# LINC

# Review

2020

## LINC Review

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# Introduction

**The 16th Leipzig Interventional Course, held 28–31 January 2020, saw almost 5,000 participants fill the Trade Fair Leipzig in order to witness a renowned international meeting committed to advancing the scientific and clinical evaluation and treatment of patients with complex vascular disease through an interdisciplinary discussion of novel endovascular techniques.**

**Over four days, all in attendance were exposed to explorations of cutting-edge interventional practice, formed over a multidisciplinary programme of lectures, debates, trial updates, device innovations and expert-driven narrative. Of course, LINC also included dedicated "First-time data release" sessions, running throughout the programme, which offered the first glimpses of data from the latest important studies and technologies.**

**Live cases also featured in abundance, with satellite transmissions from Italy, Ireland, USA, France, Switzerland, as well as centres in Leipzig and across Germany. Ever engaging, and always exciting to watch, these cases placed a spotlight on the latest-and-greatest techniques, devices, tips and tricks, and demonstrated how to tackle challenging situations head on.**

**LINC also welcomed collaborators from leading vascular courses around the world, including: The Charing Cross (CX) Symposium, Vascular InterVentional Advances (VIVA); the International Congress of Interventional Surgery (CICE); the International Symposium on Endovascular Therapeutics (SITE); Complex Cardiovascular Therapeutics (CCT); the China Endovascular Course (CEC); the Japan Endovascular Treatment (JET) Conference; the VEITHsymposium; the Pan Arab Interventional Radiology Society (PAIRS); the German Society for Angiology/Vascular Medicine (DGA); as well as the online learning Vascupedia platform and the Aortic and Peripheral Surgery "How to do it" congress.**

**The *LINC Review* brings you just some of the highlights from the hundreds and hundreds of presentations, cases, discussions and debates that took place during the entire LINC 2020 meeting. For even more, we encourage you to head to the LINC website and dedicated LINC App to view a selection of key sessions, live cases and presentation slides.**

**Thank you to all delegates and industry sponsors for your continued support. We look forward to seeing you next year at LINC 2021, held January 25–30!**

## Contents

# Society and association accreditation

## LINC 2020 was accredited by:

The Sächsische Landesärztekammer with 21 cmE points.
www.slaek.de

The Swiss Society for Angiology with 20 Credits.
www.angioweb.ch

The Dutch Association for Vascular Surgery with 20 accreditation points in Category I.
www.vaat-chirurgie.nl

## LINC 2020 was endorsed by

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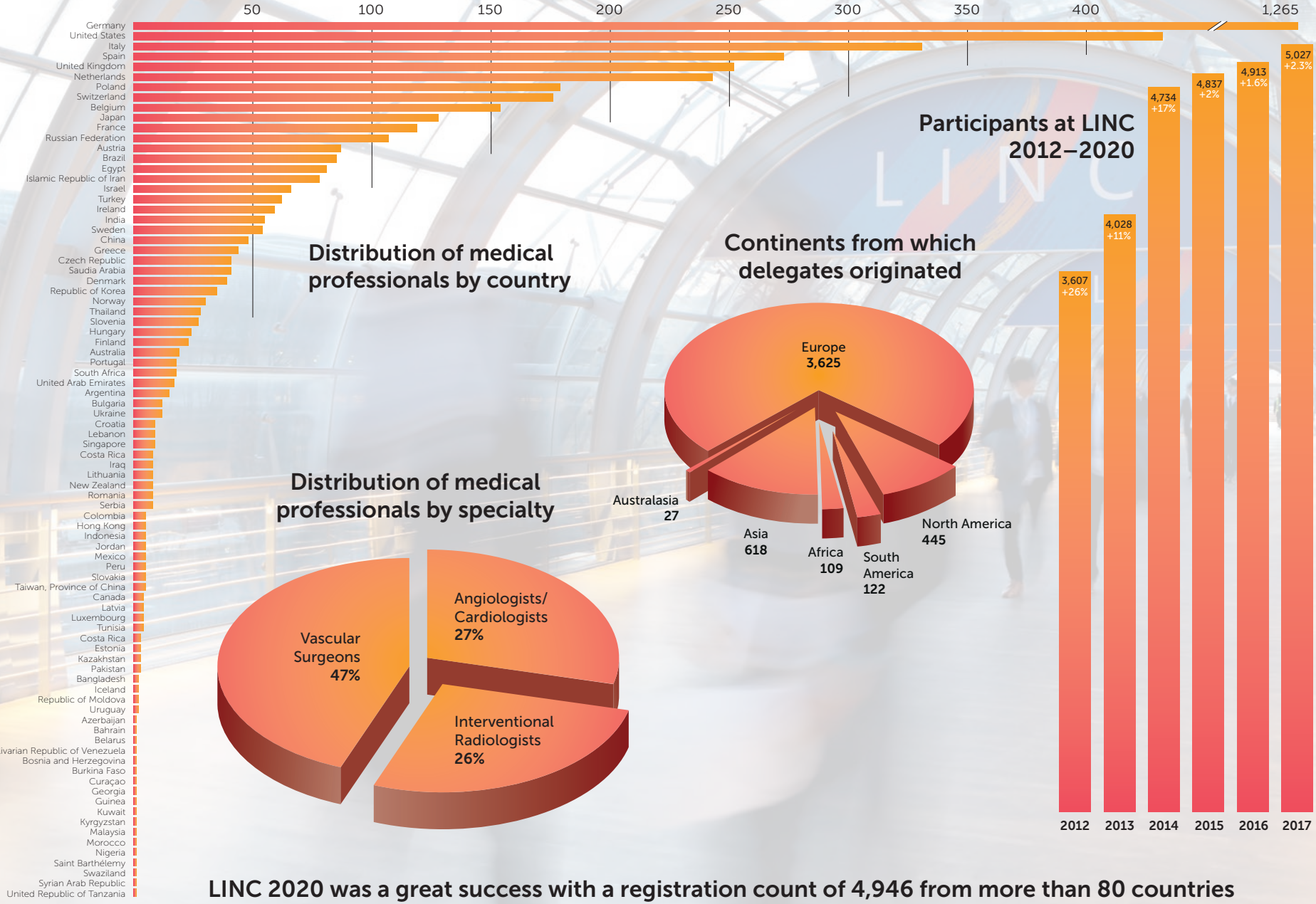
# LINC in numbers




## Distribution of medical professionals by country

## Continents from which delegates originated




## Distribution of medical professionals by specialty




## Participants at LINC 2012–2020




**LINC 2020 was a great success with a registration count of 4,946 from more than 80 countries**

# Independent analysis of Lutonix DCB

## Data reveals no plausible link between paclitaxel and mortality

Latest insights into the safety and efficacy of drug-coated devices took centre stage on the first day of LINC 2020, with a large proportion of the session dedicated to paclitaxel safety.

Speaking during the session was Kenneth Ouriel, Founder, President and CEO of Syntactx (New York, NY, USA), a full-service Clinical Research Organisation (CRO) that delivers high-quality clinical research services, including heading-up clinical trials for medical device and pharmaceutical companies.

"The need for a CRO is exactly what my talk is about because it is useful for medical device and pharmaceutical companies to have an independent assessor of data," Dr Ouriel told the *LINC Review* ahead of his presentation. "And the reason for that is more to do with perceived, rather that real, conflicts of interest."

In other words, CROs ensure that any perceived bias that people may have of company-sponsored trial data is put to bed via robust and independently verified analyses of datasets.

In his talk, Dr Ouriel presented in-depth independent safety analysis of the Lutonix (BD, USA) drug-coated balloon (DCB) – a 2 µg/mm$^2$ paclitaxel-eluting balloon catheter which has been extensively studied in the LEVANT 1[1], LEVANT 2[2] and LEVANT Japan[3] series of trials.

"Lutonix was the first DCB approved by the Food and Drug Administration in the US," said Dr Ouriel. "Approval was based on a rigorous preclinical and clinical scientific programme that demonstrated both safety and effectiveness."

The independent Lutonix analysis Dr Ouriel presented is in part a response to the questions raised about paclitaxel safety by the Katsanos *et al*. meta-analysis (2018) which found a late all-cause mortality signal for patients treated with paclitaxel balloons and stents.[4] As Dr Ouriel noted, Syntactx has since been doing an independent analysis of the Katsanos data as well – a task which has proven challenging indeed: "It's been a lot of work but it has been intellectually rewarding," he said.

"However, we haven't been able to figure out, when you have two groups of patients, one with an uncoated balloon and one with a paclitaxel-coated balloon, why there is a mortality signal? Some of the smartest people in the field have been asking the same question. There definitely is a signal there, but not a single clinician that I know believes that it's related to the small amount of paclitaxel which is found on the balloon.

"Most of us, myself included,

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*"There is no significant increase in the hazard ratio for mortality in any analysis of the Lutonix DCB, nor any plausible mechanism for mortality or evidence of paclitaxel causation."*

**Kenneth Ouriel**

believe that it's probably related to some facet of trial design – more than likely due to missed follow-up visits (that are not at random). As we work towards more complete follow-up on virtually every patient, the mortality signal almost disappears once the vital statistics on patient survival become clear."

Indeed, several of the trials from leading manufacturers that fed into the meta-analysis had patients lost to follow-up, noted Dr Ouriel, which could have impacted the apparent mortality signal observed. Not least, he added, given that follow-up was different for the DCB cohorts versus non-DCBs.

Crucially, patient-level data was not included in the Katsanos *et al*. meta-analysis, leading many to question if differences in follow-up care in DCB versus percutaneous transluminal angioplasty (PTA) comparators could be driving at least some of the mortality signal.


Focusing back on Syntactx's independent analysis of Lutonix data, Dr Ouriel relayed that patient-level data was used to compare safety outcomes from 1,093 Lutonix and 250 PTA patients across the LEVANT series of trials, including the LEVANT 2 Continued Access cohort – enrolled specifically to assess paclitaxel safety.

"We utilised additional statistical methods to assess the data, including propensity adjustment when pooling the data from the Continued Access cohort," noted Dr Ouriel. "This is an appropriate way to remove the bias associated with differences in the make-up of patient groups that are not from the same RCT. We also performed time-dependent analyses to account for factors that change over time, and performed multivariable analyses to identify key predictors of mortality."

Cutting to the chase with regards to whether any mortality signal could be seen with the Lutonix data, Dr Ouriel asserted that, of the 173 deaths seen in the LEVANT 1 and 2 datasets, no deaths were classified as related to paclitaxel based upon the known side-effects of the drug. "Mechanistically, if paclitaxel caused death, there should be a disproportionate frequency of mortality in one category or a group of related categories," explained Dr Ouriel. "That was not observed. Thus, without clustering of death within a category, causation is not supported."

Staying on the topic of causality, Dr Ouriel underlined the importance of using Bradford Hill criteria – a nine-point system that explores epidemiologic evidence of a causal relationship between a presumed cause and an observed effect. Criteria span consistency, strength of effect, specificity, plausibility, coherence, biological gradient (dose response), coherence, temporality (does mortality increase following index procedure?) and analogy (could the effects be due to immunogenic particulates?).

Save for the last two criteria (temporality is present, and particulates have been implicated in other situations), the rest of the criteria can be ruled out, commented Dr Ouriel: "The absence of seven of the nine criteria is consistent with association, but not causation."

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# Independent analysis of Lutonix DCB

*"People have felt reasonably comfortable going back to using paclitaxel devices, although I'm sure the market isn't anywhere near what it was before."*

**Kenneth Ouriel**

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He went on to explore whether there were patient or treatment-related variables associated with increased risk, i.e. is there a plausible mechanism for mortality associated with paclitaxel – or with any other biological feature of DCB treatment – even through some unknown mechanism?

Using a propensity-adjusted multivariate analysis of mortality out to five years in the LEVANT 2 data, Dr Ouriel and colleagues identified several variables as predictors of mortality, including age, Rutherford category, left limb, diabetes, anticoagulants at discharge and prior treatment. However, these variables were shown to be predictors of mortality irrespective of treatment arm, i.e. DCB or PTA, thus superseded paclitaxel as predictors of outcome.

As such, the burning question remains: "Is there a relationship between additional exposure to paclitaxel and risk of mortality?" said Dr Ouriel.

Looking at the LEVANT 2 RCT and Continued Access data, the effect of initial paclitaxel dose on survival was analysed in four dose groups: > 0 to ≤ 2 mg; > 2 mg to ≤ 3.5 mg; > 3.5 mg ≤ 5 mg; and > 5 mg. "No significant dose-response relationship was identified," commented Dr Ouriel, adding that when adjusting for age – the most significant predictor of mortality in both DCB or PTA groups – no identifiable dose-relationship could be seen.

We also looked at the effect of subsequent interventions with paclitaxel devices, which increases drug exposure," continued Dr Ouriel. "Some of the other analyses that have been reported did not account for reinterventions. Almost 20% of subjects in the LEVANT 2 RCT were treated with a paclitaxel device at some point during their five-year follow-up.

"Subjects in both groups, DCB and PTA, who subsequently underwent an intervention with a paclitaxel device had higher five-year survival rates than those that did not. This finding was confirmed in our other studies, and would be counter-intuitive if additional paclitaxel exposure is indeed harmful in the long-run.

"It should be noted that the mortality rate in both the PTA and DCB groups in the LEVANT 2 study was lower than that of the PAD population as reported in the Swedish Vascular Registry (Sartipy *et al*. 2018) at five years."

What this boils down to is that subjects in clinical trials may do better with additional clinical management, said Dr Ouriel, while reducing subsequent interventions is beneficial for patients, it also reduces additional "touch points" with health care providers.

Commenting on the outlook for paclitaxel, Dr Ouriel noted that as more data is added into analyses, the proposed signal for mortality using paclitaxel becomes even weaker, thus he is optimistic that the reputation of paclitaxel will recover. "People have felt reasonably comfortable going back to using paclitaxel devices, although I'm sure the market isn't anywhere near what it was before," he said.

"I think this has really impressed upon people that you do need complete follow-up beyond the primary endpoint, especially given the primary endpoint for many trials was a year or less. Even though the primary endpoint is earlier, people are pretty much doing five-year trials now in the lower extremities."

He concluded: "There is no significant increase in the hazard ratio for mortality in any analysis of the Lutonix DCB, nor any plausible mechanism for mortality or evidence of paclitaxel causation. Based on all of our analyses to date in a large dataset, the Lutonix DCB continues to offer meaningful benefit relative to risk in indicated patients."

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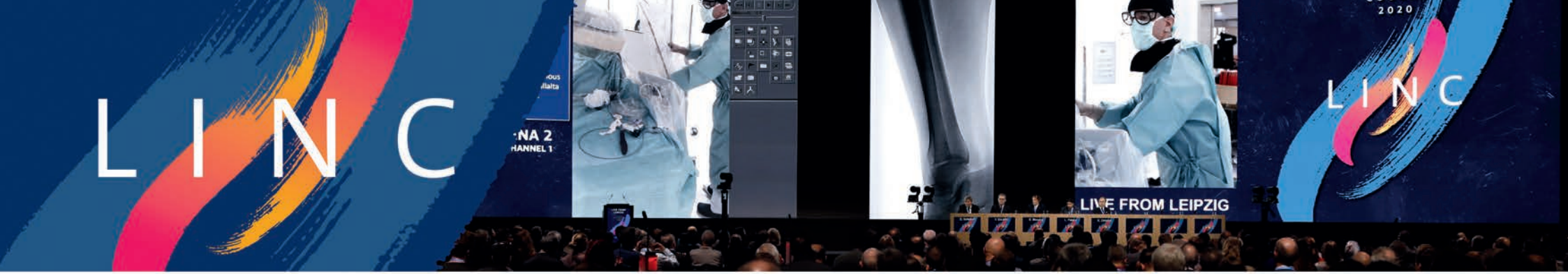


# Don‘t miss LINC LIVE webinars!

## Starting on 26 August 2020, 16:00–17:30 CET, the LINC Organisers will start a series of webinars with live case transmission from leading interventional sites.

**Key topics:**

- Treatment strategies for critical limb ischemia and BTK disease
- Treatment of challenging femoropopliteal CTOs
- Management of multilevel disease
- Differential utilisation of drug-eluting devices (DES/ DCB)
- Strategies for optimal vessel preparation and debulking
- Utilisation of covered stents for complex aortoiliac disease
- AV-access related interventions
- Venous interventions
- Latest techniques in endovascular aortic repair for challenging aortic lesions

**Learning objectives:**

- To discuss treatment strategies for complex peripheral vascular pathologies based on the patient specifics shown in the live case
- Review of latest data on available technologies in short presentations
- Review of specific techniques and alternatives in short presentations
- Discussion of all aspects with the panel of experts
- Discussion of questions raised by audience with expert panel and live case operators

***Don‘t miss the upcoming webinars on 26 August, 2 September, 9 September, 16 September, 23 September, and 28 October!***

**For more information and new webinars visit our website at: www.leipzig-interventional-course.com**
**Course Organisation: www.cong-o.com**

# ARIVA trial updates on anticoagulation after venous stenting

An eagerly awaited update from the Aspirin® Plus Rivaroxaban Versus Rivaroxaban Alone for the Prevention of Venous Stent Thrombosis in Patients With PTS (ARIVA) trial was showcased at LINC, giving all in attendance an insight as to what to expect from the multicentre study being conducted in sites in Austria, Germany and Switzerland.

Running through the details of the trial was Oliver Schlager, a medical interventionalist from the General Hospital and Medical University in Vienna, Austria. Dr Schlager, who specialises in patients with a range of chronic conditions from chronic post-thrombotic venous occlusion to non-thrombotic iliac vein lesions (NIVL), is principal investigator (PI) for the Austrian portion of the trial. The German PIs will be Christian Erbel, Houman Jalaie and Michael Lichtenberg, and Nils Kucher from University Hospital, Zurich, Switzerland is the overall PI.

ARIVA is an investigator-initiated academic trial whose primary aim is to assess different anticoagulation regimes after venous stenting in patients with chronic post-thrombotic venous lesions. "People who undergo endovascular revascularisation and venous stenting will be randomised to receive either anticoagulation-only therapy [rivaroxaban] or to receive the anticoagulant in combination with aspirin," explained Dr Schlager.

The primary outcome of the trial is patency at six months, i.e. without the occurrence of either occlusion of at least a part of the stent segment or a re-intervention to maintain patency of the treated segment.

What's important about ARIVA, noted Dr Schlager, is that it is the first trial of its kind. "To date we do not have any prospective randomised controlled studies on antithrombotic or anticoagulant treatment in patients after venous stenting," he said. "Therefore, it's very important to start this study as soon as possible."

What's apparent is that while a range of anticoagulants are used after venous stenting, there is no clear evidence on which works better. Indeed, Dr Schlager cited an interesting electronic survey conducted in the UK several years ago[1] in which medical experts were asked what anticoagulation treatment or antithrombotic treatment they would recommend after venous stenting, and the results were analysed to achieve a Delphi consensus.

*"ARIVA is very important because to date we do not have any prospective randomised controlled studies on antithrombotic or anticoagulant treatment in patients after venous stenting."*

**Oliver Schlager**

But the survey revealed that amongst experts in the UK, between 10 and 15 different anticoagulation regimes were used after venous stenting, noted Dr Schlager. Of the 106 experts, a third chose life-long anticoagulation with a vitamin-K antagonist (VKA), 19% chose life-long anticoagulation with a direct oral anticoagulant (DOAC), 7% used antiplatelet therapy (APT) following stent placement alone and 13% used APT in combination with an anticoagulant. "What was interesting in this publication was the variety of different treatment regimes after venous stenting," said Dr Schlager.

