently investigated for the quantifiable evaluation of foot perfusion post revascularisation in order to predict successful wound healing. Moreover, following various technological innovations, physicians now have the potential to intraoperatively quantify limb perfusion, and therefore, objectively evaluate the clinical impact of endovascular procedures. Peripheral FFR, a hyperaemia-inducing physiological test commonly implemented in coronary revascularisation and recently applied for the assessment of the physiological significance of iliac and superficial femoral artery stenosis and below the knee disease in critical limb ischaemia,[4,5] could also be used for the intraoperative evaluation of the impact of an apparently successful lesion revascularisation on distal foot perfusion.[6]

Interestingly, this can also be achieved indirectly with non-invasive, "wireless" methods. Jens S *et al* reported the feasibility of intraoperative 2D perfusion angiography of the foot in critical limb ischaemia patients, using software developed in collaboration with Phillips. Treatment outcome is determined by the evaluation of pre- and post-procedural changes in arrival time, time to peak, and the time–density curves in order to produce functional indices of tissue perfusion.[7] Nonetheless, absolute quantification of blood flow has not been possible. In a study by Shaw A *et al* presented at the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) annual meeting in 2013, noninvasive, real-time, intra-operative laser Doppler imaging (LDI) detected a quantifiable increase of limb perfusion following lower limb angioplasty. Figure 1 shows that quantitative functional vascular assessment depicting an angiosome-based perfusion. Gain and/or decline is also possible using p-FFR or intraoperative perfusion angiography. Figure 2 demonstrates vessel-specific papaverin-induced p-FFR values following revascularisation of the anterior tibial and peroneal arteries employing intraprocedural angiographic perfusion imaging with further post-processing of the contrast-density curves. Figure 3 demonstrates the quantification of incremental improvements of heel tissue perfusion following revascularisation of the peroneal and subsequently the posterior tibial artery again using angiographic perfusion imaging with post-processing of the background raw temporal data. Note the steep increase of flow following revascularisation, in the respective flow curves.

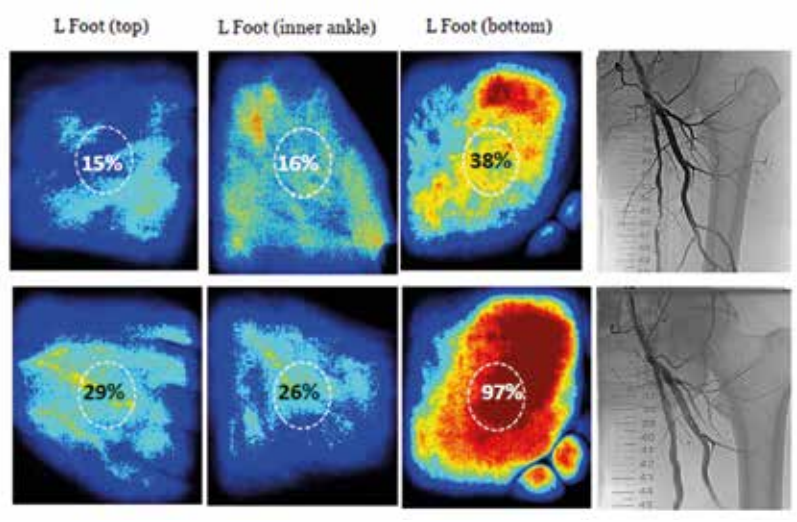


Figure 1

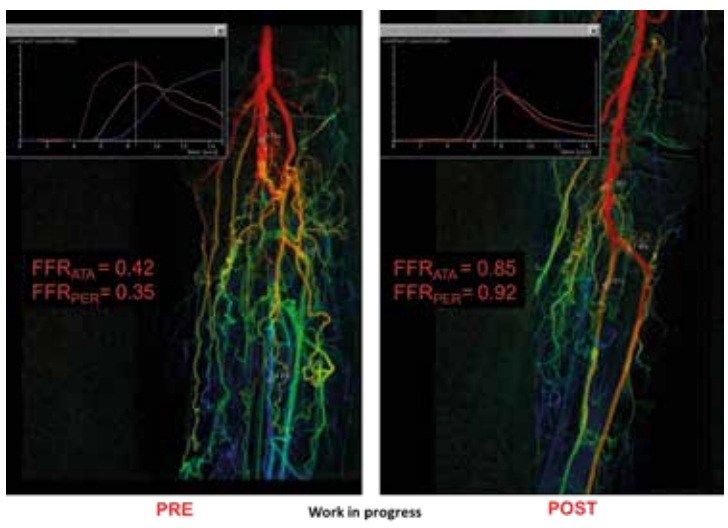


Figure 2

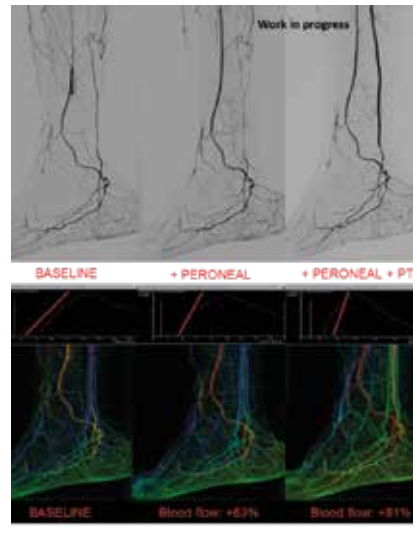


Figure 3

The above examples demonstrate the possibility of real-time, intraoperative, perfusion-guided revascularisation, enabling the physician to decide whether to stop or proceed with further improvement of remaining stenosis or the revascularisation of additional vessels and/or pedal arch angioplasty. Modern medicine requires objective measurable scientific outcomes, not subjected to misinterpretation and these new methods of quantification will most likely do away with phrases like "looks ok", or "should be enough" from everyday clinical practice, thereby producing significantly improved clinical outcomes.

Stavros Spiliopoulos is an interventional radiologist at Attikon University General Hospital, Athens, Greece. Konstantinos Katsanos is an interventional radiologist at Patras University Hospital School of Medicine, Patras, Greece. The authors have reported no disclosures pertaining to the article.

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Product News

Vasorum launches Celt ACD second generation vascular closure device in the USA

Following FDA approval of its PMA supplement, Vasorum has added a 7F Celt ACD vascular closure device to its Celt ACD 6F and Celt ACD 5F range in the USA.

Celt ACD is indicated for arterial puncture closure in both diagnostic and interventional cardiology and radiology patients. Celt ACD offers "excellent time to haemostasis in a wide variety of clinical situations," a company press release says. The second generation Celt ACD devices, now available in both the USA and Europe, have a newly improved delivery system that has been designed to enhance the user experience during deployment.

The first commercial cases in the USA were carried out by Shing-Chiu Wong, Professor of Medicine at Weill Cornell Medicine in New York. Based on his use, Wong commented, "The Celt ACD range of closure devices are addressing the clear need for quicker and more efficient methods of increasing patient throughput in healthcare facilities, and they provide doctors and patients with a solution which can efficiently manage arterial closure following vascular procedures." Clinical cases have also been carried out by Richard Kovach, Division Director, Interventional Cardiology and Medical Director, Cardiac Catheterization Laboratory at Deborah Heart and Lung, Browns Mills, New Jersey. Kovach commented that he "was impressed with the performance of Celt ACD in patients with severe arterial disease undergoing complex interventional procedures." Additionally, he believes that "Celt ACD has the potential to become the workhorse closure device in cath labs."

There are currently over eight million catheter procedures performed annually, which support an estimated US$1bn femoral artery closure device market. The number of procedures is expected to exceed 10 million by 2020. In addition to interventional cardiology procedures, the market growth is being driven by an increasing number of peripheral vascular, neurovascular and other catheter procedures which demand more patient-friendly devices and more efficient patient discharge from hospitals. Given its ease of use and wide clinical applicability, Celt ACD is well positioned to address this broad and growing market opportunity.

"To date in Europe, Celt ACD has proven itself to be a best in class arterial puncture closure device. Celt ACD allows immediate closure of multiple re-sticks in calcified vessels and is also very comfortable for patients. The launch of the expanded Celt ACD range in the USA is a very significant milestone for Vasorum," stated James Coleman, co-founder and CEO of Vasorum.

Surmodics announces global approvals of 0.014" low-profile PTA balloon dilation catheter

Surmodics has received US Food and Drug Administration (FDA) 510(k) and CE mark clearance for its 0.014" low-profile percutaneous transluminal angioplasty (PTA) balloon dilation catheter, designed for peripheral angioplasty procedures. The company is making this product available for distribution in the coming months.

Surmodics says that its 0.014" PTA balloon catheter "offers best-in-class deliverability and lesion crossing by leveraging the company's proprietary Serene hydrophilic coating, unmatched for low friction and particulates." The company's proprietary balloon and catheter technology, combined with Surmodics' advanced processes, ensures ultra-low tip entry and crossing profile with smooth transitions, to achieve best-in-class product performance.