"This underlines the need for a large multicentre prospective randomised controlled study which will give us information on which treatment regime is best and could be recommended in patients."

Back then, the authors of the survey wrote that although a number of studies have focused on technical factors associated with stent occlusion, there is a paucity of research examining the role of antithrombotic therapy in maintaining stent patency. They also commented that there were no controlled studies that previously investigated the use of anticoagulants or antiplatelet agents following venous stenting.

Today there are still several single-arm studies that assess the use of different venous stents, and patients within these studies receive anticoagulation after venous stent placement, but most are driven by venous stent companies. "None of these studies specifically address the anticoagulation regime after venous stenting," said Dr Schlager. "Existing single-arm studies focus on the stents but not on the accompanying medical treatment, which is absolutely necessary."

There are three major factors

impacting on the patency of venous stents, said Dr Schlager. One is the type of lesion – either chronic post-thrombotic, acute thrombotic, or non-thrombotic, while the second lies in haemodynamics. "This is more about the inflow coming from the veins below the inguinal ligament, which has to be granted through stent patency after stent placement," he said. "But the third most important factor, of course, is the anticoagulation treatment, for which there is no study so far."

That's why there is a need for collaboration amongst different specialties, Dr Schlager went on: "Anticoagulation treatment is a key issue for stent patency after venous stenting. The interventionalist should either be familiar with different anticoagulation regimes by themselves or should cooperate with angiologists and haematologists who are able to take care of the anticoagulation regime."

During his presentation, Dr Schlager stepped outside of the ARIVA trial to address other new research into anticoagulation. For example, a study conducted by Tim Sebastian at the University Hospital Zurich, which was published last year, looked at the duration of anticoagulation following stent placement.[2] "This is an interesting study into patients who received anticoagulation treatment for a limited period, and patients who received anticoagulation for an extended period after stent placement," said Dr Schlager.

*"Anticoagulation treatment is a key issue for stent patency after venous stenting."*

**Oliver Schlager**

"What he showed is that there was no significant difference in patency between patients who received anticoagulation for a limited period in comparison with patients who received anticoagulation for an extended period."

Of course, the study was a retrospective analysis rather than a prospective randomised control study, noted Dr Schlager. "It was a nice study, but it shows how important the ARIVA trial is."

In his concluding remarks, Dr Schlager reiterated that going forward there is a clear need for many more randomised controlled trials looking at the different anticoagulation therapies on offer. "I think that we need more prospective randomised controlled studies after venous stenting, and the ARIVA trial will help us to get this information," he said in closing.


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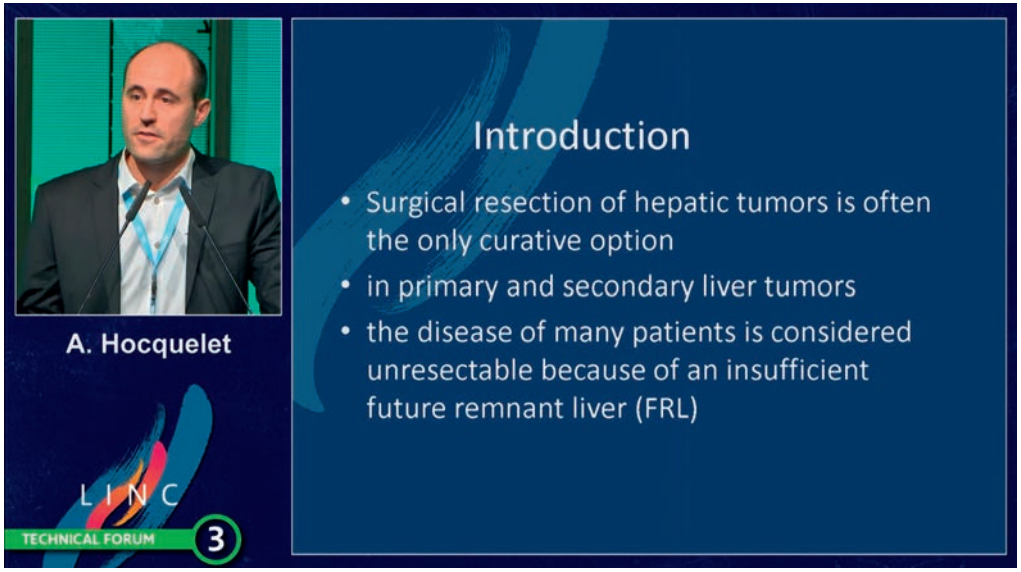
**The ARIVA trial is planned for completion in August 2022.**

# Preoperative portal vein embolisation in liver cancer

## The three cornerstones of good patient selection




Arnaud Hocquelet (CHUV, Lausanne, Switzerland) discussed indications and patient selection in preoperative portal vein embolisation (PVE).

Dr Hocquelet told audiences that surgical resection of hepatic tumours is often the only curative treatment for large primary tumours or for patients with several small secondary tumours. However, for many patients, their tumours are considered unresectable because of insufficiency of future remnant liver (FRL).

PVE serves as a potential remedy to this issue. It leads to a redistribution of flow and has been shown to induce local hypertrophy of the liver[1]. "The indication of PVE is to increase the FRL volume before resection," explained Dr Hocquelet, "In order to increase surgical margin and to improve postoperative liver function."

He outlined the three cornerstones of PVE that underpin good patient selection. The first is the type of intervention. "You have to talk with your surgeons about the amount of liver to be resected during the intervention, and the margin required. It is not the same if you are going to treat a large anterior hepatocholangiocarcinoma of 7 cm, or several small metastases of around 1 cm in the liver. Also, you have to discuss the complexity of the surgery. Indeed, a prolonged liver ischaemia period from vessel clamping is a risk factor of postoperative liver failure."

The second cornerstone, continued Dr Hocquelet, is the FRL volume percentage of total liver volume. He cited the work of Yiglitler *et al*. (2003), who identified a more difficult postoperative course in those patients left with a smaller FRL[2]: "There is a strong correlation between the amount of the liver after surgery and the overall morbidity. Under 30%, your rate of morbidity is around 50%. This correlation is well-known in several studies."

Dr Hocquel*et al*so noted more recent research demonstrating how combining the albumin-bilirubin score (the ALBI score) with FLR predicts post-hepatectomy liver failure[3]. Before major liver resection, the FRL volume can be calculated according to the equation: *FRL% = FRL / (whole functional liver volume, excluding tumour)*, where the usual cutoff is > 30% for the healthy liver, and 40% for others.

*"Now we have a cheap, fast and accurate method of assessing liver function – hepatobiliary scintigraphy."*

**Arnaud Hocquelet**

"To accurately assess your FRL, you need a good quality contrast-enhanced CT scan with hepatic vein visible, in order to perform segmentation using automatic, semi-automatic or hand-free methods – depending on what software you have available in your centre.

"One interesting thing is that a very small left lobe (< 10%) should not be considered a contraindication for PVE. Indeed, there is a very strong correlation between a small initial size of the FRL and a high degree of hypertrophy[4]."

The last cornerstone is the FRL function. "Volume is not function, it is very important to understand that," stressed Dr Hocquelet. "Obviously, for a cirrhotic patient, everybody thinks about liver function. But for a young patient receiving intra-arterial oxaliplatin, on CT you can find signs of portal hypertension without cirrhosis. This is an SOS: it should alert you about liver function. Now we have a cheap, fast and accurate method of assessing liver function – hepatobiliary scintigraphy. In our centre, we use the cutoff of 2.69 mm/min/kg for the FRL, to allow surgery.

"'Volume is not function' is true before any intervention. In one study, they found very weak correlation between liver volume and liver function[5]. This is also true after PVE. After PVE, you will observe an increase in volume, but you will have a bigger increase in function. But after ALPPS [Associating Liver Partition and Portal vein Ligation

for Staged hepatectomy] – the surgical alternative to PVE – at two weeks you will have a very strong increase in volume but no increase in liver function. If you have the volume but not the function, you will have postoperative liver failure."

He concluded: "PVE is here to improve surgery quality by improving margins, to improve postoperative outcomes by avoiding liver failure, and to bring curative treatment to unresectable patients.

"To do that, you need to talk with your surgeons, have a good CT to assess liver volume, and you have to assess liver function using hepatobiliary scintigraphy. Of course, you have to avoid treating patients with contraindications."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# Deep vein thrombosis and EKOS™

## Interventional treatment to minimise post-thrombotic syndrome and maximise outcome

Maximal reduction and treatment of post-thrombotic syndrome (PTS) by optimal interventional treatment of deep vein thrombosis (DVT), together with the safety and efficacy of EKOS™ Acoustic Pulse Thrombolysis™ treatment were the first two topics under discussion at a symposium led by BTG, now a part of Boston Scientific.

Nils Kucher (University Hospital Zurich, Switzerland) chaired the event and gave a presentation addressing how to optimise reduction in PTS numbers when treating acute DVT interventionally. He was joined by colleagues Mert Dumantepe (Acibadem University School of Medicine, Istanbul, Turkey) who discussed the treatment of femoral PTS with EKOS™, and Stefan Stortecky (Swiss Cardiovascular Centre Bern, Switzerland) who reported his centre's data on the treatment of high-risk and intermediate high-risk pulmonary embolism (PE).

Professor Kucher emphasised that interventional treatment of acute iliofemoral DVT may lead to primary patency of over 95%, and freedom from PTS of over 90% at three years, if proper patient selection and procedural/post-procedural management are performed.

Referring to data from the past three years from centres in Bern and Zurich, as collected in the Swiss Venous Stent Registry (SVSR), Professor Kucher shared his experience of the interventional treatment of acute iliofemoral DVT with venous stenting. Together the centres have treated 160 patients, comprising more women than men, with an overall mean age of 48 years old. Most (78%) DVTs were on the left side, and mainly due to May-Thurner syndrome. "I want to highlight that 16% had varicose veins as a risk factor, and already had chronic venous insufficiency. This is why the Villalta score is inappropriate in clinical trials because many patients already have increased Villalta scores," remarked Professor Kucher.

Of those treated, 44% underwent catheter-directed thrombolysis (CDT) – either EKOS™ or conventional, 21% were treated in a single session (Angiojet ZelanteDVT™ thrombectomy catheter, Boston Scientific), and the mean number of stents deployed was 1.7. "We are shifting towards single session treatment in the majority of patients now," said Professor Kucher.

*"If you're treating a patient with iliofemoral DVT, there really shouldn't be anyone with moderate or severe PTS if it's a first-time DVT and they have no chronic venous insufficiency."*

**Nils Kucher**

Primary patency rate at three years was 79.4% (CI 95% [71.7, 87.1]) with the majority of stent failures occurring early on. Assisted primary patency was 84.9% (CI 95% [78.1, 91.7]), and secondary patency at three years was 95.6% (CI 95% [91.8, 99.4]). "We did not give up if someone needed a secondary intervention because a stent became occluded. At three years almost all patients had patent stents," added Professor Kucher.

Villalta scores showed that 90% of patients had no PTS at three years, and 9% had mild PTS. Professor Kucher went on: "Two patients had higher scores. These patients had severe chronic venous insufficiency at baseline; one had an active ulcer at the time of DVT. You cannot improve the Villalta score in such a patient. If you're treating a patient with iliofemoral DVT, there really shouldn't be anyone with moderate or severe PTS if it's a first-time DVT and they have no chronic venous insufficiency."

Professor Kucher then addressed the differences between the major trials in the area: the Swiss Registry, ATTRACT and CaVenT. "Why did these trials fail so badly?" he asked.

"All of our patients [in the Swiss Registry] had descending iliofemoral DVT, and by comparison CaVenT and ATTRACT had 48% and 57%, respectively. The remainder were ascending femoropopliteal DVTs but these should not be touched – they need blood thinners.

"Also, 21% of our patients had single session treatment compared to 0% in CaVenT, and


an unknown number if ATTRACT. CDT first was used in 79% of our patients versus 100% and 59% in CaVenT and ATTRACT."

He added that 100% of patients received a stent, compared to 17% and 30% respectively in CaVenT and ATTRACT, noting: "I wonder how many patients in ATTRACT had spontaneous flow at the end of the procedure – not many I think."

Professor Kucher summarised what he felt was key to success with respect to diagnosis for descending DVT. "Colour Duplex [ultrasound] with calf compression is the only reliable imaging technique to identify the distal thrombus extent," he said. "If the popliteal cannot be compressed then it might not be thrombosed, and if it is not thrombosed then a descending iliofemoral DVT is confirmed."

*"Our results showed that 75% of patients reached the primary endpoint."*

**Mert Dumantepe**

Regarding his procedural recommendations, among the key criteria listed by Professor Kucher were: popliteal access with ultrasound guidance, deciding whether to use CDT first, or single session thrombectomy; diagnosing compressed iliac veins using venographic criteria; and using intravascular ultrasound (IVUS) in cases where venography is equivocal.

Post-procedure he recommended oral anticoagulation for at least three months, and no platelet inhibitors; oral anticoagulants stopped at 3–6 months in May-Thurner syndrome cases; while Duplex surveillance and Villalta scores need to be carried out at 2 weeks, 3, 6 and 12 months, and then annually.

Following Professor Kucher, Dr Dumantepe took to the podium and discussed how endovascular intervention using EKOS™ with Acoustic Pulse Thrombolysis™ treatment is safe and effective for patients suffering from femoral PTS.

He referred to his single-centre experience where they included over 200 patients with symptomatic femoropopliteal DVTs with more than six months of complaints who had failed on conservative therapy and had a Villalta score greater than eight.

The primary efficacy endpoint was reduction in Villalta score of over six points at day 30 versus baseline, and increased blood flow in the relevant segment. The primary safety endpoint was major bleeding within 72 hours of starting the procedure and incidence of PE within 30 days post ultrasound-assisted, catheter-directed, low-dose thrombolysis (UACDT).

A total of 202 femoropopliteal PTS patients were included with

Continued on page 16

# Deep vein thrombosis and EKOS™

*Continued from page 15*

mean DVT age of 27.1 months, and with mean dose/duration of tissue-type plasminogen activator (tPA) of 23.3 mg and 22 hours, respectively.

"Our results showed that 75% of patients reached the primary endpoint [p < 0.001]," reported Dr Dumantepe. "We only saw two major bleeding events, and nine recurrent DVTs. Doppler showed that patency was around 90% for each segment, and similar at one year."

He also highlighted the importance of freedom from ulceration: "We saw a 91% ulceration healing rate. Washout [time to washout of the femoral vein] also significantly improved after EKOS™ treatment for second day. Villalta score also showed improvement of 10.2 points from baseline at 360 days, while venous clinical severity score (VCSS) score showed a reduction of 8.1 points from baseline at 360 days. Quality of life scores also improved by 21.3 points on the VEINES scoring system."

After presenting a couple of case studies from his centre in Istanbul, he closed his presentation with a call to action. "The ACCESS PTS treatment protocol reduces PTS scores, that is Villalta and VCSS, improves quality of life, and these benefits have persisted for 365 days so far," said Dr Dumantepe. "It's time to stop saying nothing can be done."

Last on the stand was Professor Stortecky who discussed treatment of high-risk and intermediate-risk PE with Acoustic Pulse Thrombolysis™. He familiarised the audience with the EKOS™ system, explaining that it uses targeted ultrasonic waves in combination with clot-dissolving drugs. The system uses a sophisticated catheter and an ultrasonic core to effectively target an entire clot, along with fibrin separation and active drug delivery into the clot by acoustic streaming.

Professor Stortecky said the PE response team treated three-quarters of patients with EKOS™ . "Some received medical therapy, some surgical thrombectomy but very few received systemic lysis," he said. "In fact, the vast majority of patients received EKOS™ in the intermediate- and high-risk patient groups."

He referred to the ULTIMA trial led by Nils Kucher, the primary endpoint of which was reduction in the right-to-left ventricle diameter (RV/LV) ratio. Results showed that the combination of EKOS™ and heparin led to a ratio of 0.3, versus 0.03 in those patients on heparin alone over 24 hours.[1]

"There was also a significant difference seen between the heparin plus EKOS™ versus heparin alone at 90 days," noted Professor Stortecky. "There was a small and statistically non-significant increase in minor

*"You can rest assure that EKOS™ will not interfere with your procedure."*

**Stefan Stortecky**

bleeding, but you can rest assure that EKOS™ will not interfere with your procedure."

The SEATTLE II single-arm study[2] in 150 patients (31 massive PE, 119 sub-massive) showed the RV/LV ratio was significantly decreased over 48 hours, as well as the mean pulmonary artery systolic pressure continuously decreased up to 48 hours. No patients had intracranial haemorrhage and there were very low rates of major bleeding events, added Professor Stortecky.

The protocol for EKOS™ in the SEATTLE II study involved patients having symptoms less than 14 days due to massive or sub-massive PE, and a RV/LV diameter of > 0.9. The PE was confirmed by CT scan. UACDT was used with a total tPA dose of 24 mg. Outcomes included a 25% decrease in CT-measured RV/LV diameter ratio over 48 hours, a 30% decrease in pulmonary arterial systolic pressure by procedure end and a 30% decrease in pulmonary angiographic obstruction over 48 hours, without any intracranial haemorrhage.

Moreover, the OPTALYSE Trial was able to show that also very low doses of tPA over a very short treatment period was able to effectively decrease RV/LV ratio. Indeed, a tPA rate as low as 1mg/hour/catheter over a 4 hour treatment period was able to significantly decrease RV/LV ratio by 0.35 and was as effective as a higher dose regimen. Based on the data, it is likely that EKOS™ is also effective in reducing RV/LV ratio with even lower dose tPA regimens and shorter treatment times, Professor Stortecky concluded.

Optimising the reduction in PTS numbers when treating acute DVT interventionally, or treating PE with EKOS™, these results serve to further reinforce the benefits of using ultrasound-assisted CDT and add to an increasing wealth of evidence to support its growing use.

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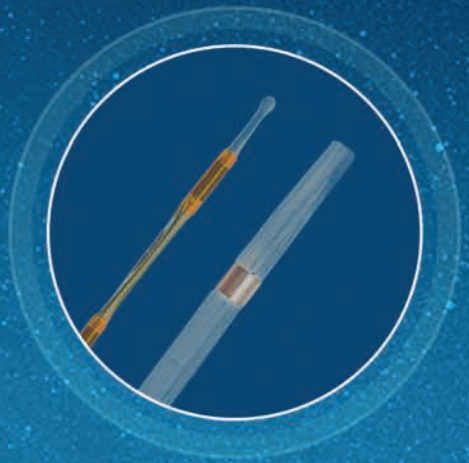

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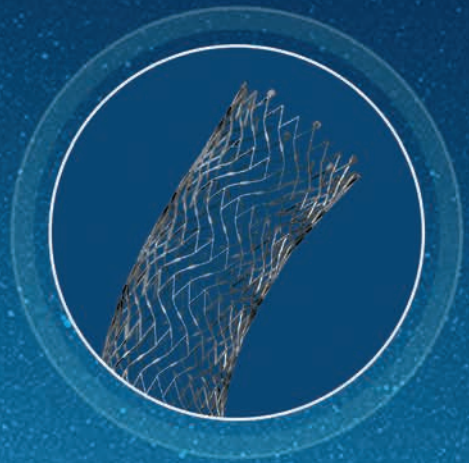

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# ‘Incredible efficacy’ of DES treatment in long BTK lesions

During an update on clinical trials and new data in peripheral vascular disease, including femoral, below-the-knee (BTK) and critical limb ischaemia (CLI), Robert Lookstein (Icahn School of Medicine at Mount Sinai, New York City, USA) presented 10-year findings of the LONG DES-BTK study of the use of drug-eluting stents (DES) in the treatment of BTK disease.