"Surmodics is focused on providing next-generation devices to address the growing need for minimally invasive treatment of peripheral artery disease," said Gary Maharaj, President and CEO of Surmodics. "We are confident this highly deliverable, low-profile PTA catheter will provide physicians an effective new tool for accessing and crossing even the most complex peripheral lesions."

The development of the Surmodics 0.014" low-profile PTA catheter is a step forward in the company's strategy to be a provider of whole-product vascular solutions for its medical device customers. Following acquisitions of Creagh Medical and NorMedix, Surmodics says that it will now have "complete capabilities for design, development and high-volume manufacturing of a wide variety of highly differentiated balloon catheter and specialty catheter solutions".

Gecko Biomedical receives CE mark clearance for Setalum sealant

Gecko Biomedical has received CE mark approval for its Setalum sealant allowing the company to market its technology in Europe.

The Setalum sealant is a biocompatible, bioresorbable and on-demand activated sealant usable in wet and dynamic environments as an add-on to sutures during vascular surgery. The polymer is applied to tissue *in situ* and activated using a proprietary light activation pen.

The technology at the foundation of the Setalum sealant was developed at the Massachusetts Institute of Technology, Harvard Medical School, and Brigham and Women's Hospital, Boston, USA. Setalum sealant is the most recent successful example of bio-inspired technology in medicine, and is based on the adhesive mechanisms found in nature that work in wet and dynamic environments.

The granting of the CE mark for the vascular sealant is the first regulatory validation of the safety and performance of Gecko Biomedical's scalable and innovative polymer platform.

"The Setalum sealant can be precisely and easily applied thanks to its viscosity and hydrophobicity and then activated at will to provide an instant hermetic barrier and effective haemostasis. The key features of this polymer technology were selected with physicians and patients in mind, and significantly improves upon the latest generation of haemostatic agents to become a gold standard in vascular surgery," said Jean-Marc Alsac, vascular surgeon at the Hôpital Européen Georges Pompidou in Paris, France, and the principal investigator of Gecko Biomedical's BlueSeal clinical study.

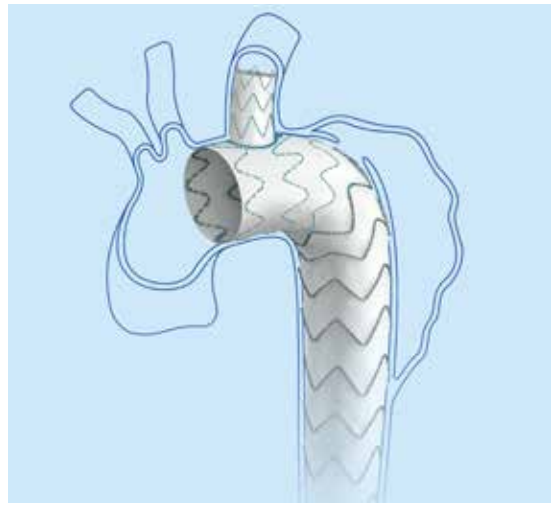
The BlueSeal clinical study was a prospective, single-arm and multicentre clinical investigation performed at four French university hospitals and undertaken in patients necessitating a carotid endarterectomy. Performance of the sealant was evaluated by the percentage of immediate haemostasis following clamp removal. Based on a sequential Bayesian design, the recruitment was stopped at 22 enrolled patients given the fulfilled performance criteria and the optimal safety profile of the sealant. Immediate haemostasis was achieved in 85% of patients and all recorded adverse events were found to be representative of those commonly occurring in patients necessitating vascular reconstruction with none considered as related to the sealant.

Christophe Bancel, Gecko's CEO, said, "We are delighted to receive the CE mark for our first product, Setalum sealant, as this will allow us to bring new and innovative solutions to the market to improve patient care. As a result, we are now ramping up our manufacturing capabilities and selection of strategic partners to bring this innovation to patients."

The company is swiftly expanding its applications, targeting new functionalities and tissue types to develop solutions for new clinical indications and geographic markets.

"Our ability to bring an entire new family of innovative polymers from the bench to the bedside in less than two and a half years, is a testimony of the versatility and scalability of our platform. We are now ready to fully expand, internally and through partnerships, into new therapeutic areas to design disruptive, surgical solutions for patients," Bancel added.

Castor branched aortic stent graft gains CFDA approval



The Castor branched aortic stent graft system, developed by MicroPort Endovascular, has obtained the regulatory approval from China Food and Drug Administration (CFDA), formally entering the Chinese market.

Thoracic endovascular aortic repair (TEVAR) for the treatment of aortic dissection has experienced rapid development and been widely accepted in the past 20 years. However, MicroPort Endovascular says "there still does not exist a stent graft especially designed for aortic arch, which can dispose with challenges inherent with the anatomy of the aortic arch." Such challenges include:

- How to get to and precisely locate in the tortuous aortic arch;
- How to deal with anatomy diversity of the aortic arch;
- How to reconstruct the supra-arch vessels.

President Zhenghua Miao from MicroPort Endovascular said, "From 2006 on, MicroPort Endovascular started on the development of Castor, which is globally the first branched stent graft especially designed for the aortic arch, with the single branch extending into the left subclavian artery."

Castor is for the treatment of thoracic dissection encroaching into the left subclavian artery or the original tear located within 20mm distal to the left subclavian artery and 15mm distal to the left carotid artery. Thus treatment in zone 2 can be completed without any adjunctive surgical procedure.

The device adopts the "unibody design", which sews the main body and branch stent together to make it possible to deploy and release at the same time, effectively avoiding type III endoleak and long-term migration.

Castor employs standardised design with high compatibility to various arch anatomies. The tapered size is exclusive to aortic dissection. The delivery system employs a dual-sheath design and the stent graft is delivered to the aortic arch under the protection of a soft sheath. The orientation and position of the branched stent is assured by patented wire-controlled, pull-in design. Accurate and fast deployment is achieved by a wire-controlled mechanism

Zaiping Jing from Shanghai Changhai Hospital said, "Castor is the first stent graft that can simultaneously repair the aortic arch, left subclavian artery and the descending aorta, whose clinical safety and performance has been fully supported by a 73-case premarket clinical study with 97.6% technical success, 5.5% 12-month all-cause mortality, 4.1% 12-month endoleak and 2.7% 12-month stroke, 69% of which are acute aortic dissection. Although there have been several ways to treat thoracic dissection involving the left subclavian artery, branched stent grafts offer the most promising technique in the near future. Applying Castor in combination with chimney or fenestration technique can deal with dissections encroach-

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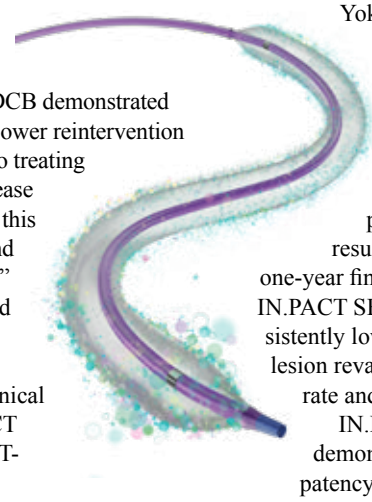
Product News

ing left carotid artery or innominate artery, achieving a complete endovascular repair of the aortic arch."

IN.PACT Admiral drug-coated balloon is approved in Japan

Medtronic announced on 8 September 2017 that the IN.PACT Admiral drug-coated balloon (DCB) received approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of peripheral artery disease in the superficial femoral and popliteal arteries. Before Medtronic can begin commercialisation, it must partner with Japanese MHLW to gain reimbursement to ensure broader access to this therapy.

"The IN.PACT Admiral DCB has demonstrated superior one-year clinical outcomes in Japan and across Medtronic IN.PACT SFA clinical trials, providing patients with an improved restoration of blood flow and reduced need for additional revascularisation compared to plain balloon angioplasty, a current standard of care," said Hiroyoshi Yokoi, Fukuoka Sannou Hospital, Japan. "In the IN.PACT SFA Japan Trial, the DCB demonstrated superior patency and lower reintervention rates. I look forward to treating peripheral arterial disease patients in Japan with this durable, consistent, and safe DCB technology."



The MHLW granted approval for the IN.PACT Admiral DCB based on the clinical data from the IN.PACT SFA Japan Trial (MDT-2113 SFA Japan Trial) led by Osamu Iida, Kansai Rosai Hospital, Japan and Yokoi.

The study enrolled 100 patients across 11 sites in Japan and randomised treatment to either DCB (n=68) or plain balloon angioplasty (PTA) (n=32). The results were consistent with one-year findings from the pivotal IN.PACT SFA Trial, showing a consistently low clinically-driven target lesion revascularisation (CD-TLR) rate and high patency rate.