The study seeks to expand on the existing datasets of DES, as part of continuing efforts to determine when and in whom this technology is best suited.

“We hope that this LONG-DES dataset will inform practitioners that even in lesions where you require three overlapping coronary stents, results are safe and effective in achieving limb salvage with very, very low rates of reintervention,” Dr Lookstein told the *LINC Review* ahead of the session.

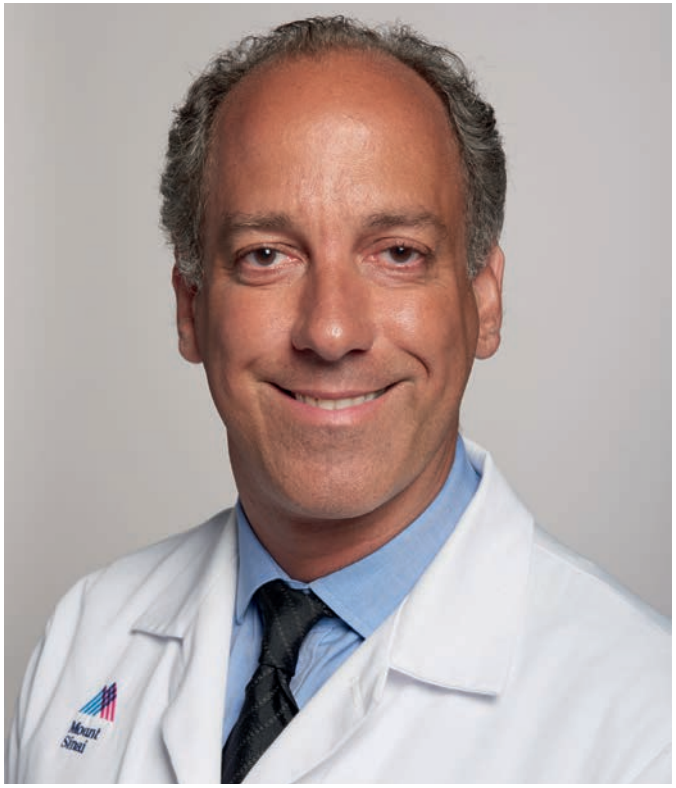
In infrapopliteal disease, the use of balloon angioplasty with bail-out bare metal stenting (BMS) in cases of residual stenosis or flow-limiting dissection is associated with poor long-term patency and the need for reintervention. Patients with BTK disease frequently have comorbid diabetes, renal insufficiency, and have a history of tobacco smoking – all of which are associated with long, calcified stenoses and occlusions that are difficult to treat with balloon angioplasty.[1]

“For those patients who are failing balloon angioplasty, we have yet to realise the ideal technology to overcome these limitations,” Dr Lookstein commented.

Exploring BTK treatment options to date, he further explained that investigations of drug-coated balloons (DCB) have so far been unsuccessful in improving upon outcomes of balloon angioplasty. “We have two negative prospective randomised trials and a third trial where we don’t have 12-month follow up yet.”

The first of these two prospective randomised trials, IN.PACT DEEP, included 358 CLI patients randomised to receive IN.PACT Amphirion DCB (Medtronic, Ireland) or plain balloon angioplasty. No statistically significant differences were detected in the primary efficacy outcomes of clinically-driven target lesion revascularisation and late lumen loss at one year.[2]

The second prospective randomised trial of BTK DCB was BIOLUX P-II, which included 72 patients randomised to receive either the Passeo-18 Lux DCB (Biotronik, Germany) or plain balloon. Here, the primary endpoint of six-month patency loss was not significantly inferior in the DCB group relative to plain balloon. Major amputations were also similar at 12 months.[3]



*“The only implants to date that have demonstrated efficacy have been balloon-expandable coronary DES.”*

**Robert Lookstein**

As such, he continued, numerous investigators globally have looked to scaffolds as a viable solution. “The only implants to date that have demonstrated efficacy have been balloon-expandable coronary DES,” he said.

“There are ongoing studies evaluating novel technologies. One of these is a self-expanding polymer-based drug-eluting paclitaxel stent – [studied in] the Saval trial[4]. Another is on the MicroStent [Micro Medical Solutions, USA] which is a bare metal, interwoven stent for the BTK circulation. Both of these trials are currently enrolling and the preliminary results are not yet publicly available[5].”

In the meantime, the body of data on the use of short coronary balloon-expandable stents for the treatment of infrapopliteal disease has grown. These have been summarised in a systematic review and meta-analysis by Varcoe *et al*. (2019), which included data pertaining to seven randomised controlled trials with mid-term (12-month) follow-up, with the conclusion that DES significantly improved rates of primary patency, freedom from reintervention, and freedom from major amputation compared to control therapy (plain balloon angioplasty, BMS, or DCB). The investigators also found that stents coated in sirolimus analogues were more effective than paclitaxel.[1]

These randomised trials included relatively short lesions with mean lesion lengths ranging from 15.9 mm to 34 mm.[1] The only included trial with lesions over 100 mm – the IDEAS trial[6], which randomised a real-world patient cohort with long BTK lesions to DCB or coronary

DES – had multiple issues, as Dr Lookstein described: "There were multiple DES allowed in the study. The only published data that has ever been presented publicly was of the six-month follow up. Lastly, DES was compared to an arm of heterogeneous DCB. So it was much more of a real world registry dataset of all-comers, randomising two different technologies for long lesions."

> *"We have placed stents in the BTK circulation for patients with CLI in over 375 individuals now."*
>
> **Robert Lookstein**

No DCB or DES are currently approved for the BTK circulation in the US, Dr Lookstein noted. Turning to his own centre's approach, he explained: "Our clinical protocol at Mount Sinai is to cross infrapopliteal lesions, perform prolonged long balloon angioplasty, and then perform a subsequent repeat angiographic assessment of the lesion that was treated. Unfortunately, we find that in [up to] 30% of cases, there is significant elastic recoil or flow-limiting dissection requiring the use of stent implantation.

"For the past 10 years, we have been using a single coronary DES platform for infrapopliteal lesions below the knee: the Xience everolimus-eluting stent [Abbott Vascular, USA]. We have placed stents in the BTK circulation for patients with CLI in over 375 individuals now, and we have been following all of our patients with a routine clinical and imaging protocol."

A key aim of the LONG DES-BTK study at Mount Sinai was to ascertain how safety and efficacy outcomes related to the number of stents implanted in a single case. Like most coronary stents being applied in the peripheries, the Xience stent has a maximum length of 38 mm, and as such even a relatively short lesion of 45 mm would require the implantation of two overlapping stents. In the cohort of 75 patients in LONG DES-BTK, lesion lengths ranged from around 50 mm to 150 mm, requiring the tandem implantation of two to four stents.

"These were all patients that were treated with this technology not as a primary therapy, but after bail-out following suboptimal angioplasty. So the patient had to undergo revascularisation, fail balloon angioplasty (defined as either significant elastic recoil with a > 50% residual luminal narrowing, or a flow-limiting dissection).

"In this very challenging subset of long infrapopliteal lesions that have failed balloon angioplasty, amputation-free survival for the entire cohort (including Rutherford 4, 5 and 6) was 73% at one year. When you look at the cohort broken down by Rutherford category, for the Rutherford 4 and 5 patients, amputation-free survival at one year was over 90%, and for the Rutherford 6 patients this fell down to almost 50%. So we are seeing significant benefit for amputation-free survival favouring the use of this technology in Rutherford 4 and 5 patients."



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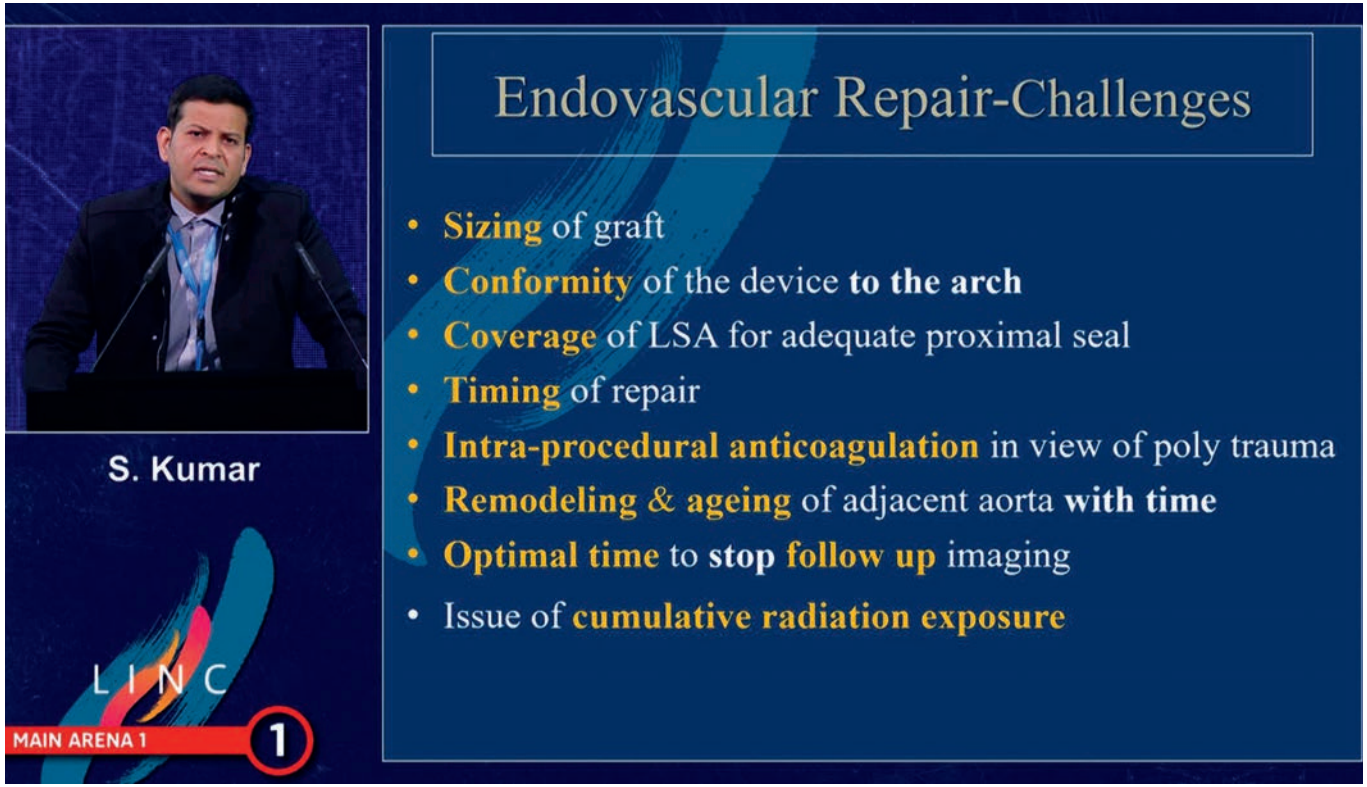
# Treating traumatic aortic injuries

Challenges and solutions in the endovascular management of traumatic aortic injuries were laid bare by Sanjeev Kumar, an interventional radiologist within the department of cardiovascular radiology and endovascular interventions at the All India Institute of Medical Sciences (AIIMS), New Delhi, India.

Dr Kumar started by highlighting the high rates of mortality for patients with traumatic aortic injuries: "Seventy percent of them die on the spot, and of those patients who reach a trauma centre, 50% will die within 24 hours – before they are treated," he said. "Hence time is crucial when you are talking about traumatic aortic injuries in this group of patients."

Dr Kumar stressed that the treatment paradigm for traumatic aortic injuries has changed drastically over the last two decades. Endovascular repair has largely replaced open repair, for example, resulting in a major reduction in mortality and procedure-related paraplegia, yet conversely it is associated with increases in early graft-related complications.

Such rises are indicative of the many challenges in carrying out endovascular repair, said Dr Kumar. The sizing of the grafting presents a particular challenge because many patients are so haemodynamically unstable. "Since patients are young with a small radius of the curvature of the aortic arch, conformity of the device to the arches is an issue," he explained.




Tears are usually located in the vicinity of the isthmus, noted Dr Kumar, thus the coverage of the subclavian artery (SCA) in emergency situations poses a great problem. "Since time is life, optimising the timing for a repair is very important for a successful outcome," he added. With polytrauma patients there is also a risk of intra-procedural haemorrhage, requiring optimum anticoagulation.

*"Since time is life, optimising the timing for a repair is very important for a successful outcome."*

**Sanjeev Kumar**

In addition, remodelling and ageing of the aorta occurs with time. "And since they are young patients, the natural history of this ageing is not widely studied," added Dr Kumar. Similarly, optimal follow-up for such patients should be addressed to limit the cumulative radiation exposure, he said.

Elaborating on each challenge in turn, Dr Kumar started by looking at the effect of hypovolaemia on device sizing. "As we know, hypovolaemia decreases aortic diameter," he said. "It's been studied in unstable patients with a mean arterial pressure (MAP) of 75 mmHg and a heart rate of more than 130 beats per minute." The aortic size in such patients has been underestimated by as much as

13%, he underlined, therefore there may be a mismatch between the aortic diameter and the endograft which could theoretically result in an increased risk of endoleak or other endograft-related complications. "In this group of patients, if they are haemodynamically unstable, we should do a 10% over-sizing over and above the normal over-sizing," he explained.

Most of these trauma patients are young, too – at least compared to patients typically experiencing aortic aneurysms. "They have a smaller radius of aorta curvature compared with aneurysmal patients," said Dr Kumar. "And, because of the sharp aortic angulation distal to the left SCA, the conformity of the device to the aortic arch – and hence provision of an adequate ceiling – is always a challenge." Too much oversizing risks graft corrugations or collapse, he added.

Dr Kumar outlined an older case in which a typical aortic arch injury – an isthmic pseudoaneurysm – was treated with a GORE TAG (WL Gore & Associates, USA) device. The follow-up CT showed poor positioning and nonconformity of the device. This led to graft collapse that was ultimately treated by a proximal overlapping stent graft (Valiant, Medronic, Ireland). "Nowadays we have a lot of devices on our shelf which improve conformability, hence when you are treating aortic trauma patient, device selection becomes very important," he explained.

Dr Kumar went on to discuss vessel diameter. "Often at times because young patients have inotropic support, you must consider the access vessel in these patients," he explained. Such patients may be on the borderline, said Dr Kumar. "But still you can consider higher thresholds in this patient because of the young and elastic nature of the vessels," he added.

> *"In higher-grade lesions, endovascular interventions are recommended."*
>
> **Sanjeev Kumar**

"However, if your access vessel is inadequate, you can always go to the iliac, for example, which was done in [one of my] patients for a successful aortic repair."

But Dr Kumar's abiding message is of prompt treatment. "Urgent repair within 24 hours is recommended in the guidelines if there are no other serious concomitant injuries," he said. "But at least the patients should be repaired before hospital discharge because non-operative management results in mortality rates as high as 50% in these patients."

He outlined coverage of the left SCA. "Because of the vicinity of the trauma, often in an emergency situation will you need to cover this left SCA and you are not able to assess the adequacy of the Circle of Willis or the dominance of the left tibial artery," he said.

"However, if the left SCA is covered, you should check the dominance of the right vertebral artery and Circle of Willis and, if the anatomy is unfavourable, surgical revascularisation should be considered in this patient," he said.

Heparinisation is a major challenge, he went on: "You know these patients are bleeding from everywhere, such as liver trauma." Indeed, heparinisation with an anti-clotting time in the range of 200 is recommended, and routine heparinisation should be provided at a lower dose than administered during elective TEVAR. Spinal drainage, on the other hand, is not routinely recommended in such patients, noted Dr Kumar.

Summing up, Dr Kumar said that the long-term natural history is still unknown in such young patients. "There are certain morphological changes of the aorta which take place over time," he said. "And also, the follow-up strategy and the cumulation of radiation exposure is a key component in managing this patient with endovascular repair."

In his concluding remarks, Dr Kumar said that minimal aortic injury, i.e. patients with grade I and grade II lesions without external contour abnormality, should be managed conservatively. "Endovascular repair is still considered a procedure of choice in suitable morphology patients," he said. "In higher-grade lesions, endovascular interventions are recommended.

"Urgent repair should be carried out within 24 hours or at least before the hospital discharge. This is the ideal time for the treatment," he said. "We still need to devise the optimal follow-up and understand the natural history of these patients, and see how they progress over a period of time."

# Femoral-popliteal atherectomy

## How to use lesion type to inform therapeutic decisions

As part of a VIVA@LINC session, John Rundback (Managing Partner of Advanced Interventional & Vascular Services LLP, Teaneck, NJ, USA) discussed how to determine when atherectomy might be beneficial for femoral-popliteal lesions, and if so, which technique to choose.

Setting the scene for the session, Dr Rundback introduced atherectomy in the context of other endovascular therapies, including plain old balloon angioplasty (POBA), drug-coated balloons (DCBs), covered or drug-eluting stents, tacks, and so on. "When we're discussing endovascular therapy for femoral-popliteal lesions, there is a fairly broad toolset," he told the *LINC Review*. "What distinguishes atherectomy from these other technologies is that it's a vessel preparation or plaque modification tool, which can be an adjunct to subsequent, definitive therapy."

Dr Rundback explained that the decision of whether to use atherectomy, either as a standalone or adjunctive therapy, depends on the pattern of disease in each patient. "The plaque morphology, the locations of the lesions, and the extent of the lesions all determine what will be the best therapy in a given case."

Consideration of these factors often reveals that atherectomy is not an appropriate therapeutic choice, Dr Rundback noted. "I would say that in our practice, we use atherectomy in a femoral-popliteal distribution in a third to 50% of cases," he estimated.

There are two common scenarios in which Dr Rundback would advise against atherectomy.

> *"What distinguishes atherectomy from [other endovascular] technologies is that it's a vessel preparation or plaque modification tool, which can be an adjunct to subsequent, definitive therapy."*
>
> **John Rundback**

The first is the situation in which long, flush occlusions require subintimal recanalisation. "Atherectomy is less appropriate in these cases, given the risk of damage to the adventitia, the chance of vessel rupture, and the fact that you're not working in the atheromatous plane," he said, asserting that another endovascular therapy would be more appropriate in such cases.

The second situation in which Dr Rundback would avoid atherectomy is in short, uncomplicated lesions. "If you have relatively short lesions, say up to 10–15 cm, that are less complex, less calcified, and smoother, the data has yet to support a clear-cut benefit for atherectomy on a routine basis," he noted.

Amongst longer, more complex lesions that do not require subintimal recanalisation, however, there is a growing evidence-base for the value of atherectomy. Four main types of atherectomy device are now in clinical use, and Dr Rundback gave his perspective on each in turn, drawing on the available evidence and his clinical experience.

Directional atherectomy, in which the atherosclerotic plaque is removed by carbide rotating cutter discs, is now supported by a strong evidence-base. For example, the DEFINITIVE LE trial,

the largest atherectomy trial to date utilising an independent core laboratory analysis of clinical outcomes, yielded very encouraging results. The study enrolled 800 patients and demonstrated an overall patency rate of 78% in claudicant patients at 12 months, as well as 95% freedom from major unplanned amputation in patients with critical limb ischaemia.[1]

A subsequent smaller trial, DEFINITIVE AR (n = 121), assessed outcomes after directional atherectomy followed by DCB. Results showed a potential patency benefit of adjunctive directional atherectomy for longer and severely calcified lesions, though the study was not sufficiently powered to show statistically significant differences between the treatment groups at 12-month follow-up.[2]

Taking this evidence into account, Dr Rundback often uses directional atherectomy for long stenoses or occlusions. "Where you have longer lesions with a good landing zone, then we tend to use directional atherectomy," he explained. "Certainly, it seems to provide the greatest amount of debulking."

Another technique is laser atherectomy, which utilises a high-energy light beam to vaporise the plaque. An advantage of this method is that, in addition to debulking, it allows penetration of the proximal fibrous cap in chronic total occlusions (CTOs).

Highlighting the potential of the latest laser atherectomy technology, Dr Rundback described his work in the recent Investigational Device Exemption (IDE) study for the B-laser atherectomy catheter (Eximo Medical Ltd., Israel). Within the study population of 97 patients, the patency rate at six months was 85.6%, and high safety and efficacy was observed in both de-novo and restenotic infrainguinal arterial lesions. Importantly, there was no significant difference in patency results between CTOs and in-stent restenosis lesions, or between those treated with POBA or DCB angioplasty.[3] "This is very exciting," noted Dr Rundback. "It is suggesting that in a wide range of lesions, laser-based atherectomy platforms can be very effective."

Some of the newer laser atherectomy devices now have the capability for aspiration, a significant advantage that is also offered by rotational atherectomy. "Aspirational atherectomy is very suitable in patients where there might be an element of acuity to the lesion, a thrombotic component," Dr Rundback reasoned, "because you get both the aspiration of any fresh thrombus as well as the atherectomy effect for more chronic disease." Evidence for the efficacy of rotational atherectomy comes from the Pathway PVD trial, a multicentre study of 172 patients which showed a 99% device success rate and a one-year restenosis rate of 38%.[4]

The final type of atherectomy, orbital atherectomy, utilises an eccentrically-mounted crown that orbits within the vessel to achieve circumferential plaque removal.

> *"It is so challenging to pass balloons or stents in these lesions. You need some debulking and plaque modification prior to doing anything."*
>
> **John Rundback**

Dr Rundback stated that this technique is particularly useful as a vessel pre-treatment tool in long, densely calcified lesions, as was demonstrated in the CONFIRM registry series (3,135 patients).[5]

"This clearly showed that for lesions that are densely calcified, the ability to successfully complete the case and achieve a satisfactory angiographic outcome is improved with orbital atherectomy," he said, going on to emphasise the value of effective pre-treatment in such cases. "Otherwise, it is so challenging to pass balloons or stents in these lesions. You need some debulking and plaque modification prior to doing anything. Orbital atherectomy in these cases also allows low pressure uniform balloon inflation, which maximizes lumen gain and limits dissections."

After discussing the differential value of the four main atherectomy techniques in specific lesion types, Dr Rundback acknowledged the other factors involved in choosing which approach to take in a given situation. Cost can be a significant factor, he said, as well as the individual practitioner's experience with the different devices.

Concluding his conversation with the *LINC Review*, Dr Rundback gave his outlook on the likely future developments in the evolving landscape of atherectomy research. "I think the REALITY trial is going to be very influential in providing a second level of evidence for the benefit of atherectomy in what are really the most challenging lesions," he predicted.

This prospective study is evaluating the safety and efficacy of directional atherectomy followed by DCB angioplasty in moderately and severely calcified femoral-popliteal lesions. However, Dr Rundback highlighted that the REALITY trial, like many other atherectomy studies, will only assess one type of technique. Comparative head-to-head trials, while harder to perform, could prove immensely useful to inform therapeutic decisions.

"We don't necessarily need a single-arm trial, but a series of small trials, in which comparisons are made between the prevailing technologies. In this way, we can advance our understanding of what works best in different scenarios," he concluded.

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# Atherectomy below the knee: how to do it safely

*"We can prepare the vessel and change the vessel compliance, enabling lower balloon inflation pressure."*

**Daniela Branzan**

Daniela Branzan (University Hospital, Leipzig, Germany) presented a summary of knowledge to date on the use of atherectomy in the treatment of below-the-knee (BTK) and below-the-ankle (BTA) disease.

BTK atherectomy encompasses laser atherectomy, directional atherectomy devices such as the Hawk series (including the SilverHawk, TurboHawk and HawkOne; Medtronic, Ireland), the Jetstream (Boston Scientific, USA), the CSI orbital atherectomy device (Cardiovascular Systems, Inc., USA) and the Phoenix (Philips Healthcare, the Netherlands).

Dr Branzan began by explaining that, while registry data exists for all of these devices, patency data is only available for the SilverHawk and TurboHawk*. Moreover, only one randomised controlled study – for the CSI device – shows the difference between atherectomy and plain balloon angioplasty (POBA) BTK*. This trial, Calcium 360 (Shammas *et al*, 2012), compared one-year outcomes of the treatment of calcified infrapopliteal arteries in patients with critical limb ischaemia (CLI) with CSI orbital atherectomy against plain balloon angioplasty, failing to find a significant difference in rates of bailout stenting between groups[1].

Speaking of the challenges of calcified BTK lesions, Dr Branzan cited Baumann *et al*. (2014), whose study to assess the extent of early recoil in patients with CLI undergoing conventional tibial balloon angioplasty found that 97% of treated lesions in a group of 30 consecutive patients showed > 10% recoil at 15 minutes post-procedure, with an average vessel recoil of 29%[2].

"We can address this problem using the atherectomy device," said Dr Branzan, returning to Shammas *et al*. (2012)[1]: "We can prepare the vessel and change the vessel compliance, enabling lower balloon inflation pressure. Rotational atherectomy uses differential sanding to prepare the vessel, whereas orbital atherectomy uses, besides that, pulsatile forces. Besides calcium, this can also treat plaques with thrombus (commonly found in chronic total occlusions).

"The question now is, which specific lesion subset profits from atherectomy BTK? In my opinion, we have to look at calcified lesions, distal BTA lesions, bifurcational BTK lesions and long lesions."

The CONFIRM Registry explored the use of the CSI device in the real-world setting. The registry's CLI BTK subanalysis, which included 523 patients with 712 lesions and a mean lesion length of 8.4 ± 7.6 cm, found a post-procedural residual stenosis of 9 ± 10%.[3]

BTA lesions pose a unique set of pressing challenges, noted Dr Branzan. "We know that 95% of patients of Rutherford 5 and 6 have BTK disease. If you look at diabetes patients, 52% have BTA disease, and a quarter of these patients have arch disease. If you add to the diabetes group end-stage renal disease, three-quarters of patients have BTA disease and half have arch disease. So we need a technology that addresses this BTA and arch disease."

She went on to illustrate the limitations of POBA in BTA disease, noting the difficulties in both inflating balloons and advancing them at this level. She added that the CSI orbital atherectomy device is designed for vessel bends, and as such may serve to facilitate subsequent balloon dilatation in affected BTA lesions.

POBA in bifurcational lesions present similar issues, continued Dr Branzan, such as restenosis and vessel recoil. "You can place drug-eluting stents, but they can crush and you can have restenosis," she said, referring to the study of Werner *et al*. (2012), who investigated bifurcational stenting after failed angioplasty in a small series of 11 patients. At six months, they reported an 81.8% primary patency rate if a single vessel was treated, and 54.5% if two vessels were treated. "We don't think this is a good solution for these bifurcational lesions,"

stressed Dr Branzan.[4]

Turning to data relating to the BTK performance of the SilverHawk and TurboHawk, Dr Branzan cited Zeller *et al*. (2007), who treated 49 lesions (36 patients) of average lesion length 48 ± 28 mm, with the outcomes of 67% primary patency at one year and 60% at two years[5]. In Rastan *et al*. (2015), a DEFINITIVE-LE subgroup analysis into directional atherectomy for the

*"We need a technology that addresses this BTA and arch disease."*

**Daniela Branzan**

treatment of infrapopliteal lesions, one-year primary patency was reportedly 84% in a set of 189 lesions (145 subjects) with an average lesion length of 58 ± 44 mm.[6]

"Is this the answer for all lesions? Basically, not always," continued Dr Branzan. "Drug-coated balloon (DCB) angioplasty has been tested up to today, but it has failed to demonstrate any benefit over standard POBA. The question is, why? One of the theories is that as circumferential calcium increases, the effectiveness of DCB decreases. There are some studies looking at DCB alone, and DCB after atherectomy BTK. You can see that there is a much greater drug uptake after pretreatment with atherectomy in these studies[7,8]."

Dr Branzan concluded by citing two studies currently ongoing comparing atherectomy with DCB: OPTIMIZE-BTK (Orbital Preparation to Maximize DCB Efficacy in Calcified BTK Lesions)[9] and Prestige Pilot (The Phoenix Atherectomy and Stellarex DCB Clinical Investigation in Infrapopliteal Interventions)[10].

"Atherectomy is extremely helpful in specific lesion subsets BTK," summarised Dr Branzan.

"The type of atherectomy device depends on the location of the plaque and on its histopathological characteristics. The future may show that combination therapy is beneficial."

***At the time of presentation: LINC, January 2020.**

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# Pooled analysis of DCB makes Total IN.PACT

The durability, safety, and efficacy of drug-coated balloons (DCB) for the treatment of peripheral arterial disease in the superficial femoral artery (SFA) was presented during a Deep dive session into lower limb interventions. The speaker, Osamu Iida, is an interventional cardiologist at Kansai Rosai Hospital Cardiovascular Center in Amagasaki (Hyogo, Japan) and one of the moderators of the session.

Dr Iida has been involved in many clinical trials for device approval in Japan such as the coronary stent studies ENDEAVOUR Japan and RESOLUTE Japan, and was the principal investigator during the recent IN.PACT SFA Japan trial using the IN.PACT Admiral paclitaxel DCB (Medtronic, Ireland). "Multiple clinical trials have already showed good results for DCBs, however, we have not found out what is really causing restenosis after the use of a DCB," explained Dr Iida. In his presentation, Dr Iida looked at insights, to find an answer.

Research gaps exist, said Dr Iida, because the many analyses on DCBs haven't used core-lab adjudicated clinical trial data for TASC A and B lesions, or more complex real-world registries.

"I believe it is still important to evaluate the predictors for restenosis after DCB treatment by using trial and registry data together," he said.

That's why Dr Iida's presentation focused on the outcomes from Total IN.PACT – a pooled subject-level analysis of the IN.PACT Admiral DCB. "The pooled analysis [examines] heterogeneous ethnic populations included in two RCTs [IN.PACT SFA and SFA Japan] and two prospective single-arm studies [IN.PACT China and Global] from 148 sites in 28 countries across six continents," he explained. "Analysis from Total IN.PACT is clinically meaningful because it considers data from more real-world patients, in which DCB shows a clear superiority against PTA."

Importantly, Dr Iida talked about the results of a multivariable analysis focused on predictors of restenosis after DCB treatment – a vital evaluation of DCB performance. "This is very important information which has not been looked at in such detail before," he added.

Indeed, the multivariable analysis of Total IN.PACT shows that the predictors of restenosis were different in the PTA group compared to the DCB group. In the PTA group, for example, the lesion length and previous peripheral revascularisation of the iliac were revealed as predictors of restenosis. On the other hand, in the DCB group there were four predictors: diabetes mellitus, previous peripheral revascularisation in the common femoral artery (CFA), lesion morphology (restenotic vs *de novo*) and lastly, pre-procedural percentage diameter stenosis.

> *"Multiple clinical trials have already showed good results for DCBs, however, we have not found out what is really causing restenosis after the use of a DCB."*
>
> **Osamu Iida**

"Also, in this analysis, lesion length, lesion calcification and vessel diameter were not predictors in the DCB group," continued Dr Iida. "Those characteristics are usually considered as risk factors for the occurrence of restenosis in the SFA."

What Dr Iida suggests now is that patients with those DCB-specific predictors need to be followed up closely. "I believe we need further evaluation on vessel dissection and the level of calcification," he reasoned, adding that he is particularly interested in the relationship between dissection and patency.

Of paramount importance, he said, is to understand the link between residual stenosis, with or without calcification, and patency after the use of a DCB: "In this analysis, neither emerged as a predictor, which I believe is a very meaningful finding because these had been the general prognostic factors after plain angioplasty."

Determining predictors is important, because Japan has such a unique reimbursement landscape where the use of a DCB and a stent on the same lesion is not permitted. "Under these conditions, we are expected to finish the first session with DCB alone, if there is no flow-limiting dissection," said Dr Iida. "In real-world practice, we often see vessel dissections or residual stenosis, however, and we also see the positive remodeling of the vessel and the healing of dissections after DCB treatment in

long-term follow-up.

"Japanese physicians are keen to know what the predictors of positive remodeling are, and of the healing of dissections, so we can finish with DCB alone, with confidence. Our question is, can we finish and leave nothing behind?"

Dr Iida stressed that in the future he'd like to investigate DCB after atherectomy in more complex femoropopliteal lesions, even with claudicants. In addition, said Dr Iida, there is still no standard criteria for the evaluation of below-the-knee (BTK) and below-the-ankle (BTA) treatment, such as patency. "We need to find out the optimal therapy BTK and BTA," he affirmed. "I believe evaluation and analysis on every new device is required according to the new global vascular guidelines on chronic limb-threatening ischaemia."

Dr Iida's presentation featured two case scenarios: a chronic total occlusion (CTO) in a small diameter vessel with no restenosis after DCB, and a CTO which showed vessel dissection after DCB, but healed in the long term. "The first case shows that use of DCBs is very encouraging when we have limitations for stenting in small vessels," he said. "The second case shows the possibility of finishing with DCB alone even with substantial dissection, if it is not flow limiting."

In conclusion, Dr Iida said the large pool of data from all the IN.PACT studies is uncovering valuable insights into clinical outcomes across a broad selection of patients and lesion types that go well beyond Investigational Device Exemption (IDE) trials. "The pooled data from Total IN.PACT is a good opportunity to learn more about DCB performance, which wasn't observed from each individual study," he said.

*"The pooled data from Total IN.PACT is a good opportunity to learn more about DCB performance."*

**Osamu Iida**

These kinds of data can help develop knowledge on how best to proceed in more complex cases in future, he concluded: "In my practice, there are more complex examples of calcification and dissection, which I believe we can still treat with DCB alone. Further evaluation is needed in these complex lesion morphologies."

# $CO_2$ angiography is efficient – but beware limitations and risks!

Tips and tricks in $CO_2$ angiography in endovascular aortic repair (EVAR) were discussed by Eric Ducasse (Universitary Hospital Pellegrin, Bordeaux, France).

$CO_2$ has been used as a contrast agent in vascular imaging since the advent of digital subtraction angiography (DSA). $CO_2$ offers certain advantages in diagnostic accuracy and patient outcomes in some settings, however it also carries a number of drawbacks, and its adoption requires an understanding of its unique properties and indications[1].

Despite its lack of toxicity, the popularity of $CO_2$ in angiography has in the past been hampered by suboptimal methods of administration that have carried risks, for example, of introducing room air into the vascular circulation, or overdose. While automated injectors have emerged onto the market seeking to overcome these risks, its use remains in a minority of institutions only.[2]

"We use $CO_2$ angiography in approximately 5–15% of cases," said Dr Ducasse in an interview with the *LINC Review*. "We use the Angiodroid system (Angiodroid, Italy); this is the only one we have in our unit.

"But these numbers are growing, due to two main reasons. First, we now have [overcome] the learning curve, and second, we are treating more and more patients with renal insufficiency and/or patients with iodinated product allergy."

Partial or complete use of $CO_2$ angiographic imaging can be adopted, he added, for those patients at risk of either contrast-induced nephropathy or allergic reaction to iodinated contrast. "There is a very low level of clearance in renal insufficiency (nowadays adopted in our pre-operative check-list), and we are very limited in the quantity of contrast we can inject in those patients. But, now, renal insufficiency and allergies are no longer a contraindication for EVAR or fenestrated EVAR (FEVAR), due to $CO_2$ angiography. It is as efficient as contrast injection."

He added: "We have not seen any contraindications in our patients. If you are respecting the instructions for use, there is really no contraindication for using $CO_2$ injection."

Angiograms created using $CO_2$ are similar in appearance to traditional iodinated contrast angiograms. Due to its relatively low atomic number and density, however, $CO_2$ absorbs X-ray radiation to a lesser extent than surrounding tissues, and as such is a negative contrast agent. Moreover, its quick passage through the body demands greater temporal resolution, and this higher image acquisition rate naturally increases radiation exposure (unless images are acquired remotely).[1]

*"Although $CO_2$ angiography is very 'sexy', there is a learning curve... It also increases the rate of radiation exposure."*

**Eric Ducasse**

Furthermore, the properties of $CO_2$ and iodinated contrast differ, giving rise to unique technical considerations. As a gas, $CO_2$ displaces blood where liquid contrast mixes. It is both buoyant and of drastically lower viscosity than liquid contrast agent. Its properties can be advantageous, for example, in visualising narrow stenoses or in identifying low-flow endoleaks following EVAR[3].

However, due to risk of cerebral air embolism, $CO_2$ cannot be used above the level of the diaphragm (it is also for this reason that patients are placed in slight Trendellenberg position). Due to its buoyancy, it may also be necessary to reposition the patient depending on the artery of interest. Song *et al*. (1999) found that gas flow dynamics and dispersion, as well as the extent of vessel filling, depended on factors including vessel size and degree of inclination. Incomplete fluid displacement when vessels were directed posteriorly (e.g. the renal arteries with the patient in supine position), while better images were acquired for anteriorly-oriented vessels such as the celiac and superior mesenteric arteries (Figure 1).[4]

Dr Ducasse noted that some of these idiosyncrasies can be dealt with in straightforward ways. For example: "What we have developed in the unit – these are some very tricky things – is to put the target artery (e.g. the highest or the lowest renal artery) above the baseline of the patient, to be sure that the $CO_2$ will be injected into that target artery. The $CO_2$ acts like oil sliding on water – it fills the targeted artery

perfectly, making a perfect image and visualisation to complete the procedure."

He further cited the work of Mauro Gargiulo, whose group at the University of Bologna, Italy, have recently reported on the efficacy of a new standardised $CO_2$ injection method in standard EVAR procedures[4] and in FEVAR.[5] They also demonstrated that $CO_2$ shows better agreement with contrast-enhanced ultrasound than iodinated contrast angiography in the detection of endoleaks after EVAR.[3]

Dr Gargiulo and others have also recently initiated a European registry aiming to study image quality using $CO_2$ angiography during various stages of stent graft deployment and implantation, as well as to improve renal artery visualisation, and to standardise EVAR protocol. Data will be gathered from centres in Bologna, Muenster, Malmo, Athens, Bordeaux, Aalst and Ourense, with a target enrolment of 160 patients.[8]

In his concluding remarks, Dr Ducasse stressed that $CO_2$ comes with drawbacks as well as advantages in certain patient groups: "Although $CO_2$ angiography is very 'sexy', there is a learning curve, which is always very tricky. This is very important. It also increases the rate of radiation exposure during the procedure, for the patient and also therefore for the team."

Figure 1. Principle underlying poor visualisation in posteriorly-oriented anatomy (Figures courtesy of Dr Ducasse).