IN.PACT Admiral SFA Japan demonstrated 93.9% primary patency in the DCB group as compared to 46.9% in the PTA group at one year based on Kaplan-Meier Estimate ($p<0.001$). Additionally, one-year results demonstrated a CD-TLR rate of 2.9% for the DCB group compared to 18.8% in the PTA group ($p=0.012$). In IN.PACT SFA Japan, major adverse events were also lower for the DCB at one year (4.4% compared to 18.8% in the PTA group; $p=0.028$), with no major target limb amputations.

"Medtronic has long been committed to providing life-saving therapies to the more than 200 million patients suffering from peripheral arterial disease worldwide," said Mark Pacyna, vice president and general manager of the Peripheral business in the Medtronic Cardiac & Vascular Group. "IN.PACT Admiral was launched more than seven years ago in Europe. Now, with more than 200,000 patients treated, we are excited to bring IN.PACT Admiral DCB to patients in Japan."

The IN.PACT Admiral drug-coated balloon is a clinically-proven primary endovascular therapy. It has been approved in Japan to treat *de novo* and non-stented restenotic lesions with length ≤200mm in superficial femoral and popliteal arteries with reference vessel diameters of ≥4mm and ≤7mm. The DCB's primary mode of action is physical dilatation of the vessel lumen by PTA, and the proven paclitaxel drug is intended to prevent artery narrowing by minimising scar tissue formation.

RD Global-Invamed receives CE mark to market Extender DCB and Temren atherectomy with CTO catheter

RD Global-Invamed has announced it has received CE mark to market the Extender drug-coated balloon (DCB) and Temren atherectomy with CTO catheter for treating arterial occlusions.

According to RD Global-Invamed, with the new Extender DCB and Temren atherectomy with CTO catheter, Invamed is expanding its venous product portfolio to include arterial treatments.

A company press release says that the Temren atherectomy with CTO catheter has a revolutionary tip design that can both cut and trim diseased tissue segment. It cuts, captures, and clears diseased tissue by aspiration with the Archimedes screw principle with one insertion. Temren treats a broad range of tissue types, from soft plaque to calcified arteries, and can be

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Vascular & Endovascular

Controversies Update

CONTROVERSIES CHALLENGES CONSENSUS

14 YEARS OF LOOKING FORWARD

EDUCATION INNOVATION EVIDENCE

- Aortic Controversies
- Peripheral Arterial Controversies — 10 Years of iLeg
- Venous Controversies — 10 Years of CX Venous Workshop
- Acute Stroke Controversies

"CX is optimal education! The symposium provides us with really strong evidence for what we are doing every day, leading to appropriate decision-making for patients."

Dittmar Böckler, *Heidelberg, Germany*

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CX 2018 Preliminary Programme Highlights

3 Days of Aortic Controversies update and techniques and technology update

Day 1: **CX Aortic Edited Cases** – Tuesday, 24 April 2018

- Open thoracoabdominal repair after failed TEVAR
- Advanced techniques in the endovascular management of visceral aneurysms
- Chimney EVAS
- Open conversion after EVAR/EVAS

Day 2: **Plenary Programme** – Wednesday, 25 April 2018

CX Abdominal Aortic Aneurysm Controversies update, including complex management, debate and roundtables

- New data on causation of aneurysmal disease
- Clinical and cost-effectiveness of EVAR
- EVAR follow-up: detection and correction of endoleaks
- Optimal management of mycotic aneurysms
- How not to treat ruptured aneurysms
- EVAR in women vs men

Late-breaking aortic trials

Day 3: **Plenary Programme** – Thursday, 26 April 2018

CX Total endovascular aortic replacement and leading-edge controversies, debates and roundtables.

- Connective tissue disorders
- Remodelling of the thoracic aorta
- Controversies in the management of short, angulated, wide and challenging proximal necks
- Prediction of myocardial infarction after FEVAR
- Radiation controversies
- Stroke from Thoracic Endovascular Procedures (STEP)

Additional Aortic Sessions

NEW CX Aortic Village with one-to-one hands-on demonstration led by Stéphan Haulon

CX Global Stars and Rising Stars

CX Abstracts and E-posters

3 Days of Venous Controversies update, techniques and technologies

Day 1: **Plenary Programme** – Tuesday, 24 April 2018

CX Venous Controversises update with debates and roundtables.

- Different techniques for ultrasound-guided foam sclerotherapy
- Thrombectomy of peripheral veins and pulmonary arteries – indications, technique and results
- Criteria for vein incompetence on transvaginal duplex and retrograde venography
- Venous outflow obstruction

Late-breaking trials for venous disease

Additional Venous Sessions

Day 2: NEW Venous Techniques & Technologies (Edited Cases)

Wednesday, 25 April 2018

Days 2 and 3: NEW CX VENOUS WORLD. Under the glass roof dome, techniques and technologies demonstrated by the world-class CX Venous Faculty, interspersed with CX Venous Edited Live cases with discussions.

Wednesday, 25 April and Thursday, 26 April 2018

CX Global Stars and Rising Stars

CX Abstracts and E-posters

2 Days of Vascular Access Course

Day 1: **Plenary Programme** – Wednesday, 25 April 2018

Complex and end-stage vascular access

- Classification and aetiology
- Upper limb complex access
- Lower limb access
- Failed central veins
- Innovations in vascular access: technologies, techniques and trial updates

Late-breaking trials in vascular access

Additional Vascular Access Sessions

Day 2: CX Vascular Access Workshop – Techniques & Technologies

Thursday, 26 April 2018

CX Global Stars and Rising Stars

CX Abstracts and E-posters

3 Days of Peripheral Arterial Controversies update and techniques and technologies update

Day 1: **Plenary Programme** – Tuesday, 24 April 2018

CX Peripheral Arterial Disease Controversies update with debates and round tables

- Decision making in claudication
- Endovascular first for critical limb ischaemia
- 2017 ESC/ESVS guidelines on peripheral arterial disease and Global Vascular Guidelines on chronic life-threatening ischaemia

Late-breaking peripheral arterial and wound healing trials

Additional Peripheral Sessions

Day 2: CX Live and Edited peripheral techniques and technologies from leading endovascular surgery, angiology, interventional cardiology and interventional radiological centres

Wednesday, 25 April 2018

Day 3: Interdisciplinary leg management, 10-year celebration with controversies, debates and roundtables with live cases, techniques and technologies, and collaboration with the CLI Global Society

Thursday, 26 April 2018

NEW CX Peripheral Village with one-to-one hands-on classes on Days 1, 2 and 3 led by Andrew Holden. This will be an opportunity to use technologies seen in Live and Edited Peripheral Cases.

CX Global Stars and Rising Stars

CX Abstracts and E-posters

Acute Stroke Controversies

Day 1: **Plenary Programme** – Friday 27, April 2018

Carotid and Vertebral Controversies

- Carotid endarterectomy and stenting safety in the early period after onset of symptoms
- Surveillance and reintervention after endarterectomy and stenting
- The role of screening to detect asymptomatic carotid stenosis

Acute Stroke Controversies

- Stroke from Thoracic Endovascular Procedures (STEP) – Incidence and global collaboration for optimal results

Additional Acute Stroke Sessions

CX Global Stars and Rising Stars

CX Abstracts and E-posters

Additional CX Courses and Sessions

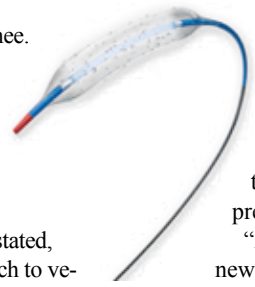
Additional CX Course	Additional CX Sessions
CX Congenital Vascular Malformations	CX Innovation Showcase
	CX Meets Latin America
	CX Meets China

40 YEARS OF LOOKING FORWARD PARTY

CX will host the "40 Years of Looking Forward" party on the evening of Thursday 26 April 2018. The party will take place at the Science Museum in South Kensington. Tickets will be available for CX attendees to purchase. More information coming soon.

Product News

used for lesions above and below the knee. It has a novel tip design that centres the active tip of the device in vessel and minimises the risk of rupture. The Extender DCB has a novel design to deliver paclitaxel into the diseased vessel segment.



Rasit Dinc, president of RD Global, stated, "Our experience and innovative approach to venous therapy has been successful in the treatment of venous insufficiency embolisation with VenaBlock and in deep vein thrombosis and pulmonary embolism treatment with hybrid thrombectomy therapy. Our innovative approach and experience has also provided a new approach to the treatment of arterial vascular diseases. In 2018 we will expand our arterial product portfolio with stent and graft products."