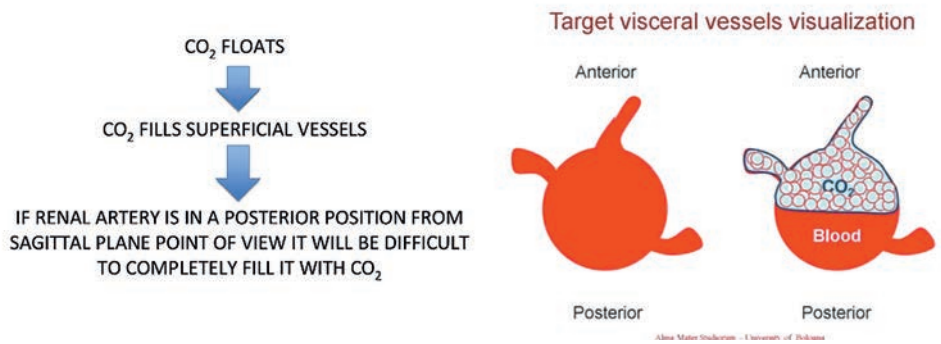
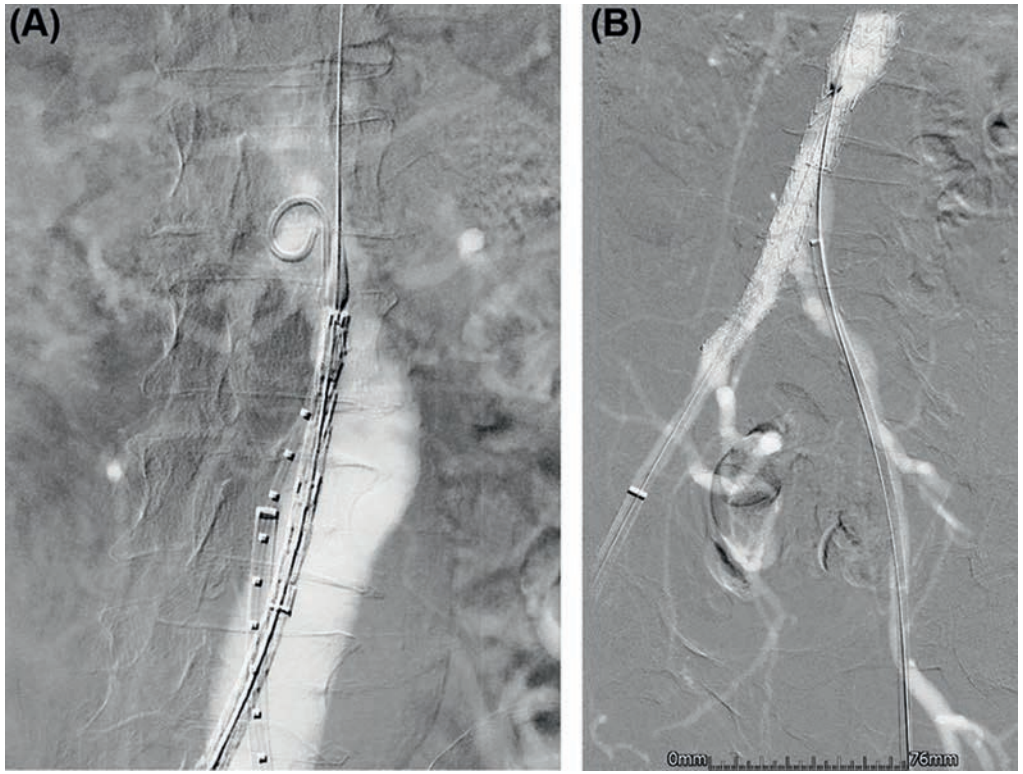



Figure 2. Procedural angiographic images acquired using $CO_2$ contrast medium

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# Failing TEVAR, keep up the surgical work

The failure of thoracic endovascular aortic repair (TEVAR) was addressed by Roberto Chiesa, a vascular surgeon who has led the vascular surgery department at San Raffaele Hospital in Milan, Italy since 1993. His department has been an Italian referral centre for aortic disease, performing about 500 aortic interventions per year (including open and endovascular treatment of the aortic arch, descending thoracic, thoracoabdominal, and abdominal pathology). "Cases of failed TEVAR have been increasing in recent years with the spread of endovascular approaches," began Professor Chiesa in conversation with the *LINC Review*.

Failure of TEVAR may be due to stent-graft related complications or the progression of aortic disease, and requires reintervention that can be performed by secondary endovascular procedures, where possible, such as endograft relining. "However, in a significant number of cases, more complex procedures including open conversion are required," said Professor Chiesa. "The number has grown incredibly over the last 20 years with the increasing diffusion of TEVAR, and surgery represents a challenge for the vascular surgeon and his/her team."

By way of evidence, Professor Chiesa talked about his team's experience in performing open conversion after TEVAR, presenting results of procedures performed between 1995 and 2019. Open conversion was carried out when there was a clear progression of aortic disease or following acquired complications. "All cases represent a technical challenge with acceptable results in high-volume centres," he noted. "Increased mortality is observed in the case of retrograde dissection and infection."

> *"Close follow-up after TEVAR is essential."*
>
> **Roberto Chiesa**

Specifically, Professor Chiesa presented two cases from his series, illustrating the issues his team typically face. The first case – a dissected thoracoabdominal aortic aneurysm (TAAA) – had already submitted to multiple failed endovascular attempts, but the patient underwent successful open conversion with a thoracoabdominal complex open aortic reconstruction.

The second case was a young patient with Marfan syndrome who underwent TEVAR and the PETTICOAT technique for an acute Type B aortic dissection. "After two years we observed an enlargement of the thoracic and abdominal aorta, and we decided to proceed with open conversion, performing reconstruction with a multibranched surgical graft," Professor Chiesa explained.

Each case is different in its own way, he added: "The technical difficulty, diversity and rarity of each patient's condition means that each case represents a big challenge for a vascular surgeon." That's why Professor Chiesa relayed what he and his team have learned from carrying out such complex procedures.

Firstly, preventing failed TEVAR is key, he said, and to do so, each case of aortic thoracic disease should be carefully evaluated, and the choice of the material should be based on the anatomical characteristics of each patient. Often, however, open conversion is necessary – particularly when there are unsuitable or multiple failed endovascular approaches, or in cases of fistulae, infection or retrograde dissection. In such cases, procedures must


> *"Cases of failed TEVAR have been increasing in recent years."*
>
> **Roberto Chiesa**

performed in a referral centre with a multidisciplinary approach. "Here, open conversion is the only solution," said Professor Chiesa. "But there must be a strict collaboration between the vascular surgeon and other professionals, i.e. anaesthesiologists, cardiac surgeons, neurophysiologists and perfusionists."

Professor Chiesa said the development of endovascular techniques has inevitably reduced the number of patients treated by open surgery in recent years, but that doesn't mean surgical expertise is redundant. "Treating endovascular complications still means open surgery, and that challenge must be addressed in highly specialised centres," he underlined.

He advises those newer to the profession to hone and maintain their surgical skills so that they can carry out open conversions well. In other words, surgeons should continue to perform the techniques regularly in well-run multidisciplinary centres. "Surgical skills will still remain of paramount importance in the future, given the increasing number of observed TEVAR failures that require open conversion," he said.

Professor Chiesa also touched on organ protection, in particular the heart, kidneys and spinal cord. "In all open thoracic and thoracoabdominal aortic interventions performed at our department, multiple adjuncts are used to ensure the best organ protection," he explained.

Giving examples of these adjuncts, he noted that cardiac function and perfusion are usually investigated pre-operatively by coronary-CT or coronary angiography and, during interventions, via transoesophageal echocardiography, for example. "Renal ischaemia is protected by cold intraoperative perfusion of Custodiol solution," he added. "Continuous monitoring of somatosensory and motor evoked potentials is routinely used to reduce the risk of spinal cord ischaemia, in association with automated cerebrospinal fluid drainage with dedicated equipment."

Indeed, much of the research into open surgery is traditionally oriented towards the study of organ protection, added Professor Chiesa, and he suggested specific organ protection strategies during open thoracic and thoracoabdominal aortic conversion might be investigated in future.

Most importantly, however, Professor Chiesa suggested more research be channelled into preventing failed TEVAR in the first place. He suggests more studies to improve the prompt diagnosis of TEVAR failure, strategic techniques that should be employed, especially within open surgical conversion, and how best to treat this specific subset of patients: "An interesting research topic could be to assess specific risk factors that are associated with the need for open conversion after TEVAR.

"Strict follow-up for patients treated by new endovascular techniques and materials should be performed by referral centres to guarantee a prompt diagnosis of any complications. Close follow-up after TEVAR is essential."

*"Surgical skills will still remain of paramount importance in the future, given the increasing number of observed TEVAR failures that require open conversion."*

**Roberto Chiesa**

# Endo AV access


## New data emerge on the WavelinQ system

LINC 2020 saw a first time data release from the prospective, multicentre study to evaluate the WavelinQ endoAVF system (BD, USA), used to create endovascular arteriovenous fistula (endoAVF) for patients requiring vascular access for haemodialysis[1].

This real-world, multicentre, prospective study represents the largest WavelinQ analysis to date, including the rigour of an independent ultrasound core lab and clinical events committee.

WavelinQ is a dual catheter system that uses radiofrequency (RF) energy to create an autologous fistula. Two catheters are aligned in the desired artery and its adjacent deep vein in the proximal forearm with the use of rare earth magnets. The venous catheter has a discrete electrode which corresponds to a ceramic backstop in the arterial catheter, employing a sub-second burst of RF energy for the creation of an endoAVF.[2]

Surgical fistula creation is recommended in the forearm first, as this does not preclude later attempts at upper arm fistula placement should the forearm placement fail. However, the rate of forearm failure is relatively high. EndoAVF presents a potentially viable first option in vascular access because it does not interfere with the possibility of subsequent surgical radiocephalic or elbow fistula placement.[2]

With endoAVF, the site of fistula creation is typically in the proximal to mid forearm – potentially the radial, ulnar or interosseous vessels. The blood flow from the endoAVF enters the deep venous system and cross-fills across the forearm and the arm's deep and superficial systems via perforating and communicating venous branches.[2]

A number of studies of the WavelinQ have explored its potential. Most recently, a single centre observational study by Inston *et al*. (2020) compared three-year data of a cohort of patients receiving endoAVF fistula (n = 30) matched with a contemporary cohort receiving surgical radiocephalic arteriovenous fistulas (n = 40). Herein, superior performance of the endoAVF was found, in terms of primary outcomes measures such as time to fistula formation, with a trend for improved primary patency and 6 and 12 months for the WavelinQ group.[2]

Other small-scale retrospective studies, including Rajan *et al*. (2015)[3] and Yang *et al*. (2017)[4] support the notion that an endoAVF requires fewer interventions to maintain patency than surgical AVF at 12 months. In 2017, Lok *et al*. published findings of the prospective, multicentre single-arm Novel Endovascular Access Trial (NEAT), finding minimal complications association with the endoAVF approach, and high 12-month cumulative patencies[5].

Data from WavelinQ's three-year post-market study were presented at LINC 2020 by Rob Jones (Queen Elizabeth Hospital, Birmingham, UK). The study, which completed in September 2019, involved 100 participants with chronic kidney disease who underwent endoAVF placement using WavelinQ (both 4 F and 6 F systems were used). Patients were followed up at 3, 6 and 12 months. Primary outcome measures included time to first intervention to maintain patency, or time of successful endoAVF creation until any intervention designed to maintain or re-establish patency or loss of endoAVF patency.[1]

> *"The evidence to date suggests fewer interventions, and therefore fewer visits to the hospital are required to maintain functionality."*
>
> **Rob Jones**

Describing the importance of devices that can permit percutaneous endovascular arteriovenous fistula (AVF) formation, Dr Jones said: "The importance to the patient is that it is minimally invasive to create and doesn't involve an incision in


the skin.

"It is also cosmetically more acceptable than the conventional fistula because it does not become aneurysmal. And, most importantly, the evidence to date suggests fewer interventions, and therefore fewer visits to the hospital are required to maintain functionality."

Discussing the results of post-market study, he continued: "The new data demonstrate that in a real-world population, in multiple countries, in the hands of different operators and different disciplines, the WavelinQ device is highly successful both in terms of creating the fistula, but also in its functionality and cannulation. Ninety-five percent functional patency [was achieved] at six months.

"The true measure of endoAVF is the ability to cannulate, and the patient to receive dialysis, which is demonstrated in this study. The implications [of this study are] that the results of the earlier trials are reproducible in the real world, including with the use of the new 4 F device. We are able to create percutaneous fistulae that are useable for dialysis, offering patients more options."

*"The true measure of endoAVF is the ability to cannulate, and the patient to receive dialysis, which is demonstrated in this study."*

**Rob Jones**

Indeed the next generation 4 F device received the CE Mark in 2017. Commenting on how this lower profile device expands upon the applicability of the 6 F WavelinQ device, Dr Jones noted: "From the patient's perspective, this has made the procedure a safer alternative. The access is of a narrower calibre and therefore haemostasis following the procedure is easier to achieve, and less likely to cause bleeding complications.

"From the operator's perspective, there is added confidence when it comes to haemostasis. It also opens up the options of fistula creation, because we can now use the wrist vessels for access to the target site, which we couldn't with the 6 F device. Also … there is no noticeable difference between the 4 F and 6 F WavelinQ in terms of successful fistula creation."

Concluding with an outlook of upcoming studies of the WavelinQ device, Dr Jones noted that two new trials will continue its investigation, one based in the US and a second that will include global enrolment.

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# Can silver surfers benefit from EVAR's golden age?

## Encouraging data from nonagenarian registry

This year's JET@LINC session featured Japanese perspectives on a range of topics. The Japan Endovascular Treatment Conference (JET) has become the largest conference on peripheral vascular intervention in Japan with more than 2,000 delegates participating in recent years.

At LINC 2020, moderators Giancarlo Biamino and Hiroyoshi Yokoi were joined by discussants Naoki Fujimura, Masahiko Fujihara, Shigeo Ichihashi, Daizo Kawasaki and Osamu Iida. As well as tackling contemporary questions in lower limb interventions, the session looked at aortic interventions for super senile patients.

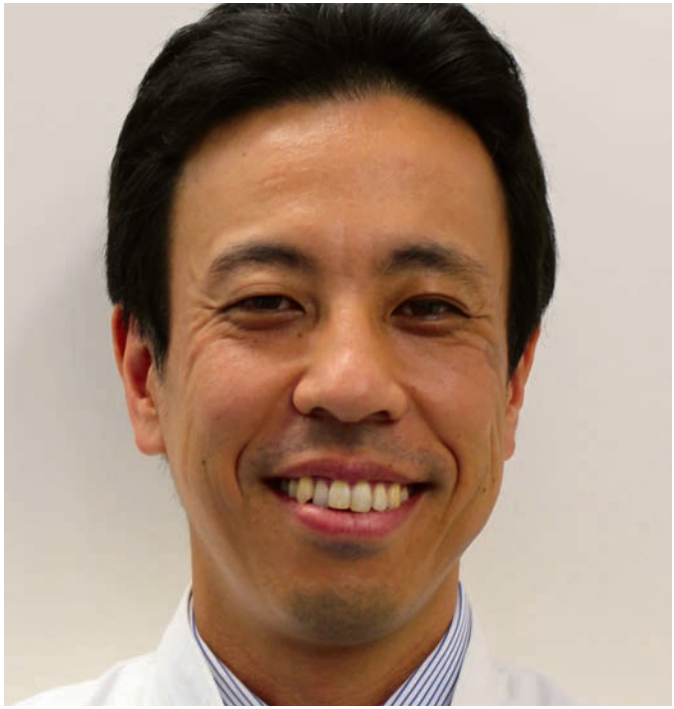
Naoki Fujimura (Division of Vascular Surgery, Saiseikai Central Hospital, and the Department of Surgery, Keio University School of Medicine, Japan) presented findings supporting the notion that nonagenarians have comparable good early results as octogenarians after elective EVAR.

A significant number of countries in both Asia and Europe face an aging population, and Japan is estimated to be the most advanced in age. Globally, the number of persons aged 80 years or over is projected to increase more than threefold between 2017 and 2050, rising from 137 million to 425 million.[1]

The feasibility of EVAR in the octogenarian population has previously been demonstrated in selected patients[2-4]. Less has been published on the nonagenarian population[5,6], however, and Dr Fujimura and colleagues sought to address this paucity of data.

They conducted a retrospective analysis using prospectively collected data from a Japanese multicentre registry relating to patients treated between the years 2007 and 2018, including elective EVAR performed for abdominal aortic aneurysms (AAA) and iliac artery aneurysms. Data relating to ruptured AAAs, inflammatory and mycotic AAAs and debranching EVAR were excluded from the analysis.[7]

Out of a total of 1,828 EVARs performed during this study period (mean patient age, 75.5 ± 8.4 years [81.5% male]), 48 EVARs were performed in nonagenarians (mean patient age, 92.2 ± 2.2 years, 68.8% male). Forty nonagenarians conforming to inclusion and exclusion criteria were analysed in a comparison with 563 octogenarians, all having undergone elective EVAR.[7]



Compared to octogenarians, nonagenarians had significantly larger AAA diameter (57.1 ± 12.5 mm vs 52.1 ± 11.5 mm, p = .040), and a greater proportion of them were assigned an American Society of Anesthesiologists (ASA) score of > 3 (30.0% vs 15.6%, p = .018). Despite this, no perioperative mortality occurred in nonagenarians (0.0% vs 1.1%, p = .512). No difference was found in the incidence of either intraoperative complications (5.3% vs 2.5%, p = .434), or 30-day major adverse events (7.5% vs 4.8%, p = .447). Strikingly, one-year all-cause mortality was no different, according to Kaplan Meier curve and log rank analysis (one-year survival rate: 94.6% vs 91.0%, p = .640) (Figure 1).[7]

And while nonagenarians did show a significantly lower five-year survival rate compared to octogenarians (14.4% vs 61.2%, p < .001), Dr Fujimura explained that this probably simply reflects the greater frailty and shorter life expectancy of nonagenarians. Indeed, the most frequent etiology of death was decrepitude.[7]

In a UK-based systematic review of nonagenarians and EVAR, Wigley *et al*. (2014) emphasised the importance of patient selection, specifying that EVAR should be conducted in "exceptional circumstances" only[6]. Commenting on this view, Dr Fujimura told the *LINC Review*: "I believe the patient should not have dementia and should have sustained activities of daily living (ADL), i.e. independent to some degree, but may be having some assistance.

"Furthermore, patients should be able to receive good care after discharge, either from family or via a paid service."

Elaborating on the decision-making process leading up to the treatment of the most

*"The success of EVAR for nonagenarians should primarily focus on the level of ADL (activities of daily living) at discharge and at one year – not long-term survival."*

**Naoki Fujimura**

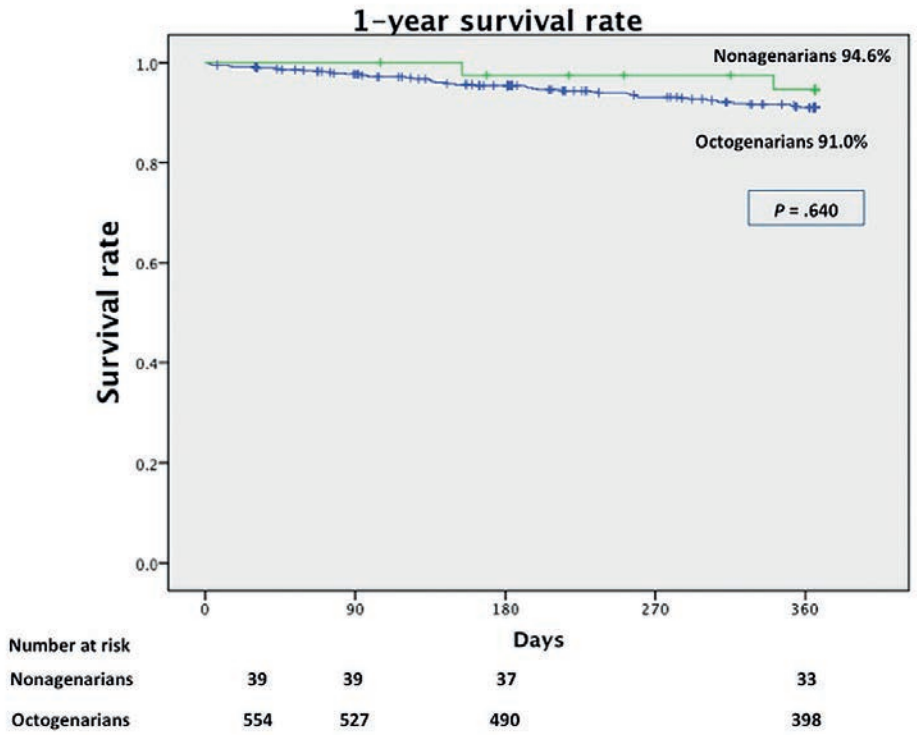



Figure 1. Kaplan Meier curves of patient survival over one year post-EVAR (both nonagenarian and octogenarian EVAR patient cohorts). Log rank analysis revealed no significant difference in one-year survival rate (94.6% vs 91.0%, p = .640).

elderly patients, he continued: "Multidisciplinary conference is mandatory before the treatment. Furthermore, informed consent should be given not only by the patient, but also by the patient's family.

"Since EVAR is a very expensive treatment, the medical community tend to withhold treatment from this group of patients. However, improvements in life expectancy – and also our results – show that one-year outcomes are no different from those of octogenarians. Thus, the decision to intervene should be dependent on individual patient status, not age."

Last year, at LINC 2019, Dr Fujimura presented perhaps the oldest TEVAR case, carried out for a 106-year-old female patient. The patient, who presented with a 6-cm saccular aneurysm of the descending thoracic aorta, and whose history included hypertension and pacemaker implantation, was nevertheless living relatively independently. The procedure was carried out via femoral cutdown. Operative time was 71 minutes, and 10 ml of blood loss occurred. The patient was discharged on post-operative day 11. Dr Fujimura highlighted the importance of tailoring procedural care to the needs of particular elderly patients, for example with respect to intubation and anaesthesia: "If the patient seems fragile, like this TEVAR case for the 106 year-old, local anaesthesia along with sedation using a sleeping agent is recommended."

*"The decision to intervene should be dependent on individual patient status, not age."*

**Naoki Fujimura**

On the relevance of the endpoint of long-term survival in the very elderly population, and the way in which EVAR benefit should be framed in a population that face death due to frailty, Dr Fujimura emphasised that long-term survival is a very important measure, but only in younger patient groups. "I believe that the success of EVAR for nonagenarians should primarily focus on the level of ADL at discharge and at one year – not long-term survival.

"As long as the patient's ADL is sustained for at least one year, I believe this is a success because the patient's fear of rupture has been removed."

In conclusion, Dr Fujimura outlined the questions that remain unanswered in this very elderly patient cohort: "To confirm that EVAR can avoid rupture and also at the same time sustain ADL level even in nonagenarians, prospective study – which includes not only mortality, but also evaluation of patient's ADL level and satisfactory status – should be done in the near future."

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# Pave-and-crack technique update at seven years

A novel endovascular strategy to target severe calcified occlusions, the so-called "pave-and-crack" technique, was the focus of a presentation this afternoon by Manuela Matschuck from University Hospital Leipzig. "We want to show that this technique is a safe alternative to open surgery, treating these patients with a bypass," she told the *LINC Review*.

Dr Matschuck, who works alongside Dierk Scheinert and Andrej Schmidt at the interventional angiology labs in Leipzig, provided key technical tips as well as the latest long-term data evaluating the technique.

The pave-and-crack technique was first described by the Malmö group for iliac arteries to enable aortic stent-grafts to be passed safely through diseased access vessels. Without this technique, severe calcification risks compromising the intraluminal passage of guidewires and balloon catheters and could also block stents and anti-restenotic therapies such as drug-coated balloons (DCBs).

Dr Matschuck presented the latest results from a retrospective analysis for patients who underwent the adapted version of the technique for heavily calcified femoropopliteal lesions. Here, a Viabahn stent-graft (WL Gore & Associates, USA), was implanted to pave heavily calcified femoropopliteal lesions. Paving acts as a kind of scaffolding that prevents vessel rupture, while aggressive predilatation is carried out until the calcified plaque is cracked.

The entire lesion is then lined in preparation for the delivery of a Supera (Abbott, USA) interwoven stent. "We adapted the technique for the kind of lesions we were unable to treat before due to severe calcification," she explained. "These were cases where we weren't able to do the endovascular procedure before."

At LINC, Dr Matschuck presented long-term data, building on 12-month data already published.[1] Her group collected retrospective data on 67 consecutive patients treated between November 2011 and February 2017 in Leipzig. A third of the patients had critical limb ischaemia, most lesions were TASC D, and 92% were occlusions. The mean lesion length was 26.9 ± 11.2 cm and 62% of the patients had grade 4 calcification, according to the peripheral arterial calcium scoring system (PACSS).

"In these patients who are usually treated with a bypass, the technique we developed is an endovascular alternative showing good results at seven years," she said. Indeed, at one year the primary and secondary patency estimates were 79% and 91% respectively; freedom from TLR was 85%. In other words, despite having extremely long and complex calcified lesions, at 12 months the patients experienced what the researchers described as excellent technical success, safety and durable results.

> *"We adapted the technique for the kind of lesions we were unable to treat before due to severe calcification."*
>
> **Manuela Matschuck**

The primary patency and secondary patency at up to seven years to be presented is a continuation from the 12-month results, said Dr Matschuck. "It tells us this is a good alternative for patients with severe disease," she said.

Indeed, a primary reason to avoid bypass is that so many of the patients undergoing the pave-and-crack technique also suffer from several comorbidities. "For a bypass you have to put patients under anaesthesia resulting in a higher risk for them," she explained. "But this procedure can be performed without anaesthesia."

Dr Matschuck noted that other groups have started to adopt the technique, however, learning to properly carry out the technique is vital." You have to train in order to become familiar with this technique, but it's getting more and more popular," she said. "Many other hospitals have started using it."

During her talk, Dr Matschuck provided technical advice on how to carry out pave-and-crack. "The technique itself is very challenging, passing a severely calcified occluded lesion," she explained. "Sometimes you have to puncture the lower limb below the knee in a retrograde approach."

Getting the hang of the technique pays dividend however, said Dr Matschuck. "This is a feasible alternative for patients with severely calcified lesions, compared to open surgery under special circumstances."

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# Controlled expansion TIPS improves transplant survival

## 12-month results from Bonn

Daniel Thomas (University Hospital Bonn, Germany) presented the final 12-month results of the Viatorr CX Case-control Study for Complications of Portal Hypertension (Viatorr-CX)[1], as well as sharing his practical experience with the novel Viatorr Controlled Expansion device (W. L. Gore & Associates, Inc., USA).

Transjugular intrahepatic portosystemic stent-shunt (TIPS) reduces portal pressure gradient and is known to improve survival in selected patients with variceal bleeding and intractable or refractory ascites. There are potential downsides to TIPS creation, however, such as deterioration of liver function, increased cardiac load and new or worsening hepatic encephalopathy (HE), the latter being the most well-known complication[2-6].

Addressing the LINC audience, Dr Thomas explained that, aside from patient-related factors, the most important procedure-related parameter ultimately influencing outcome is the portal-to-systemic pressure gradient, also known as the portosystemic gradient. "A number of studies have tried to identify an ideal pressure gradient (especially for patients that have bled) that should be achieved following TIPS implantation," he said. "This is > 8 mmHg and < 12 mmHg."

TIPS diameter naturally influences portosystemic gradient reduction, and complications such as HE can arise from excessive portosystemic shunting. As such, underdilation of stents is thought to reduce incidence of portosystemic encephalopathy without compromising desired outcomes.[7]

Dr Thomas continued: "It has become a very common approach to underdilate the stent. However, we have shown – first retrospectively, then also prospectively – that those TIPS stents of 10 mm nominal diameter will ultimately dilate to their full nominal diameter[8]. This happens very early after implantation, and to a high degree after day seven."

More recent study by Silva-Junior *et al*. (2017) has also shown a statistically significant reduction in gradient as early as 24 hours following TIPS[9].

The Viatorr Controlled Expansion (VCX) stent was introduced approximately three years ago with the aim of addressing the issue of post-TIPS gradient reduction. "The VCX is basically the same conventional Viatorr (VTS) stent that has been around for more than 20 years, but a control expansion sleeve has been added to the platform," said Dr Thomas. "This makes sure that if you inflate the balloon inside of the stent to 8 mm, it will stay exactly there. But if you feel that you need to lower the portosystemic gradient more, you can go on and dilate to 9 or 10 mm.

> *"With the new stent design there is a clear reduction for ascites, HE and sepsis."*
>
> **Daniel Thomas**

"Our initial experience was reported in 2017. We found that the TIPS implantation procedure was no different to the old stent model, with a comparable rate of stent thrombosis. There was really no passive expansion of the TIPS stent. We did pressure measurements in a subgroup of patients and demonstrated that the portosystemic gradient remains unchanged at 3–10 days following implantation. So VCX really holds its promise."[10]

Late 2019 saw the publication of one-year data on the VCX versus the VTS, in a cohort of patients who received 10-mm stents that were submaximal dilated to 8 mm. Forty-six consecutive patients received the VCX, and were matched by gender, age, aetiology of liver cirrhosis and MELD-score to patients who had previously received the VTS stent. The two groups did not differ in terms of blood work and history of ascites and bleeding, while the VCX group contained a higher number of HE cases.[11]

Describing the study's main findings, Dr Thomas noted: "At one year, if you look at follow-up for readmissions, you can see that there is a significantly higher readmission rate for patients with the old stent design, while with the new stent design there is a clear reduction for ascites, HE and sepsis. The same holds true for recurrence of ascites, if you implant the VCX stent at 8 mm. There are also less episodes of HE with the VCX compared to the old stent.[11]

"As you look at cardiac function, it is noticeable that patients who received VCX had a smaller right ventricular volume (a marker for cardiac load) after TIPS implantation. Left ventricular (LV) contractility

also benefits from a smaller TIPS diameter, and patients had a better LV contractility post-TIPS implantation with the VCX, while contractility actually deteriorated a little bit in the VTS group after TIPS.[11]

"All these things translate to better transplant survival in the VCX group compared to the VTS group after one year, with a P-value of 0.03."

Dr Thomas concluded that the findings of this study corroborates pre-existing evidence from the Bonn-Freiberg registry that smaller TIPS diameter leads to improved survival. He added: "When we talk about 'smaller', I mean 8 mm, not 6 mm, as we have seen that 6 mm is probably too small.

"The advantage of VCX is that you have a smaller diameter at the beginning. You can begin with 8 mm, but you can always increase it as needed, so that you probably won't run into the situation where you need to occlude the stent or put in a reduction stent."

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# First presentation of global, real-world Lutonix data

The prospective, single arm multicentre Lutonix real world registry aims to demonstrate the safety and assess the clinical use and outcomes of the Lutonix drug-coated balloon (DCB; BD, USA) for the treatment of stenosis or occlusion of native below-the-knee (BTK) arteries in a heterogeneous patient population in real world clinical practice[1].

Two-year results of the Lutonix registry were presented by Dierk Scheinert (University Hospital Leipzig), who is the study's co-principal investigator alongside Michael Lichtenberg (Klinikum Arnsberg, Germany).

"The Lutonix registry was carried out in parallel with the randomised clinical trial (RCT)[2]," Professor Scheinert told the LINC audience. "Its total enrolment was 371 subjects at 26 international sites in 11 countries.

"The inclusion and exclusion criteria were relatively closely matching those of the RCT, [including] Rutherford 3–5 patients. The requirement was that lesions could be stenotic or occlusions below the knee (BTK), but the vessel had to reconstitute at the ankle. So, below the ankle disease was excluded."

Lesions were included with ≥ 70% stenosis, with target vessels reconstituting above or at the ankle. Exclusion criteria included neurotrophic ulcer, heel pressure ulcer or ulcer potentially involving calcaneus of the index limb.

*"This is a real world population, far beyond the short lesions that are otherwise typically studied in RCTs."*

**Dierk Scheinert**

The primary safety endpoint was a composite of freedom from BTK major adverse limb events and perioperative death at 30 days. The primary efficacy endpoint was freedom from target lesion revascularisation (TLR) at six months.

Secondary endpoints included reintervention for the treatment of thrombosis of the target vessel(s), reintervention for embolisation to distal vasculature, unexpected device or drug-related adverse events, change or improvement in Rutherford class of the target limb, and freedom from all-cause death.

"Baseline clinical characteristics were typical features of a challenging critical limb ischaemia (CLI) cohort with BTK disease," said Professor Scheinert, noting that 63.9% of patients were diabetic. 65.4% of patients were Rutherford 5, 10.5% were Rutherford 4 and 24.1% were Rutherford 3.

Professor Scheinert continued on to describe lesion characteristics. "Most of the treatments were carried out in the anterior tibial artery. That is something that we typically see. And then there is a spread between the posterior tibial, peroneal and tibioperoneal trunk arteries."

"The total target lesion length was 12 cm on average, which I think is showing that this is a real-world population, far beyond the short lesions that are otherwise typically studied in RCTs. Calcification was present in 68% of lesions.

Six-month results have previously been published[3], while at LINC 2020 the 24-month results were discussed. On Kaplan Meier analysis of freedom from primary safety events, Professor Scheinert commented: "I think [these are] very respectable. There is a very high rate of freedom from such events – 98.4% at the two-year time point – reinforcing that this treatment was really safe in the hands of these operators."

He continued: "In terms of efficacy, freedom from TLR was 78.9% at the two-year time point. Beyond the one-year timepoint, there have been relatively few additional events being recorded; the curve seems to flatten quite nicely. So for those patients who didn't have early events, a good durability is demonstrated."

Going on to discuss secondary endpoints, he noted a rate of freedom from major amputation of 93.4%, and a rate of freedom from reintervention for distal embolisation of 100%.

On the subject of all-cause death, he said: "Of course, in such a challenging CLI cohort, we have to expect a higher death rate than what we typically see when we discuss claudicants. At the two-year time point, we had a total survival rate of 80.5%, which I think is in line with previous reports of such cohorts.

"The Rutherford [category] improvement was impressive. Many patients improved by several levels of Rutherford category. In fact, 81.9% improved by at least one Rutherford category, and 59.5% improved by three or more Rutherford categories. So the fact of the treatment was, from a clinical standpoint, impressive.

"In summary, this was a safe treatment."

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# Treating genetic aortic disorders with endovascular techniques?

Tilo Kölbel (German Aortic Centre, University Heart Centre Hamburg, Germany) questioned the dogma that rejects the use of endovascular treatment of connective tissue disorders during a session on the latest techniques for endovascular repair of thoracoabdominal aneurysms and the management of aortic ruptured or infected aneurysms.

Connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome and Loeys-Dietz syndrome are associated with aortic aneurysmal disease that often first manifests at a young age. Marfan syndrome, for example, comes with cardiovascular manifestations including progressive dilatation of the aortic root, as well as descending thoracic and abdominal aortic dilatation.[1]

Speaking to the *LINC Review*, Dr Kölbel explained that the traditional mainstay of open surgical repair for patients with genetic syndromes leading to thoracoabdominal disease is gradually giving way to endovascular repair in well-selected patients managed at experienced centres.

The reasons underpinning this shift are several, as he explained. "Open thoracoabdominal surgery is a very invasive procedure, which carries a significant morbidity and mortality and is usually only feasible in very young and fit patients. But fewer and fewer surgeons are able to do this.

"Another disadvantage besides its invasiveness is the cost of this procedure, which comes from the significant intensive care that is needed by these patients, even though the implant is cheaper compared to [those of] modern endovascular techniques.

*"The reality is that these patients are frequently older, and they very frequently have had multiple previous operations."*

**Tilo Kölbel**

Patients are also more frequently discharged to nursing homes and have ongoing disabilities related to that kind of surgery. Endovascular repair is associated with much less trauma."

It is within the context of this shift away from open repair that certain traditionally held views about patients with genetic aortic syndromes deserve equal questioning, explained Dr Kölbel.

One such view is that these patients do not react well to endovascular grafts, because of the nature of their native vessels being less resistant to the radial forces that form the mechanism by which grafts achieve sealing. However, Dr Kölbel noted that such an issue is complex: different genetic aortic syndromes are more or less vulnerable to this phenomenon; in addition, other factors play a role, such as the location of the graft's landing zones.

Another misconception surrounds the notion that such patients are young and fit and able to tolerate open surgery: "I would call this a dogma," said Dr Kölbel. "Today they get to much older ages. And they also require treatment of aortic disease in the stage and age when they are no longer fit for open surgery."

As examples of further dogmas, he cited the notions that patients with genetic aortic syndrome patients do not tolerate stent grafts in native landing zones, and that endovascular therapy cannot offer good long-term results.

"That is what everybody has been thinking for a long time," Dr Kölbel said. "And these ideas are built on the very early experience, in which first generation devices were used in patients with genetic aortic syndrome without good technique, without good knowledge – with catastrophic results."

Further detailing the experience of patients with genetic aortic syndromes today, Dr Kölbel explained: "The reality is that these patients are frequently older, and they very frequently have had multiple previous operations. Many of them are cardiopulmonarily compromised. These are not the young fit patients the cardiac surgeon sees for the first time. So they may also benefit from less invasive repair.

"Open thoracoabdominal repair is not well tolerated by these patients, and they are often turned down for open repair. Even the surgeons that advocate open repair turn down a significant number of them, because they say they are not fit enough."

He added: "Patients with genetic aortic syndromes also request minimally invasive

treatment, because they have frequently had difficult experiences with open surgery.

"Even the experts, when they report their results, show that it has a significant mortality. And this is something that is very hard to sell, even to genetic syndrome patients. If you know one in five doesn't wake up, this is not really good enough. And these are the ones that they think can tolerate open surgery. Michael Jacobs – one of the titans of open thoracoabdominal surgery – says the thoracoabdominal surgery in genetic patients has a high risk of mortality and morbidity, but that there is no other option. The last part is what I would like to challenge, because there frequently is another option for those patients."

Dr Kölbel noted that, in his experience, patients can tolerate stent grafts well, even in native landing zones, under certain circumstances. "The landing zones are not all the same," he explained. "For instance, a landing zone in zone 2 of the aortic arch is frequently well tolerated. If the landing zone is in a straight segment, it is also well tolerated. And I have seen a significant number of patients with good long-term results with endovascular therapy."

He added that, in some patients where adequate landing zones are absent, additional surgical work can be necessary, such as debranching: "The reason we do this in the endovascular procedure is that we would otherwise need to land with the stent graft in a native vessel – but because we don't like to do this in a patient with genetic aortic syndrome, we replace this vessel first with a surgical graft, and then we land in the replaced vessel. In that way, we can mitigate the risk of landing in native vessel.