Rasit Dinc also said, "RD Global is a research and development institute. Our aim is to develop new and better treatment options for all humans around the world. We are in a dynamic world and necessity for a new treatment options are increasing; our golden rule is, 'Read, think, apply and follow', in order to catch up with global needs."

TVA Medical receives CE mark for everlinQ 4 endovascular AVF system

TVA Medical's everlinQ 4 endovascular arteriovenous fistula (AVF) system has received CE mark in the European Union. The technology uses a 4F catheter system with

enhanced visual indicators to create haemodialysis access using an endovascular technique without open surgery.

In a prospective, single-arm, single-centre study evaluating the everlinQ 4 endoAVF system, 97% of endovascular AVF procedures were successful, and fistula maturation was achieved in 83% of patients.

Tobias Steinke, chief of Vascular and Endovascular Surgery, Schön Klinik, Düsseldorf, Germany, performed the first case in Europe using the everlinQ 4 system. "The new system with smaller profile catheters and radiopaque visual indicators was extremely easy to use," he said. "This new approach streamlines the procedure for providing patients a functional AV fistula without open surgery."

"We are pleased to achieve this next regulatory milestone that broadens availability of the everlinQ endoAVF system for patients," said Adam L Berman, president and CEO of TVA Medical. "We are now offering the 4F catheter system in Europe, as well as in the everlinQ endoAVF EU Study, which is gathering additional clinical data to support future clinician education, patient access, and reimbursement of the everlinQ endoAVF System."

Lombard's Aorfix IntelliFlex LP delivery system launched in Japan

Lombard Medical has announced the full commercial launch in Japan of its new low-profile IntelliFlex LP delivery system for the Aorfix abdominal aortic aneurysm (AAA) system.

The new delivery system, used to deliver Lombard's Aorfix AAA stent graft, is exclusively marketed in Japan by Osaka-based Medico's Hirata, a supplier of medical devices for the Japanese healthcare industry.

Clinical cases confirming the performance and ease-of-use of the IntelliFlex LP delivery catheter in complex aortic aneurysm anatomies were presented at this year's Japanese Endovascular Symposium (23–24 August; Tokyo, Japan). Makoto Sumi, of Saitama Cardiovascular and Respiratory Center for Vascular Surgery, Saitama, Japan, presented the data.

"After a carefully controlled release of Lombard's new delivery catheter for Aorfix, positive first-hand customer experience is increasing demand in our domestic market. We are confident that the investment made by Lombard in the technology—and our firm in sales and marketing—will pay dividends in terms of increased sales for the balance of 2017 and beyond," says Masataka Hirata, president of Medico's Hirata. "In addition, early data from the Medico's-sponsored Japanese clinical study (JANIS) recently presented at the Japanese Society for Vascular Surgery independently confirmed the excellent clinical data in the clinical study which led to Lombard's US Food and Drug (FDA) approval (PYTHAGORAS)."

Kurt Lemvigh, chief executive officer of Lombard, comments, "Japan is perhaps the most demanding market in the world in terms of quality of products and clinical outcomes…by focusing on our UK home market and the fast-growing AAA markets in Japan and China, we believe we can achieve cash flow breakeven and profitability on rather modest revenue. The operational turnaround at Lombard is tangible."

iVascular SLU receives Indian clearance for peripheral products

iVascular SLU has announced that it has received approval for selling its coronary and peripheral products in India.

The Indian medical devices market is the fourth largest in Asia and part of the global top 20.

"iVascular's product portfolio was created with the latest technologies to improve patients' outcomes and provide physicians with the solution for the challenges that they meet daily. We are now excited to expand our presence further into Asian market", said Lluis Duocastella, iVascular's CEO.

The approval will cover iVascular's peripheral drug-coated balloons and drug-eluting stents, which are now available for sale on the Indian subcontinent.

Luminor drug-coated balloon receives Canadian Medical Device Licence

iVascular has announced that its Luminor 14m peripheral balloon catheter with paclitaxel elution has received the Canadian Medical Device Licence (MDL).

Luminor 14m is a drug-coated balloon (DCB) with the combination of an extra low cross profile and iVascular proprietary technology for drug release "TransferTech".

Lluis Duocastella, CEO of iVascular asserted: "The receipt of MDL for Luminor 14m represents a milestone for iVascular on the Canadian market. It opens a new horizon for the endovascular product portfolio and allows us to provide the Canadian market with the best DCB on the market."

Also during CIRSE, iVascular clinical data were presented from the EffPAC randomised controlled trial. The trial enrolled 171 patients at 11 German centres who were randomised to treatment with either the Luminor DCB or percutaneous transluminal angioplasty. The comparison with other published randomised controlled trials indicated that the Luminor DCB demonstrates higher efficacy than most other available DCBs.

Medtronic launches Concerto 3D detachable coil system in USA and Europe

Medtronic is expanding its embolisation product portfolio with the launch of the Concerto 3D detachable coil system. The system was launched at the Cardiovascular and Interventional Radiological Society of Europe annual meeting (CIRSE; 16–20 September, Copenhagen, Denmark).

The Concerto 3D coil is a new coil in the Medtronic Concerto platform and is indicated for arterial and venous embolisations in the peripheral vasculature. The product is now available in both the USA and Europe.

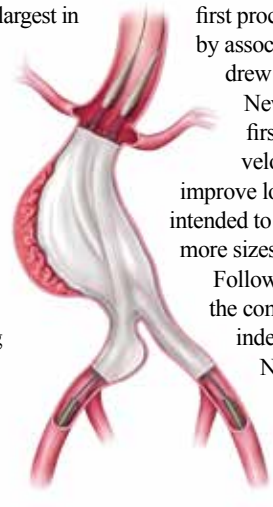
The new 3D coil has a complex shape that is designed to give physicians the ability to frame the treatment area by creating a scaffold. The Concerto 3D coil is used to form a frame while treating aneurysms. This is similar to the way neurovascular aneurysms are treated. According to a press release, the 3D coils may also be:

- Helpful in obtaining a focal occlusion during vessel take-down with scaffold forming
- Used interchangeably with the existing Helix line in other applications.

The Concerto 3D coil has the same softness and detachment system as the Concerto Helix, which is intended to allow the coil to navigate smoothly through tortuous anatomies and detach instantly for ease, precision, and control during embolization. In addition, the coil also contains fibres that increase thrombogenicity (clotting) of the coil compared to bare metal equivalents. The Nylon and PGLA fibres system features the LatticeFX technology, which is designed to promote thrombosis response.

Endologix' Nellix receives CE mark with refined Instructions for Use

Endologix has been granted CE mark approval for its Nellix endovascular aneurysm sealing system, with refined Instructions for Use (IFU). Nellix is being studied in the USA under a US Food and Drug Administration (FDA) Investigational Device Exemption (IDE).



Nellix originally received CE mark last year. The first procedures with the system were performed by associate professor Andrew Holden and Andrew Hill at Auckland City Hospital, Auckland, New Zealand. Endologix says that it is "the first and only EVAS product" and was "developed to reduce all types of endoleaks and improve long-term patient outcomes". The system is intended to enhance ease of use and offers physicians more sizes to treat more patients with AAA.

Following a review of supporting clinical data, the company's notified body, together with an independent clinical reviewer, determined that Nellix—with this refined IFU—meets the applicable safety and clinical performance requirements. As a result of these evaluations, the notified body granted a CE mark for Nellix with the refined IFU.

"We are very pleased with the clinical outcomes generated by the Nellix endovascular aneurysm sealing system utilising the refined IFU," comments John McDermott, Endologix's chief executive officer. "The Nellix CE mark with the refined IFU provides patients and physicians in Europe with continued access to…complete aneurysm sealing, including low rates of endoleaks and all-cause mortality."

US FDA clears Adhezion Biomedical's SecurePortIV catheter adhesive

The US Food and Drug Administration has cleared Adhezion Biomedical's SecurePortIV catheter securement adhesive for marketing.

The adhesive is comprised of a cyanoacrylate formulation. It can be used with short-term or long-term vascular access devices to enhance device securement, seal the catheter insertion site, protect the patient from catheter related blood stream infection, and provide a water-resistant barrier. SecurePortIV comes in a patented ergonomic applicator.

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- Peripheral Arterial Controversies — 10 Years of ileg
- Aortic Controversies
- Venous Controversies — 10 Years of CX Venous Workshop
- Acute Stroke Controversies

"At CX we discuss clinical science getting information about what is up to date with regards to new developments and technologies in the light of what is considered as being the benchmark. The opportunity to discuss new data in the light of what is established is unique to this meeting."

Thomas Zeller, *Bad Krozingen, Germany*

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Product News

The adhesive is applied to the skin under the hub of vascular access devices, and forms a film that holds the catheter to the skin to reduce catheter movement, migration, and/or dislodgment.

SecurePortIV is also applied over the catheter-skin insertion site forming a seal proven to immobilise surface bacteria and fungi, preventing them from entering into the catheter skin entry site while also providing a moisture-proof barrier.