Early data on the endovascular treatment of patients with genetic aortic syndromes was collectively analysed as part of a systematic review by Böckler *et al*. (2017)[2]. These data were based largely on patients who were treated before receiving their diagnosis of connective tissue disorder, as well as patients unfit for open repair. In Böckler *et al*. (2017), the authors conclude that conservative therapy, monitoring and possibly also conventional surgical treatment should be considered standard in the management of these patients[2]. "In their meta-analysis, they found that the majority of patients needed conversion or died after endovascular repair," commented Dr Kölbel. "One of the conclusions of the study is that they should not be treated endovascularly.

"But there are also publications that show good results of endovascular repair in genetic aortic syndrome patients. As such, we should not throw out the baby with the bathwater for these patients."

Indeed, Clough *et al*. (2017) report a retrospective study of patients with connective tissue disease who underwent thoracoabdominal or arch aneurysm repair using a fenestrated and/or branched endograft in a single, high-volume centre between 2004 and 2015. No early mortality or stroke occurred in this cohort, and mid-term follow up of a mean of 3.4 years was deemed favourable.[3]

> *"We should not throw out the baby with the bathwater for these patients."*
>
> **Tilo Kölbel**

Dr Kölbel also discussed data from his centre in Hamburg, reported by Tsilimparis *et al*. (2019). In this cohort of 54 patients who underwent branched arch procedures, five had connective tissue disorders. Within this subset, no deaths occurred (while overall in the cohort of 54 patients mortality was 6% [n = 3]) and one patient had a stroke (in the overall cohort the stroke rate was 11% [n = 6]) within 30 days.[4]

More recently acquired data is in preparation for publication*, Dr Kölbel noted, of 30 patients treated endovascular in Hamburg over an eight-year period (2010–2018). The majority of these patients had Marfan syndrome (n = 23), while others had Loeys-Dietz syndrome (n = 5) or Ehlers-Danlos syndrome (n = 2). "I don't think anything like this has been reported, because we also did six complex procedures in those patients," commented Dr Kölbel. "The types of disease treated where aneurysms and dissections, and a significant proportion of those were urgent treatments for rupture or symptoms."

Summarising the treatment strategy adopted in Hamburg, he continued: "We consider endovascular treatment as a first option in all genetic patients if it can be done without significant risks. We prefer endovascular treatment in all genetic patients when EVAR can be done by bridging graft-replaced aortic segments (landing with an endovascular graft in previously-grafted aorta is a safe thing to do, and the genetic patient is no different to any other patient in this case).

"Another conclusion is that zone 2 in the aortic arch, in my experience, seems to be a relatively stable landing zone in genetic patients, as we have not seen significant problems as long as we use non-bare stent devices. In contrast to other patients, the oversizing should probably be somewhat lower, and we should take even more care to land in straight aortic segments, because landing in curvature is dangerous due to the excessive forces in the outer curvature."

An important part of the recipe of successful endovascular treatment in genetic syndromes, he stressed, is good patient selection, as well as knowing which devices work and do not work. He further emphasised that treatments of genetic aortic syndromes should be centralised to aortic centres that can offer these treatment options: "There is some necessary experience with these techniques too, and there are not too many centres that can offer that."

He concluded: "There is no place for dogma in aortic surgery. Patients with genetic aortic syndromes should be offered contemporary, minimally invasive techniques when justifiable."

* At the time of LINC, January 2020.

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# Pedal-plantar loop techniques: Lessons from a maestro

Below-the-ankle revascularisation and the pedal-plantar loop (PPL) technique was discussed by Marco Manzi, director of the Interventional Radiology Unit at Foot & Ankle Clinic of Policlinico Abano Terme (Padua, Italy).

Dr Manzi, who spoke via satellite from Abano Terme, has specialised in diabetic patients with critical limb ischaemia (CLI) and wounds of the foot since 2001. "In our regional referral centre we treat more than 800 diabetic patients with CLI and wounds every year, following the multidisciplinary approach model," he said in conversation with the *LINC Review*. "That's why we have been so deeply involved in extreme revascularisation procedures."

The PPL technique is such a procedure, said Dr Manzi, who talked about the origins of this particular technique, especially about the father of the technique, Dr Lanfroi Graziani, who performed the first case in 2005. He also described the story of how the technique was developed, as well as the importance of the PPL or arch reconstruction, together with its limitations.

As Dr Manzi underlined, recent articles stress the importance of focus on the pedal arch. One study [1] found that patients with CLI who underwent pedal artery angioplasty (PAA) showed a higher rate of wound healing and shorter time to wound healing, especially in the moderate-risk population.

Another study [2] reported on clinical implications (wound healing, time to healing, and survival) according to the pedal arch status at the end of an infrainguinal endovascular procedure. It concluded that the pedal arch status has a positive impact on time to healing, limb salvage, and survival in diabetic patients with foot wounds undergoing infrainguinal endovascular revascularisation. "The authors underline the improvement in patients' wound healing whenever the patency of the arch is achieved," explained Dr Manzi.

Importantly, there is another study[3] where researchers retrospectively reviewed 1,915 limbs of 1,613 patients with symptomatic peripheral artery disease (PAD) who underwent angiography between September 2009 and November 2013. Here, they hypothesised a scenario where two different diseases might be present in PAD patients, big artery disease (BAD) and small artery disease (SAD), overlapping at the foot level. The study looked for prevalence and correlation with risk factors and CLI.

Interestingly, the researchers found SAD in 414 patients (25.2%) and that SAD was strongly and independently associated with CLI, diabetes and dialysis. "Thus, SAD should be regarded as a leading actor in CLI," they concluded.

And, here is where the PPL technique has its limitations, according to Dr Manzi. "The authors explain how it is not efficient in patients with disease of the small vessels in the forefoot [i.e. SAD] because of the failure of the blood distribution system in the foot," he said.

*"Whenever there is a clinical need for wound healing, we should try to achieve arch revascularisation."*

**Marco Manzi**

That's why it's critical to distinguish between patients said Dr Manzi. "We must consider the difference in disease between the SAD and BAD patient when approaching revascularisation procedures," he explained. "For SAD patients, traditional endovascular treatment is of no value."

In his his talk, Dr Manzi described a case that may help further understand the concept of treating SAD. Specifically, he discussed a patient where it had been possible to reconstruct the arch, but with a very bad clinical outcome.


Given the outcomes for such patients, Dr Manzi argued that considerable research is required today to explore alternative revascularisation techniques. "Determining the value of deep (foot) vein arterialisation (DVA) is actually one of the main research topics now," he said. "It is an alternative treatment for SAD patients defined as no-option patients."

DVA might be an option for CLI patients facing amputation. Indeed, in patients with no outflow distal targets permitting bypass, DVA involves creating a connection between a proximal arterial inflow and a distal venous outflow in conjunction with disruption of the vein valves in the foot.[4] This helps blood flow to reach the foot, resolve rest pain and promotes healing of a chronic wound. DVA requires much more research, however, said Dr Manzi. "Of course there is still little clinical data and absolutely

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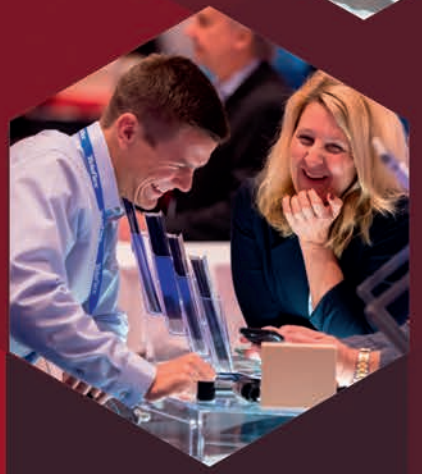

# Pedal-plantar loop techniques: Lessons from a maestro

*Continued from page 44*

no randomised controlled trials," he remarked.

In the future, Dr Manzi would like to see more consistency in treatments: "The amount of calcium and the length of occlusions represents the main limitations for every below-the-knee, -ankle and PPL procedure and really, it's always a challenging situation," he explained. "I would like to see the standardisation of both the traditional procedure and DVA too; only with standardisation we can properly evaluate the value of techniques and clinical outcomes."

Dr Manzi explained how standardisation might be achieved. "To standardise a procedure means starting from the diagnostic angiogram," he said. In other words, using the right projections to evaluate anatomical conditions and variations is crucial, as is using the proper amount and injection pressure of contrast medium or carbon dioxide. "Standard flowcharts in decision making processes and crossing strategies are important as well the use of devices," he explained.

*"We must consider the difference in disease between the SAD and BAD patient when approaching revascularisation procedures."*

**Marco Manzi**

In conclusion, Dr Manzi emphasised the importance of focus on the PPL technique. "Whenever there is a clinical need for wound healing, we should try to achieve arch revascularisation," he said. "However, we must avoid it in SAD patients who probably need a different treatment such as DVA."

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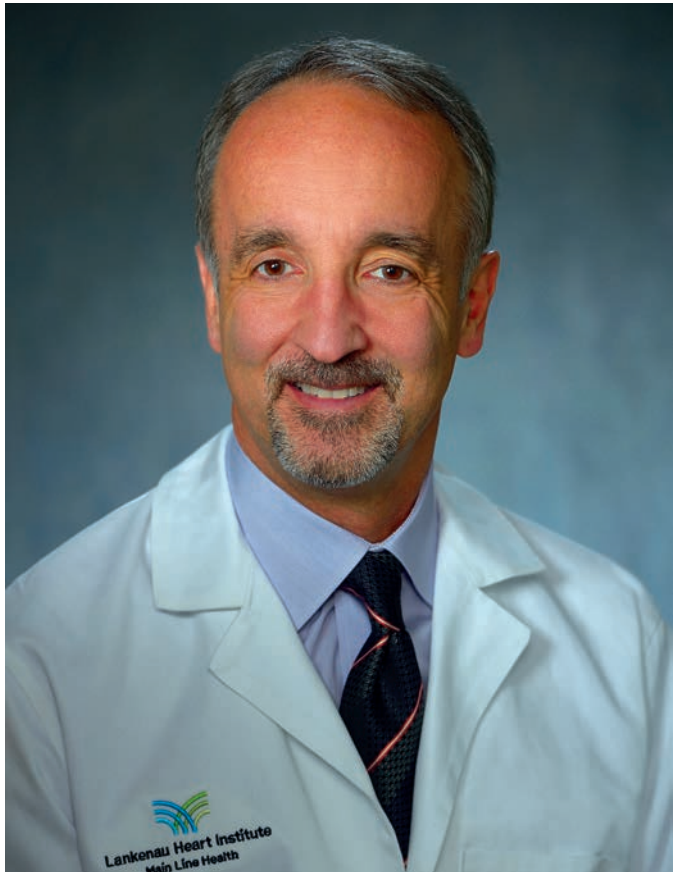
# TOBA trials round-up: An impressive Tack record

William A Gray (Lankenau Heart Institute, Wynnewood, Pennsylvania, USA) presented the latest findings from clinical trials of the Tack Endovascular System (Intact Vascular, Inc., USA) for post-percutaneous transluminal angioplasty (PTA) dissection repair.

The Tack System is a purpose-built device that addresses the issue of focal lesion dissection following PTA, such lesions reportedly being three and a half times more likely to require revascularisation than lesions without dissection[1].

Dr Gray began by comparing Tacks to stents, noting that the latter have both biological and clinical drawbacks. "It is pretty clear that lower outward force is more biologically inert, and the Tack has been designed to be like that. I think that explains a lot of the positive outcomes."

First results of investigations of the Tack in above-the-knee (ATK) dissection emerged in 2016 with the Tack Optimised Balloon Angioplasty (TOBA) dissection repair trial from Bosiers *et al*.[2] This was followed by the pivotal IDE TOBA II trial, which again focussed on ATK dissection repair following either PTA or Lutonix drug-coated balloon (DCB; BD/Bard, USA)[3]. TOBA III investigated its performance following treatment with the IN.PACT Admiral balloon




(Medtronic, Ireland)[4].

Investigations of a Tack device custom-built for below-the-knee (BTK) dissection include the TOBA BTK and TOBA II BTK studies[5].

Dr Gray discussed in detail the study design and findings of TOBA II. "This is the first trial to enrol only 100% dissected vessels," he said. "All patients had to have a qualifying post-PTA dissection. That is unique in this trial. In most DCB trials, this has not been an inclusion."

The prospective, single-arm, multicentre TOBA II study enrolled 213 patients. Safety and efficacy endpoints were very similar to standard ATK trials, explained Dr Gray. In addition, the target lesion set was fairly typical, with an approximately 7.5 cm lesion length, and around 60% moderate to severe calcification. Around 40% of patients were diabetic.

He continued: "This trial differs from TOBA III in that a little more than a third of the patients had balloon angioplasty alone with the Tack, and then the other folks had Lutonix DCB angioplasty with the Tack. This is because there was still a transition going on in the US from plain old balloon angioplasty (POBA) to DCB, and we had to accommodate all the investigators."

> *"It is pretty clear that lower outward force is more biologically inert, and the Tack has been designed to be like that."*
>
> **William A Gray**

Both primary endpoints were met at 12 months, with Kaplan-Meier primary patency and freedom from clinically driven target lesion revascularisation (CD-TLR) at 79.3% and 86.5%, respectively. In addition, no device fractures or clinically significant migrations occurred, and significant improvements were noted in Rutherford category, ankle-brachial index, and quality of life.

"There were two dissections per patient," detailed Dr Gray. "Of those dissections, more than two thirds of them were of a severe grade (greater than C). After Tack was implanted, 92.1% of them resolved completely without further evidence of dissection on angiography. The bailout stent rate in TOBA II was 0.5% (1/213). There was one patient with one stent placed. All of the other 212 patients didn't require a stent to achieve their dissection relief. There was only a 0.1% migration of a Tack, which moved just a tick."

Moving on to discuss analysis of a complex lesion subset, Dr Gray explained: "The DCB group in the TOBA II trial was similar in patency to the LEVANT II trial[6], which was the predicate comparator. In a POBA lesion set, which was about the same level of complexity as the POBA arm of the LEVANT II trial, the patency rate was significantly higher at 89.6%. For a non-antiproliferative drug group, this was quite remarkable."

Dr Gray also briefly discussed TOBA III, which had a similar trial design to TOBA II except that all patients had been treated with the IN.PACT Admiral. In this trial, mean lesion length was around 10 cm, and long lesion lengths were also included (around 22 cm in length),

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# TOBA trials round-up: An impressive Tack record

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half of which were chronic total occlusions. At one year, 97.7% of dissections in the standard lesion set were resolved, and 98.8% in the long lesion subset. The bailout stent rate was 1/169 (0.6%) in the standard lesion group and nil in the long lesion subset. Primary patency in the standard lesion set was 95% at one year, and freedom from CD-TLR was 100%. In the long lesion subset, almost 90% of patients had primary patency at one year, and freedom from CD-TLR was 97%.

"The TOBA II BTK set of data is similarly remarkable," Dr Gray went on. Six-month data from the prospective, single-arm TOBA II BTK study were presented at VIVA 2019[5]. The study included 233 patients treated at 41 international sites. "The Rutherford classification was largely Rutherford 4 and 5. There was a fairly significant number of smokers and diabetics with chronic renal insufficiency, in about one quarter of the patients."

Detailing the core-lab adjudicated angiography at baseline in TOBA II BTK, Dr Gray noted the significant vessel tapering of BTK vessels: "The proximal and distal disease segments were materially different in terms of their diameter. The Tack is designed to treat from 1.5 mm up to 4.0 mm diameters, so you can have a variability and still use the same device."

Highlighting key results, he added that, at six months, the bailout stent rate was 1.3% overall, and < 1% within Tack segments. The Tack dissection resolution rate was 100%. Safety and efficacy endpoints were met. The Tack segment patency and target lesion patency rates were similar at almost 88%. Target limb salvage and freedom from CD-TLR were 99% and 92%, respectively.

Dr Gray concluded with a reiteration of the benefits the Tack confers alongside its impressive performance in dissection resolution: "The Tack preserves future treatment options. And, in my lab, because it has one stock keeping unit, we don't have to order different types of Tacks to treat ATK and – hopefully it is soon to be approved – BTK lesions."

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*"The Tack preserves future treatment options."*

**William A Gray**

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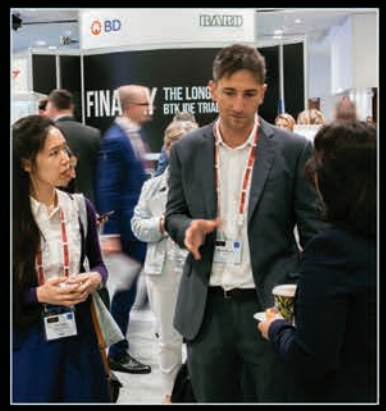




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# First-time results from COMPARE trial revealed at LINC

One-year results from the COMPARE trial were showcased on the first morning of LINC, shedding new light on the impact of high- vs low dose paclitaxel in drug-eluting balloon (DCB) treatment of femoropopliteal disease. Presentation of the first-time data came on the same day as publication of the results online in the European Heart Journal.[1]

The COMPARE trial is a prospective, multicentre, non-inferiority, clinical trial of 414 patients with symptomatic femoropopliteal lesions (Rutherford classification 2–4) randomly assigned in a 1:1 ratio to endovascular treatment with either the low-dose (2.0 µg/mm$^2$) Ranger DCB (Boston Scientific, USA) or high-dose (3.5 µg/mm$^2$) IN.PACT Admiral or Pacific DCBs (Medtronic, Ireland). Patients were stratified according to lesion length (≤ 10 cm, > 10 cm and ≤ 20 cm, > 20 cm and ≤ 30 cm) in order to ensure inclusion of a relevant proportion of complex lesions.

Talking through the results of COMPARE was Sabine Steiner (University Hospital Leipzig), who introduced the genesis of the trial. "Currently marketed DCBs have been designed based on a similar functional concept using paclitaxel as the active drug, together with an excipient to facilitate the release and transfer of the drug to the vessel wall," she told the *LINC Review*. "Besides drug dose, the drug and excipient formulations used in their coatings, and the manner in which coatings are applied to the balloons differ between commercially available DCBs."

The coating technology and formulation of the active drug may affect the extent of drug delivery and clinical efficacy, she added, particularly the dosing of paclitaxel which could have a relevant impact on the antiproliferative capacity of these devices.

"Comparability between trials is limited as lesion characteristics and bailout stenting rates differ substantially," continued Dr Steiner, "and it is unclear thus far if heterogeneity between DCBs translates to meaningful clinical differences. Prior meta-analyses[2,3] have suggested such an effect: reduced restenosis and target lesion revascularisation (TLR) rates were suggested for high-dose DCBs based on these analyses."

COMPARE was born out of the realisation that comparative effectiveness of high- vs low-dose DCBs has not been tested within a clinical trial. Its primary efficacy and safety endpoints comprised of primary patency and freedom from major adverse events (i.e. device and procedure-related deaths through one month, major amputations, and clinically driven TLR through 12 months).[1] A non-inferiority margin of –10% at 12 months was set.


*"This was the first head-to-head comparison of two DCBs with different paclitaxel dosages and coating technologies for femoropopliteal interventions."*

*Sabine Steiner*

Total occlusions were observed frequently (> 40%) and provisional stenting was performed in every fourth intervention, noted Dr Steiner. Non-inferiority was determined for both primary efficacy and safety endpoints at 12 months. Patient demographics included a mean age of 68 years, around two thirds male, one third diabetics and current smoking in over 40% of patients. Mean lesion length was > 12 cm, with around 40% incidence of chronic total occlusions (CTOs). Calcification Grade 3 or 4 according to PACSS criteria was present in > 50% of lesions.