The sealing effect could also help reduce the frequency of dressing changes.

Endurant II/IIs stent graft receives FDA approval for short neck anatomies with Heli-FX EndoAnchor

Medtronic has received US Food and Drug Administration (FDA) approval for the Endurant II/IIs stent graft system to treat abdominal aortic aneurysm (AAA) patients with neck lengths down to 4mm and <=60 degrees infrarenal angulation when used in combination with the Heli-FX EndoAnchor system. The expanded indication enables the Endurant II/IIs stent graft to be used in conjunction with the Heli-FX EndoAnchor system to treat a wider range of patients with short, hostile aortic neck anatomies, independent of renal stenting.

Until now, some patients with short infrarenal necks (<10mm) were considered ineligible for endovascular aneurysm repair (EVAR), leaving them with limited treatment options. Up to 30–40% of patients with AAA disease are considered unsuitable candidates for conventional EVAR. According to estimates from physicians across Europe and the USA, more than one-third of these patients have AAA proximal neck anatomies <=10mm.

"Due to the complex and hostile proximal aortic neck anatomy, this patient population remains a challenge to treat," said William Jordan, Jr, professor of surgery and chief, Division of Vascular Surgery and Endovascular Therapy at Emory University School of Medicine, Atlanta, USA, and co-principal investigator of the ANCHOR registry. "With minimal time added to the procedure, EndoAnchor fixation has been proven to enhance outcomes and durability, establishing a new treatment approach that addresses this critical patient need."

The FDA approval is supported by a short neck cohort of the ANCHOR registry, a global multicentre, multi-arm, prospective, post-market registry evaluating the real-world applicability of the Heli-FX EndoAnchor system. Led by co-principal investigators Jordan and Jean-Paul de Vries, chief of Vascular Surgery at St. Antonious Hospital in Nieuwegein, the Netherlands, outcomes from a sub-analysis of 70 patients with proximal AAA neck lengths <10mm down to 4mm who were treated with Endurant and Heli-FX demonstrated a technical success rate of 88.6%, based on delivery and deployment of the stent graft and each EndoAnchor implant used, and a 97.1% procedural success rate (investigator-assessed), with a rate of 1.9% proximal type Ia endoleaks at one year. Additionally, there was only one type Ia endoleak that resulted in a secondary procedure through one year.

At one year there were no AAA expansions or instances of main body migration and through one year, no instances of AAA ruptures. There was minimal EndoAnchor implant time added to the overall procedure, with an average of 17 minutes.

HyperMed Imaging announces US sales availability of HyperView

HyperMed Imaging is now selling its new HyperView imaging system to customers in the USA.

The HyperView system is US Food and Drug Administration (FDA)-cleared, and, according to a company press release, represents "a new standard of performance when assessing tissue oxygenation and perfusion in patients with potential circulatory compromise."

The HyperView is a handheld, battery operated, non-invasive and portable diagnostic imaging device that is used to assess tissue oxygenation without contacting the patient and without the need for injectable contrast. The system uses proprietary technology to capture colour-coded images containing data that provides the clinician critical information such as oxyhaemoglobin levels (Oxy), deoxyhaemoglobin levels (Deoxy) and oxygen saturation (O2Sat) in superficial tissue. Such information may assist clinicians when determining if a patient has adequate blood perfusion to heal a wound or maintain healthy tissue. Understanding both arterial and venous sufficiency in the surface tissue may enable clinicians to make more informed decisions regarding when to intervene, the company says. The HyperView system also helps document perfusion levels before and after vascular interventional procedures such as: peripheral bypass, stent placement, or balloon angioplasty.

HyperMed's vice president of sales, Annette Plishka, commented, "There are many important applications for this exciting new diagnostic imaging device in wound care, vascular intervention and reconstructive surgery."

HyperMed's president and chief executive officer, Mark Darty, added, "Early market feedback from customers has confirmed that HyperView is a game changer. It is a product poised to impact a number of important market segments. The low cost, speed, portability, ease of use and high-quality data and imagery provide clinicians a new class of tool to rapidly assess perfusion and locate ischaemic tissue. This information helps caregivers better understand potential circulatory compromise and allow more informed treatment of complications of vascular disease and diabetes."

Clinical News

Luminor EffPAC study shows efficacy at six months

Data have been announced demonstrating the efficacy of iVascular's Luminor drug-coated balloon (DCB) in patients with peripheral artery disease (PAD) at six months. The results from the full clinical cohort of the EffPAC randomised study were presented in the DCB session at the Cardiovascular and Interventional Radiological Society of Europe (CIRSE; 16-20 September, Copenhagen, Denmark).

Ulf Teichgräber, director of the Departement of Radiology of the University Hospital Jena, Germany, presented the new, primary endpoint late lumen loss and the clinical six-months results from the full cohort of the EFFPAC Randomized Control Study, demonstrating the effectiveness of Luminor DCB versus plain balloon angioplasty (POBA) in the superficial femoral artery (SFA).

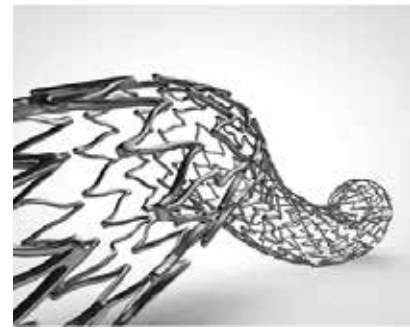
Primary and secondary endpoints were achieved with high statistical significance. Primary endpoint revealed a late lumen loss (LLL) of 0.14mm in the DCB group vs 1.06mm in the POBA group (p<0.001). Target lesions revascularisation (TLR) was 1.3% (DCB) vs 17.1% (POBA) (p<0.001). Primary patency was 94.7% (DCB) vs 75% (POBA) (p<0.001). Rutherford stages were overall improved for 85.2% patients (DCB) vs 75% (POBA) (p=0.021), and by 3 stages for 44.6% patients (DCB) vs 27.8% (POBA) There was no amputation nor any product related adverse event in the DCB group. "The comparison with other published randomised controlled trials underline that Luminor DCB demonstrates higher efficacy than most other available DCBs," according to an iVascular press release.

As stated by Teichgräber, "These incomparable outcomes are the result of the innovative coating technology of Luminor DCB, which is shown not only in the patency, LLL and TLR data, but also in significant improvement of patients' clinical status". The EffPAC trial enrolled 171 patients at 11 German centres who were randomised to treatment with either the Luminor DCB or PTA. The six-month data include a total of 153 patients (77 DCB and 76 PTA).

New Mimics data support use of the BioMimics 3D swirling flow stent in primary stenting of complex lesions

New significant outcomes from the Mimics study have been presented at the 15th annual conference on Vascular Interventional Advances (VIVA; 11-14 September, Las Vegas, USA). The data were presented by Thomas Zeller (Unversitaets Herzzentrum, Freiburg, Bad-Krozingen, Germany).

The BioMimics 3D vascular stent (Veryan) with unique helical curvature to generate swirling blood flow was evaluated in the Mimics study, which randomised 76 patients with symptomatic peripheral artery disease 2:1 to either BioMimics 3D swirling flow stent or LifeStent (Bard). A statistically significant difference was



observed in primary patency through 24 months (p=0.05) between BioMimics 3D and the straight stent control and in clinically-driven target lesion revascularisation between 12 and 24 months (p=0.03).

A post-hoc analysis was conducted to assess how performance of the BioMimics 3D stent was affected by the outcome-confounding factors of calcification, lesion length, occlusion and diabetes. The presence of target lesion calcification did not affect curvature of the BioMimics 3D stented segment nor the generation of swirling flow within. Kaplan-Meier survival estimates for freedom from loss of primary patency through 24 months in femoropopliteal segments treated with BioMimics 3D stents demonstrate independence from each of the confounding factors of severity of calcium, lesion length, occlusion and diabetes.

Zeller commented that the Mimics' randomised controlled trial data "support use of the BioMimics 3D swirling flow stent in primary stenting of complex lesions and point to potential for complementary use with drug-coated balloons".

Contego Medical announces ENTRAP Study initiation for Vanguard IEP peripheral balloon angioplasty system with integrated embolic protection

Contego Medical has announced the initiation of the ENTRAP Study evaluating usage of its Vanguard IEP peripheral balloon angioplasty system with integrated embolic protection in patients receiving peripheral angioplasty. The first cases with the device were performed by Ralf Langhoff (Sankt Gertrauden Krankenhaus, Berlin, Germany) with the first enrolled patient treated by Koen Deloose (AZ Sint Blasius, Dendermonde, Belgium). The Vanguard IEP system received CE mark in April 2017.

Contego says that the Vanguard IEP system represents the latest innovation of the company's Integrated Embolic Protection (IEP) technology, incorporating a peripheral angioplasty balloon and distal embolic filter on the same catheter. The system protects the lower limbs during angioplasty without the need for additional devices or exchanges. "The device is very straightforward and intuitive which makes handling simple and easy; no extra working steps at all," said Ralf Langhoff, following initial use.

The ENTRAP Study is a prospective, single-arm, multicentre study using the

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Vanguard IEP system and has been designed to evaluate acute safety and device performance. The study plans to enrol up to 130 subjects in centres throughout Belgium and Germany. Koen Deloose commented, "Visual debris was noted in the first cases I performed with the Vanguard IEP system, underscoring the need for embolic protection during complex femoropopliteal angioplasty."

Gardia Medical demonstrates enhanced safety in lower extremity interventions

Gardia Medical has announced that, according to the independent Clinical Events Committee (CEC), the company has successfully met the primary endpoint in its WISE-LE study.

The WISE-LE study's objective is to demonstrate the safety and performance of the Wirion EPS in subjects undergoing lower extremity atherectomy for the treatment of peripheral artery disease (PAD). The primary investigator of the Study is Bill Gray from Lankenau Heart Institute in Philadelphia, USA.

According to the IDE-approved study protocol, the primary endpoint for the WISE-LE performance-goal study is freedom from major adverse events (MAEs) to 30 days post-procedure. The performance goal was based on Covidien's DEFINITIVE LE and DEFINITIVE Ca++ trials. Currently, Covidien's SpiderFX in the only embolic protection system cleared for the lower extremity indication in the USA.

The study protocol specified enrolment of 153 patients with the primary endpoint successfully met if 18 (12%) or fewer MAEs occurred according to CEC adjudication. An interim analysis was performed at 100 patients and the study was stopped for success at interim given the single MAE versus the nine (9%) allowed for success.

Gardia is expecting to receive an atherectomy independent labelling that will cover use with all atherectomy devices. The SpiderFX, the only FDA-cleared EPD for the lower extremity indication is limited for use with a specific atherectomy device.

iVascular initiates TINTIN Luminor trial

iVascular SLU has announced the initiation of the TINTIN trial, evaluating the combined therapy of Luminor drug-coated balloon (DCB) and iVolution self-expandable stent.

The TINTIN study is prospective, investigator-initiated, non-randomised, multicentre trial, investigating the 12-month safety and efficacy of combined Luminor DCB and iVolution self-expandable stent in TASC C and D femoropopliteal atherosclerotic lesions.

"Both Luminor and iVolution have already demonstrated their safety and efficacy in previous studies" stated Lluis Duocastella, CEO of iVascular SLU. "The TINTIN trial is the next step to prove their combined benefit for the patient with the most complex lesions".

Koen Deloose (AZ Sint Blasius Dendermonde, Belgium), is the TINTIN trial principal investigator. Deloose enrolled the first two patients on 22 September. "We are excited to drive the first multicentre study evaluating the dual therapy DCB with bare metal stent in real-life TASC C and D lesions. Performing this with a drug-eluting balloon that has shown the best results in a randomised controlled trial as of today, and a self-expandable stent that has proven its efficacy in EVOLUTION trial, we expect outstanding results in the most challenging SFA lesions" Deloose said.

Shockwave Medical reports positive results for Lithoplasty in calcified lesions below the knee

Shockwave Medical has reported positive results from the DISRUPT BTK Study, which were presented at the annual Cardiovascular and Interventional Radiological Society of Europe congress (CIRSE; 16-20 September, Copenhagen, Denmark).

"The results of this study are consistent with findings from previous studies of Lithoplasty, showing a low rate of residual stenosis with minimal complications in a predominantly critical limb ischaemic patient population," said Marianne Brodmann, of the Medical University of Graz, Austria. "These results suggest that the Lithoplasty treatment has the potential to address challenges that calcified stenosis pose below the knee, where calcium is more prevalent and different than above the knee. It can occur deeper in the artery wall, making these lesions more difficult to treat. Treatment failure can pose heightened risks for patients with critical limb ischaemia, including higher risks of amputation and death."

DISRUPT BTK, a prospective single arm study, evaluated the use of the Shockwave Medical Lithoplasty system as a treatment for peripheral artery disease (PAD) patients with calcified lesions in arteries below the knee. The study enrolled 20 patients at three sites in Europe and New Zealand.

The study enrolled patients with moderate or severe calcified lesions in below-the-knee arteries, including 80% of patients who were classified as having critical limb ischaemia. Acute performance results showed low residual stenosis (27%) with low vascular complications, including no perforations, distal embolisation, reflow complications or abrupt closure and only one grade B dissection. There were no major adverse events including death, myocardial infarction, target limb revascularisation or amputation through 30 days.

The Lithoplasty system is designed to treat calcified leg artery blockages with lithotripsy, sonic pressure waves historically used to treat patients with kidney stones. The technology is now commercially available in both the USA and Europe for the treatment of calcified

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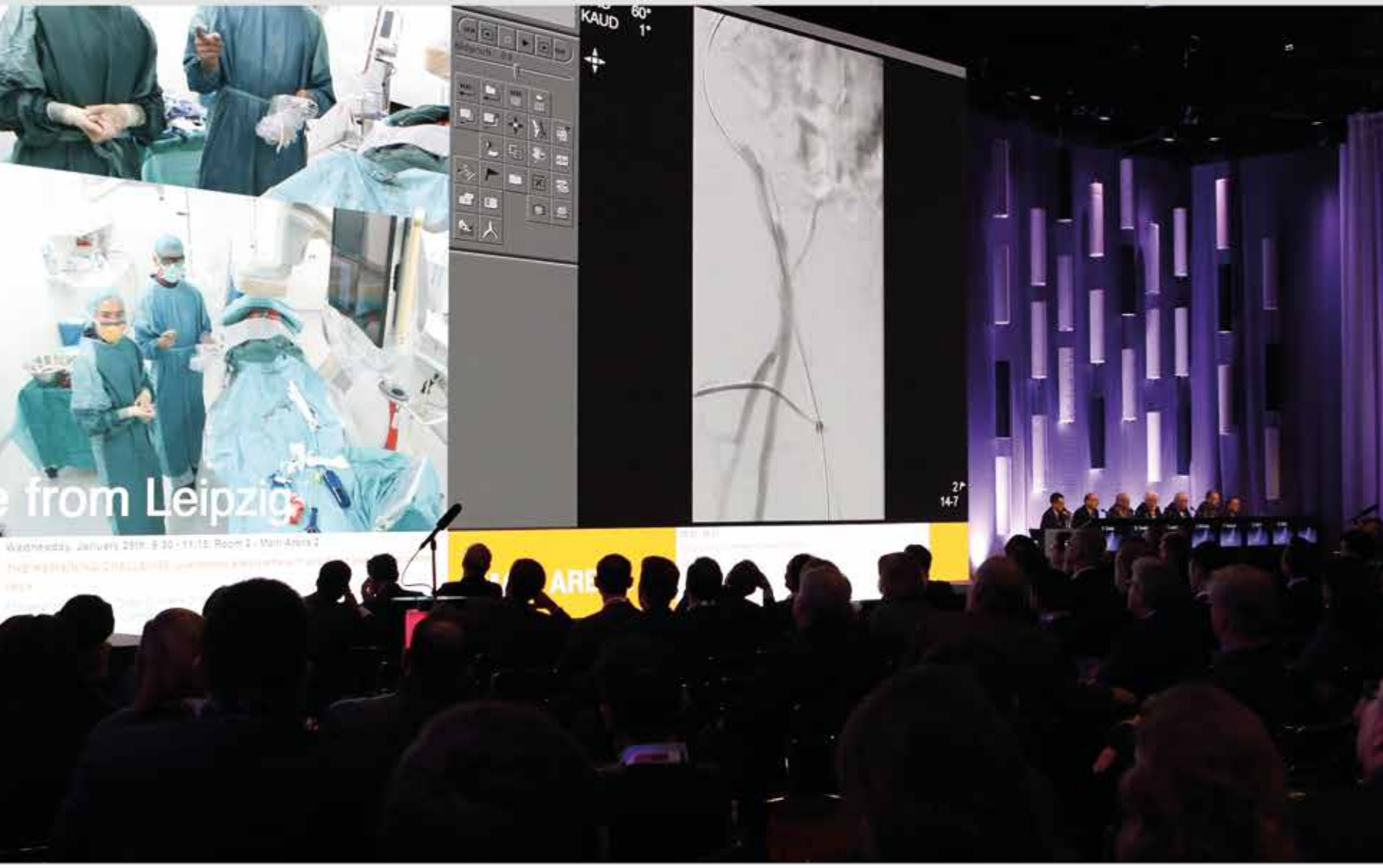

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Clinical News

plaque in peripheral arteries.

"Interventional procedures that involve moderate and severe calcium can be complex, unpredictable and costly. The previous DISRUPT PAD Study demonstrated that Lithoplasty addresses many major concerns in the treatment of problematic calcium in femoral and popliteal artery lesions, achieving a high acute gain in vessel diameter with minimal dissections, embolisation, perforation or recoil," said Doug Godshall, CEO of Shockwave Medical. "DISRUPT BTK now gives clinicians encouraging data in a high-risk patient population where calcific lesions pose different treatment challenges including the potential for limb loss."

InGeneron announces positive results from wound healing case series using regenerative cell technology

InGeneron has announced the publication of results from an investigator initiated case series in chronic leg wounds in the *Journal of the European Academy of Dermatology and Venereology*.

In the case series, InGeneron's proprietary adipose-derived regenerative cell (ADRC) technology was used for the treatment of chronic venous leg ulcers and mixed arterial-venous ulcers, the most common types of chronic leg wounds in the Western world, especially among elderly patients. Both conditions are associated with severe pain impairing quality of life and complex as well as time-consuming treatment regimes.

The case series was conducted in collaboration with the Department of Dermatology at the University Hospital rechts der Isar Munich, led by principal investigator Alexander Konstantinow, and was published in the Journal of the European Academy of Dermatology and Venereology. The publication is titled "Therapy of ulcus cruris of venous and mixed venous arterial origin with autologous, adult native progenitor cells from subcutaneous adipose tissue: a prospective clinical pilot study".

"Chronic leg wounds are associated with a complicated disease progression and severe pain, impairing quality of life. Current treatment options are complex, time consuming and require high medical expenses. New therapeutic interventions that improve outcomes in these patients could have an important therapeutic impact," said Konstantinow, senior physician at the Department of Dermatology and Allergology at Technical University Munich, Germany, and the primary investigator of the study. "The results that we have achieved in this case series are remarkable because we have been able to restore wound healing capabilities and decrease pain in multimorbid patients with large venous and mixed arterial-venous ulcers with a one-time minimally invasive application, while demonstrating a very good safety and tolerability profile. InGeneron's point-of-care system has the potential to benefit a large number of patients with wound healing disorders of vascular origin, while being more cost effective compared to currently available standards of care."

The case series comprised 16 multimorbid leg ulcer patients (12 male, four female) ranging in age from 52 to 84 years who were treated with autologous ADRCs prepared at point-of-care with InGeneron's Transpose RT system. Seven patients were presenting with venous leg ulcers, nine with mixed arterial-venous ulcers. Within 10 to 25 weeks, 11 out of the 16 patients showed complete wound closure. All seven venous leg ulcers patients showed complete epithelialisation. Moreover, the group of venous ulcer patients reported significant pain decrease by more than 90% 14 days post-treatment. After nine to 44 months of follow-up across all patients, no severe side effects were observed, demonstrating good overall safety and tolerability of the therapy in this patient population.

"This case series marks the next step in our journey to establish clinical evidence of how adipose-derived regenerative cells impact inflammation and pain as well as support healing in chronic wounds," said Ron Stubbers, President of InGeneron. "These encouraging results highlight the potential of our regenerative cell therapy approach in wound healing."

Based on the results of the investigator initiated study InGeneron plans to initiate a FDA feasibility study in the USA in the near-term. The prospective, randomised, single-site study will investigate the safety and tolerability of InGeneron's point-of-care regenerative cell therapy in venous leg ulcer patients.

First US patient treated with VentureMed Group's Flex

The first US patient has been treated with VentureMed Group's Flex scoring catheter. The catheter is used to treat patients with end-stage renal disease.

"Many end-stage renal disease patients receive many years or even decades of dialysis treatments," says John Pigott, founder and chief science officer at VentureMed Group. "This leads to the creation of arteriovenous fistulas or arteriovenous grafts, which are prone to re-interventions. The use of percutaneous interventions—such as thrombectomy, thrombolysis and/or angioplasty—have become universally included in dialysis treatment algorithms. A vessel-prep device…could potentially prolong the time between re-interventions."

Jose Vale performed the procedure at the OhioHealth Marion General Hospital in Marion, USA. "Vascular access is a haemodialysis patient's life line. Arteriovenous fistulas and arteriovenous grafts make haemodialysis treatments possible," Vale said after the procedure.

"Flex allowed me to successfully recanalise the patient's occlusion and there have been no reports of incomplete or suboptimal dialysis treatments from the dialysis unit," Vale explained. "Innovative technologies, like Flex, that potentially reduce overall procedure time, radiation exposure and allows for optimal results is a great option for this patient population."

First procedure performed in Rox Medical's CONTROL HTN-2 clinical trial

The first patient was treated in the CONTROL hypertension (HTN)-2 clinical study, the Rox Medical's pivotal study to evaluate the safety and effectiveness of the Rox Coupler used to create an arteriovenous anastomosis in the iliac vessels, in patients with high blood pressure.

A press release reports that the CONTROL HTN-2 study is a large, multicentre trial that will include up to 30 study sites in the USA. The first procedure was performed at Brookwood Baptist Health Princeton Baptist Medical Center in Birmingham, Alabama, USA, by Farrell O Mendelsohn.

Prior to CONTROL HTN-2, the press release notes, Rox Medical conducted a multicentre randomised trial in Europe. Patients treated with the Rox Coupler experienced a mean drop in blood pressure of 27mmHg which was sustained out to six months. A manuscript has been recently accepted for publication confirming a significant and durable pressure drop at one year.

The Rox Coupler and Flow procedure creates a passage between an artery and a vein in the upper thigh, which redirects a measured amount of arterial blood to the veins. This therapy is intended to reduce peripheral vascular resistance and add a compliant venous element to the arterial system through creation of a therapeutic arteriovenous anastomosis with the Rox Coupler.

Mendelsohn, the principal investigator for the research protocol, says: "Our entire research team at Cardiology, P.C. is excited about implementing this research study for our patients as the ROX Coupler technology may offer an alternative option to treat the global problem of uncontrolled hypertension."

Manta large bore vascular closure device to be evaluated in 500-patient European post-market clinical registry

Essential Medical has announced initiation of enrolment in a post-market clinical registry in the regions where Manta is commercially available.

Principal investigator Nicolas Van Mieghem, medical director of the Department of Interventional Cardiology at Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands stated, "Manta has quickly become our standard of care at the Thoraxcenter. In our experience, Manta proved to be safe, effective, and easy to use, but now it is time to confirm our results in a multicentre prospective study. We will be enrolling 500 patients in up to 20 centres from the Netherlands, Switzerland, Finland, Denmark, and Sweden."

Gary Roubin, chief medical officer of the company, stated, "We are excited to keep the momentum going with Nicolas Van Mieghem as we have just finished enrolment in our US IDE trial. We are confident these studies will continue to show that Manta will enable safer and more effective large bore closure with faster ambulation and discharge. Our goal is to show with even greater numbers that Manta will address the access site complications that continue to limit the advancement of large bore procedures because vascular closure technology has not kept pace with valve and stenting technologies."

Manta is a novel CE-marked vascular closure device designed to close punctures ranging from 10F to 25F at femoral arterial access sites after percutaneous cardiac and peripheral catheterisation procedures that use a large-bore device, such as transcatheter aortic valve implantation, endovascular aneurysm repair, ventricular assist device, and balloon aortic valvuloplasty. Manta is an investigational device in the US and Canada and is not yet commercially available.

The Manta device is CE marked and currently available for sale in the Netherlands, Norway, Finland, Denmark and Sweden. The company recently announced the completion of enrolment in its IDE study and expects to submit its PMA by the end of the first quarter 2018.

First patient enrolled in Frontier IV clinical trial of PerQseal large arteriotomy closure technology

Vivasure Medical has announced the successful enrolment of the first patient in the Frontier IV clinical study, a non-randomised multicentre international trial, designed to expand the indications of its proprietary PerQseal large arteriotomy closure technology. The patient was enrolled by Peter Crean (Blackrock Clinic, Dublin, Ireland).

Large arteriotomies (12Fr) are vessel punctures created to facilitate endovascular procedures such as transcatheter aortic valve implantation (TAVI), endovascular aneurysm repair (EVAR), balloon valvuloplasty, and ventricular assist devices. A press release reports that PerQseal is the world's first fully absorbable, patch-based large-bore percutaneous closure technology.

Christoph Naber (Contilia Heart and Vascular Centre, Essen, Germany), who is the TAVI principal investigator of Frontier IV, says: "Driven by clinical and economic outcomes data, percutaneous access-site management has become an increasingly important aspect of TAVI procedures. I strongly believe PerQseal, which is designed specifically to address large arteriotomies, will help improve outcomes for these patients."

"We are very excited to begin the Frontier IV trial as the next phase in our commitment to build the clinical experience with PerQseal. A percutaneous approach has now become the gold standard for procedures such as TAVR and EVAR, driven by clinical outcomes data. As patient volumes increase, access site management and closure has become an increasingly important aspect of complication and cost reduction. The data from this trial will be used to support our goal of expanding the indication range of the PerQseal technology," comments Gerard Brett, co-founder and CEO of Vivasure.

Industry News

BTG acquires Roxwood Medical

BTG today announces it has acquired Roxwood Medical, an innovative provider of advanced cardiovascular specialty catheters used in the treatment of patients with severe coronary and peripheral artery disease.

Roxwood's anchoring catheters (CenterCross, CenterCross Ultra, MultiCross) and microcatheters (MicroCross) offer options for physicians in the crossing of complex lesions and arterial blockages. By incorporating a self-expanding scaffold that stabilises the delivery of a guidewire, Roxwood's catheters provide positioning accuracy and support to facilitate the crossing of blockages, mitigating guidewire buckling and enabling treatments such as angioplasty, stenting or atherectomy.

BTG will pay up to US$80 million in cash to acquire Roxwood, comprising US$65 million paid on closing and up to an additional US$15m should certain future commercial milestones be achieved. The transaction is expected to be accretive to adjusted EPS from the second full year of ownership.

Shockwave Medical announces US$35 million in new financing

Shockwave Medical has reported US$35 million in new financing, an extension of the company's previously announced US$45 million Series C financing. New investor Fidelity Management & Research Company participated, along with certain funds and accounts advised by T Rowe Price Associates Inc, a returning investor.

Proceeds from the financing will be used to expand commercialisation and advance clinical development of the company's peripheral and coronary lithoplasty systems in the USA and Europe and to advance development of a program evaluating the technology as a potential treatment for aortic valve stenosis.

The peripheral lithoplasty system is an innovative therapy designed to treat calcified leg artery blockages with lithotripsy, sonic pressure waves historically used to treat patients with kidney stones. The technology is now commercially available in both the USA and Europe for the treatment of calcified plaque in peripheral arteries. In addition, the coronary lithoplasty system received CE mark earlier this year.

Lombard Medical announces restructuring and strategy to achieve profitability

Lombard Medical has announced completion of a restructuring following the implementation of its new strategy to focus sales efforts in the UK, Japan and China, and reduce operating and manufacturing costs in order to achieve cash flow breakeven in the near term.

The restructuring program is anticipated to result in a reduction of nearly US$12 million in operating expenses in 2018 when compared to 2016 expenditure levels; a reduction of more than 50%.

Lombard's strategic partnership with MicroPort Scientific is focused on two key areas: gaining CFDA regulatory approval for Lombard's endovascular portfolio in China and a significant reduction in material and labour costs. To that end, the parties have several collaborative initiatives and cost saving projects well underway. It is anticipated that based on this collaboration, Lombard will achieve industry standard gross margins within the next 24 months.

The parties intend to launch the Lombard abdominal aortic aneurysm products in China, distributed by MicroPort, following regulatory approvals currently anticipated before the end of 2018.

Endologix announces collaboration agreements with Japan Lifeline for development and commercialisation of thoracic endovascular systems in Japan

Endologix has signed a joint research and development agreement, as well as an exclusive distribution agreement, with Japan Lifeline (JLL) pertaining to the development and distribution of novel endovascular stent graft systems for the treatment of thoracic aortic diseases.

Under the terms of these agreements, the two companies will jointly invest in the development, clinical research, and commercialisation of the systems. JLL has exclusive distribution rights to the systems in Japan, and Endologix intends to commercialise and sell the systems through its existing global sales force and distribution partners in countries other than Japan. Endologix anticipates that the global market for thoracic devices could reach US$900 million by 2022, and represents a significant growth opportunity for the company.

Alvimedica obtains injunction by German court against sales of Microport drug-eluting stent featuring abluminal reservoir technology

The Court of Dusseldorf, Germany, has recognised in full the CID-Alvimedica rights on intellectual properties regarding the principles and related technology on drug release from a stent through reservoirs on the outer surface (abluminal reservoir technology) and issued an injunction against AB Handels GmbH, a dealer of Microport stent in Germany, which forbids with immediate effect any commercial action on any version of stent featuring the protected principles.

CID Spa, an Italian company, now member of Alvimedica Group, was the first company in the world to market a polymer-free drug-eluting stent (DES), and the first company to market a reservoir based DES. This knowledge, developed entirely in-house, offers interventional cardiologists the advantages brought by the combination of Co-Cr polymer-free platform, which is integrally coated by an anti-thrombotic ultra-thin pure carbon coating (Bio Inducer Surface), with the proprietary drug release system based on reservoirs on the stent's outer surface to ensure a prolonged and targeted drug release towards the vessel wall.

The above unique features are coupled with the Amphilimus formulation (sirolimus + fatty acid), another unique patented technology particularly effective in case of diabetes mellitus. In fact diabetic patient cells exhibit a resistance to standard "-limus" drug which results in lower efficacy. Cre8 and Cre8 EVO represent actually the only solution to this issue thanks to the role of fatty acid that acts as a permeation enhancer increasing the sirolimus drug intake into the cells, specifically in the diabetic patient, Alvimedica says.

Responding to the announcement from Alvimedica, a spokesperson from MicroPort said, "MicroPort categorically denies that A B Handels GmbH, the subject of the injunction, is MicroPort's distributor or dealer. MicroPort has no formal contractual relationship with and has never conducted business with A B Handels GmbH. MicroPort is actively investigating how A B Handels GmbH was able to obtain Firehawk product to sell in Germany without MicroPort's approval and any participatory role this entity has played in the granting of this injunction.

Getinge and Contego Medical announce European distributor agreement

Getinge has entered into a partnership with Contego Medical. Getinge will distribute Contego's products in Germany, France, Spain, Portugal, the UK, Netherlands, Belgium, Austria and Scandinavia, with the potential to expand into other territories.

Getinge will distribute the Paladin carotid post-dilation balloon system with integrated embolic protection and Vanguard IEPTM peripheral balloon angioplasty system with integrated embolic protection. Contego Medical's novel embolic protection devices coupling an angioplasty balloon with an integrated distal filter on the same catheter, enables more patients to benefit from embolic protection as compared to currently available methods.

Calendar of events

14–18 November
VEITHsymposium
New York, USA
Hilton Midtown
W veithsymposium.org

22–24 November
Vascular Society Annual Scientific Meeting
Manchester, UK
Manchester Central Convention Complex
W vascularsociety.org.uk

7–9 December
MAC—7th Munich Vascular Conference
Munich, Germany
Klinikum rechts der Isar
W mac-conference.com

17–20 January 2018
Southern Association for Vascular Surgery
Scottsdale, USA
The Westin Kierland
W savs.org

25–27 January 2018
CACVS—Controversies & Updates in Vascular Surgery
Paris, France
Marriott Rive Gauche and Conference Centre
W cacvs.org

30 January–2 February 2018
LINC—Leipzig Interventional Conference
Leipzig, Germany
W www.leipzig-interventional-course.com

4–6 March 2018
European Vascular Course
Maastricht, The Netherlands
W www.vascular-course.com

Featured Event
24–27 April 2018
Charing Cross International Symposium: 40 Years of Looking Forward
Olympia Grand
London, UK
W www.cxsymposium.com

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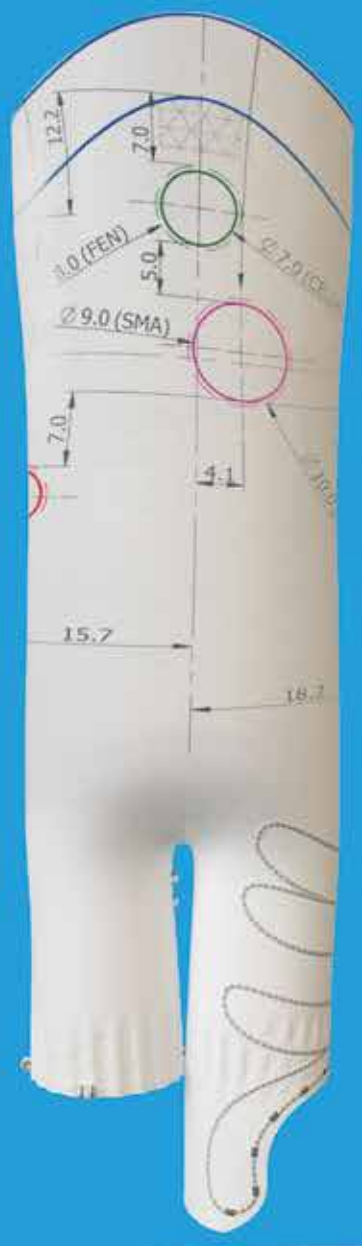

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