Dr Steiner dived into the results: "Procedural success was observed in 96% of patients, defined as residual diameter stenosis of ≤ 50% determined by angiographic core laboratory, without device malfunction and without procedural complications.

"The primary efficacy and safety endpoint met non-inferiority[1]. Primary patency was 81.5% in

the high-dose and 83.0% in the low-dose DCB group (difference: 1.5% [lower bound of the 90% two-sided confidence interval {CI} -5.2%]; P non-inferiority < 0.01). Freedom from major adverse events was determined in 92.6% of the high-dose and in 91.0% of the low-dose DCB groups (difference -1.6% [lower bound of the 90% two-sided CI -6.5%]; P non-inferiority < 0.01).

"Overall death rate was low (2.0%), and no major amputation occurred."

Briefly touching upon the limitations of COMPARE, Dr Steiner noted that the study was solely designed to assess non-inferiority for primary patency and a combined safety endpoint but not for functional outcomes. What's more, use of dedicated lesion-modifying devices was discouraged by the study protocol, but these therapeutic options are commonly used in clinical routine, thereby limiting generalisability of study results. "A general shortcoming of DCB- and other peripheral device trials is the lack of blinding of the operator who is responsible for all procedure-relevant decisions," she added.

> *"Primary patency was 81.5% in the high-dose and 83.0% in the low-dose DCB group."*
>
> **Sabine Steiner**

Turning back to the outcomes of COMPARE, Dr Steiner reiterated its take-home messages: "This was the first head-to-head comparison of two DCBs with different paclitaxel dosages and coating technologies for femoropopliteal interventions. Both the low-dose DCB (Ranger 2.0 µg/mm$^2$) and high dose DCB (IN.PACT 3.5 µg/mm$^2$) showed excellent primary patency and low TLR rates, and the primary endpoints for non-inferiority were met.

"Low mortality [was seen] at one year. Follow-up is now ongoing for up to five years."

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# Emerging data on cutting-edge approaches in CLTI

One-year results from the DISAPEAR registry[1] evaluating the Absorb bioresorbable vascular scaffold (BVS; Abbott Vascular, USA) were presented by by Steven Kum (Changi General Hospital, Singapore).

The DISAPEAR registry evaluated the safety and effectiveness of the Absorb BVS in an Asian cohort exclusively with chronic limb-threatening ischaemia (CLTI).[1]

"Metallic drug-eluting stents [DES] have been shown to be effective in short lesions in the short term," Dr Kum told the *LINC Review*. "The BVS offers the advantage over bare metal stents of leaving no permanent implant behind."

DISAPEAR was a single centre retrospective analysis including 41 patients classed with CLTI at Rutherford 4 (n = 3 [7%]), 5 (n = 23 [56%]) and 6 (n = 15 [37%]) treated with BVS between 2012 and 2017. Patients were complex: 90% had diabetes mellitus, 12% were on dialysis, and 93% had experienced tissue loss. In total, 53 lesions were treated with 69 scaffolds. Mean lesion length was 22.7 ± 17.2 mm (range, 4–88 mm). Median stenosis was 88%. Focal calcification was present in 50% of lesions, and 24% of lesions were severe.[3]

Technical success was achieved in 100% of cases. Primary patency was 95% at six months and 86% at 12 months (ascertained by duplex ultrasound peak systolic velocity ratio < 2.0). Freedom from clinically-driven target lesion revascularisation (CD-TLR) was 98% at six months and 93% at 12 months. Amputation-free survival was 93% at six months and 85% at 12 months, whereas limb salvage was 98% at both six and 12 months. Complete wound healing was achieved in 79.5% of cases at 12 months, with a median time to wound healing of four months.[3]

Compared to previous study, Dr Kum noted that similarly favourable short- and medium-term results were achieved in DISAPEAR, with slight variation in patient and lesion characteristics between cohorts. "If you look at the data out there for peripheral BVS, there are two other centres running similar studies. The first is from Ramon Varcoe[4], and the second is from a US site by Atman Shah[5]. Our data will be published over the next few months.

"In the cases that we have done, we have had a high proportion of patients with CLTI and complex, calcified lesions. Our patients had complex comorbidities, with a high proportion of diabetes and renal failure. We believe that this provides a snapshot of the experience of the BVS in patients with 'real world' CLTI.

"Collectively, the experience of BVS approaches 150 treated patients. We seem to be getting a fairly consistent experience with the BVS in terms of the ability to maintain primary patency. This has also translated into a good clinical result in these three centres."

*"We seem to be getting a fairly consistent experience with the BVS in terms of the ability to maintain primary patency."*

**Steven Kum**

Long-term results of study of the BVS in treating peripheral lesions are limited to the ABSORB-BTK study of Varcoe *et al*., who published three-year results in 2018;[4] Five-year results were presented at VIVA last November, with primary patencies of 72.9% and freedom from CD-TLR of 90.7%[6].

The BVS for coronary use was withdrawn voluntarily by Abbott for a variety of reasons, as recently explored by DeRubertis *et al*. (2018)[2]. Speaking of his experience with the Absorb BVS in DISAPEAR, Dr Kum said: "We did not see similar events in the peripheral space as in the coronaries. This is primarily because the effects of stent thrombosis are not as adverse in the peripheral space as compared to the heart."

He further noted that peripheral vascular disease is more aggressive than coronary disease, with disease progression generally asymptomatic in the peripheries. Relative to the coronaries, late stent thrombosis is also less consequential, likely manifesting long after wound healing has occurred. In addition, angioplasty alone (the only on-label treatment for below-the-knee (BTK) disease alongside atherectomy) has a meagre track record in CLTI, and most specialists are reluctant to implant metal BTK.[2]

Another point of optimism for peripheral BVS lies in the improved techniques on implantation, learned from coronary use. "Although there haven't been any major changes

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# Emerging data on cutting-edge approaches in CLTI

*Continued from page 52*

to the BVS, the implantation technique has evolved," explained Dr Kum. "Implantation technique in the peripherals has taken a leap from what we have learned in the coronary space, with regards to appropriate vessel sizing and adequate predilatation and post-dilatation.

"So far the long-term data of small studies seems to suggest a best-in-class ability to maintain long-term patency. Compared to the gold standard of plain balloon angioplasty, this gives us an idea of how a DES-based platform may potentially be a viable solution for aggressive disease BTK."

Abbott has recently announced their intention to run an FDA-approved investigational device exemption (IDE) trial, to be named LIFE-BTK. This multicentre RCT, with a planned follow-up of five years, will enrol 235 patients randomised to a new-generation BVS, Esprit (Abbott Vascular), or percutaneous transluminal angioplasty (PTA).

## First time release of two-year data from the ALPS registry of LimFlow pDVA for no-option CLTI

Another BTK approach for CLTI patients – reserved for those so-called 'no-option' cases – is percutaneous deep vein arterialisation (pDVA).

ALPS is being conducted in four centres, in Alkmaar, Leipzig, Paris and Singapore, its two-year data relating to 32 patients consecutively treated between 2014 and 2018 with the LimFlow device (LimFlow SA, France). Dr Kum commented: "The results of the PROMISE 1 study were recently presented at VIVA, with promising clinical results[7]. The ALPS registry is essentially the outside-US experience to date. The clinical results seem to be fairly similar to those found in PROMISE 1."

> *"The ALPS registry is essentially the outside-US experience [with LimFlow] to date."*
>
> **Steven Kum**

Describing the ALPS two-year analysis, Dr Kum said that 78% of patients were deemed at high risk of amputation, with 31.3% classed as Rutherford 6. Technical success was achieved in 31/32 patients. Amputation-free survival at 83.9%, 71.0% and 67.2% at six, 12 and 24 months, respectively. Complete wound healing was achieved in 36.6%, 68.2% and 72.7% at six, 12 and 24 months, respectively.

This study represents is the largest of its kind, Dr Kum noted. "This was a multicentre registry with the procedure performed by radiologists, vascular surgeons, and interventional angiologists. It seems that with the dedicated device we are able to get good technical success, as well as a promising clinical result in centres with dedicated wound care."

A US pivotal trial is currently ongoing for the LimFlow device.

## DESAFINADO registry – 12-month results of the Eluvia DES in a predominantly CLTI cohort

Dr Kum also presented on DESAFINADO, the study of the drug-eluting Eluvia stent (Boston Scientific, USA) in the femoral-popliteal artery in the treatment of diabetic foot.

Launched several years ago, the Eluvia stent is based on the Innova nitinol platform peripheral stent (Boston Scientific), with a polymer coating similar to the Synergy coronary stent (Boston Scientific) lending it a prolonged, one-year drug elution profile. Dr Kum compared this design with its principal competitor, the Zilver PTX (Cook Medical, USA) which constitutes a polymer-free paclitaxel system, a higher drug dosage (3 µg/mm$^2$ versus Eluvia's 0.167µg/mm$^2$ dose density) and a short elution time of about one month. "These stents each have a very different philosophy on drug elution," he summarised.

Citing the data to date, Dr Kum discussed the MAJESTIC registry, which included 57 patients treated with Eluvia for femoropopliteal lesions with an average length of 70.8 ± 28.1 mm. The primary patency at one year reached 96.4% (according to Kaplan-Meier estimate). Improvements in the Rutherford category were sustained at one year, with 81% (43/53) of patients exhibiting no symptoms and 13% (7/53) presenting with mild claudication.[8]

Eluvia was then compared against the Zilver PTX in IMPERIAL, the global randomised controlled multicentre trial with a single-blind, non-inferiority design. Post-hoc superiority analysis of 12-month data gave a primary patency rate of 86.8% in the Eluvia arm and 77.5% in the Zilver PTX arm (p = 0.0144).[9]

Commenting on these two studies, Dr Kum said: "These studies were based on short lesions. There is actually very little study on the use of Eluvia in long lesions in real-world cohorts."

As such, DESAFINADO focused on long lesion data. This single centre, all-comer registry included a total of 67 patients with both CLTI and claudication (predominantly CLTI) treated with Eluvia for SFA/popliteal disease between September 2016 and October 2018. Lesion lengths were a median of 200 mm (range, 20–450 mm), and 48% of lesions were occlusions. Lesions occurred over the full extent of the SFA as well as P1–P3 popliteal segments.

12-month primary patency was 84% overall, and freedom from CD-TLR was 92%. At six months, amputation-free survival was 88%. Further analysis was also conducted according to lesion coverage type: in those cases with total lesion coverage with Eluvia, primary patency was 91%; with hybrid coverage using Eluvia in combination with drug-coated balloon, primary patency was 80%; and in cases combining bare metal stent or plain balloon angioplasty with Eluvia, primary patency was 42%.

Dr Kum compared these findings with those of the IMPERIAL trial long lesion cohort, where a primary patency rate of 87.9% was achieved in lesions with a mean length of 162.8 mm[10]. He also noted similar findings coming out of the Münster registry[11]: "In this fairly complex group of patients with lesion lengths around 200 mm, they were able to achieve primary patency of around 87% with good clinical results as well."

Speaking of his own clinical experience, he continued: "We started to use the Eluvia in a group of patients with, predominantly, diabetes and CLTI, and with long lesions (approximately 200 mm). As compared to prior registries, we had more diabetics, more renal failure, more CLTI – 84% of our patients had CLTI.

"When we initially looked at our results, it was encouraging to see that we were able to replicate similar patency results in a more complex group of patients with equally complex lesions. I think it is a real snapshot of the use of the stent in the real-world context."

Dr Kum concluded with his thoughts on the changing attitude towards metal in the region of the SFA: "We do know that in theSFA the treatment options have changed over the years, from bare metal stenting to DCB with spot stenting. In real world registries of DCB, such as the IN.PACT Global registry, bailout stenting rates were approaching 50%. Over the years, we have started to re-evaluate whether the 'leave nothing behind' philosophy was truly beneficial in treating these patients with aggressive disease.

"Our initial experience with DES has given us some confidence that to treat an aggressive disease in CLTI, perhaps we need a stent with a longer elution profile with a guaranteed luminal gain and a scaffold to optimise management of the inflow. Certainly, with regard to what we would do on a daily basis, our suspicions have been reaffirmed that there is a place for a DES in CLTI with long lesions."

*"To treat an aggressive disease in CLTI, perhaps we need a stent with a longer elution profile with a guaranteed luminal gain and a scaffold."*

**Steven Kum**


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# TOPOS takes on DVTs

A study looking at early outcomes of a hybrid oblique nitinol stent for post-thrombotic syndrome (PTS) patients with common iliac vein compression was presented by Christian Erbel (Department of Cardiology and Angiology at the University Hospital Heidelberg, Germany).

Professor Erbel began by recalling that the majority of iliofemoral deep vein thromboses (DVTs) are caused by iliac vein compression. In May-Thurner syndrome the right common iliac artery crosses the left common iliac vein, causing compression.

Conventionally in May-Thurner syndrome, explained Professor Erbel, a stent ends up touching the contralateral wall of the inferior vena cava (IVC). He referred to an example study of 755 patients with Wallstent (Boston Scientific, USA) extension into the IVC, along with 29 months of follow-up antiplatelet therapy[1]. Here, 10% showed a contralateral DVT. "Is it possible to get a new stent, preventing and avoiding this risk of contralateral DVT?" questioned Professor Erbel.

To avoid the risk of contralateral DVT, he suggested use of the sinus-Obliquus stent (Optimed, Germany) because of its design as a dedicated May-Thurner stent. "It has an oblique design at 35° and a close design at the proximal part to provide a high radial force against the artery," he said. "And the distal open cell design provides flexibility and less radial force which we need for the external iliac veins."


Showing a picture of the stent in place, Professor Erbel added: "It stops right in the middle of the IVC but does not touch the contralateral wall of the IVC. With this kind of stenting we hope we will have no risk of contralateral DVT."

He went on to talk about the TOPOS (Treatment of the Postthrombotic Syndrome With the Oblique Stent) Study which was initiated in 2016 to investigate the safety, efficacy and clinical outcome of this hybrid oblique stent under routine clinical conditions. TOPOS is a non-interventional, multicentre, multinational venous stent study of the treatment of PTS with common iliac vein compression. Sixty patients with PTS were enrolled. Treatment with the Optimed stent and provisional distal stent extension was allowed.

Professor Erbel previewed the three-month patency rates obtained via duplex ultrasound. Clinical outcomes were assessed using the Chronic Venous Disease Quality-Of-Life Questionnaire (CIVIQ-20), Villalta and Revised Venous Severity (rVCSS) scores.

Speaking about demographics, Professor Erbel relayed that the average age of enrolled patients was around 46 years, body mass index was 26 and, as expected, the majority were women. In addition, there were clotting abnormalities in about a quarter of the enrolled patients, and a similar proportion had multiple episodes of DVT.

About 22% had experienced a pulmonary embolism. "This shows that these types patients were quite complex and not the easy-going patients we sometimes have," he said. The assessments revealed a Villalta score of 12.2, a rVCSS score of nine, pain intensity score 3.9 and the CIVIQ-20 score was around 46 points. Excluded from the study were stents located in the IVC and patients with abnormalities in the IVC.

There were two groups; the oblique stent-only group, and those that had received a stent extension. The common iliac vein and the external iliac vein appeared in both groups and the common femoral vein was in only 88% of the stent extension group.

Professor Erbel dived into the stent details. "The mean stent number was one in the oblique stent-only group and 2.1 in the stent extension group. The mean total length was 10 cm in the oblique stent-only group and 25 cm in the stent extension group," he said.

The majority of patients in the stent extension group used the 150 mm oblique stent and the majority of the patients in the oblique stent-only group used a 100 mm stent, he added.

Primary and secondary patency after three months was 93.1% and 100%, respectively. "If you look at the symptoms and adjunctive therapy you see the Villalta score significantly decreased from 10 to 3.5 which means there is no PTS anymore," said Professor Erbel. The VCSS score reduced from 9 to 4.8, CIVIQ-20 from 46 points to 30 and the pain intensity score from 3.9 to 1.3 (highly significant).

According to Professor Erbel, with venous ulcers there was a trend towards a significant reduction from 13% to 5%. Compression therapy was initially 83% and after three months had reduced to 55%. "On average 63% were free of PTS after the treatment which is actually quite nice," he said. "No one developed contralateral DVT, as expected, and after three months this was still the case."

In conclusion, Professor Erbel reiterated that the dedicated sinus-Oblique May-Thurner stent has a high radial force at the compression site and sufficient flexibility to accommodate the anatomy of the curved iliac vein. "This stent results in a high patency rate and improvement in PTS severity and quality of life at three months," he said. The TOPOS study will continue and results of two years results will assess the durability of this treatment. Data should be out at the end of next year.

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# ‘The biggest issue is in the diagnosis’ in PCS

From Galway University Hospital, Ireland, Gerry O’Sullivan and colleagues presented a live case of treatment of pelvic venous reflux in a patient with pelvic congestion syndrome (PCS).

The patient, a 38-year-old female, had previously had two children by vaginal delivery. Her initial complaint was chronic pelvic pain, which had been investigated by a number of specialists. Her eventual referral to interventional radiology was prompted by a CT of the abdomen and pelvis that revealed dilated gonadal veins, marked para-uterine varices and a possible left common iliac vein compression.

Speaking of the difficulty some patients encounter in reaching a diagnosis of PCS, Dr O’Sullivan began: “She has seen a pelvic floor specialist, a pain specialist, and she has also seen a psychiatrist. It is sad to say, but I see this as a common pattern with PCS.

“When I was a medical student, I didn’t know anything about varicose veins in the pelvis. Frankly, I doubt it has reached medical textbooks even now. Most of my colleagues don’t know about it. So it is up to us to ‘spread the gospel’: this is a common problem in women who have full-term normal vaginal deliveries.”


*“It is up to us to ‘spread the gospel’: this is a common problem in women who have full-term normal vaginal deliveries.”*

**Gerry O’Sullivan**

Dr O’Sullivan cited the work of vascular surgeon Mark Whiteley and radiologist Tony Lopez of the Whiteley Clinic, Guildford (Surrey, UK), alongside the clinic’s chief sonographer, Judy Holdstock, in bringing PCS to the fore. He went on to explain that the underlying retrograde flow and reflux in the internal iliac veins (IIVs) and gonadal veins can be demonstrated by transvaginal ultrasound in conjunction with doppler ultrasound or, when this is not available, by CT or MR venography with history taking.

As well as varices in and around the patient’s right perineum, CT also indicated a potential iliac vein compression (May-Thurner syndrome). Addressing the issue generally, Dr O’Sullivan said: “At the moment in the US – in my view – patients are possibly getting too many iliac vein stents.

“I think you need IVUS in this situation. In post-thrombotic patients and an acute underlying lesion, there is no doubt about them needing a stent. But in female patients who have never had a DVT who come in with pelvic varices, I personally would insist upon IVUS before I place a stent. [In this case], I have consented [the patient] for it, but I don’t know if I’m going to place it or not.”

CT also indicated parametrial varices in and around the vulva and vagina, which Dr O’Sullivan noted as typically reaching the broad ligament. “On both sides you are looking for dilated gonadal veins in front of the musculature, bilaterally,” he commented, adding: “This is – unsurprisingly – something women are not keen to talk about. Frankly, most doctors probably just underplay the symptoms.”

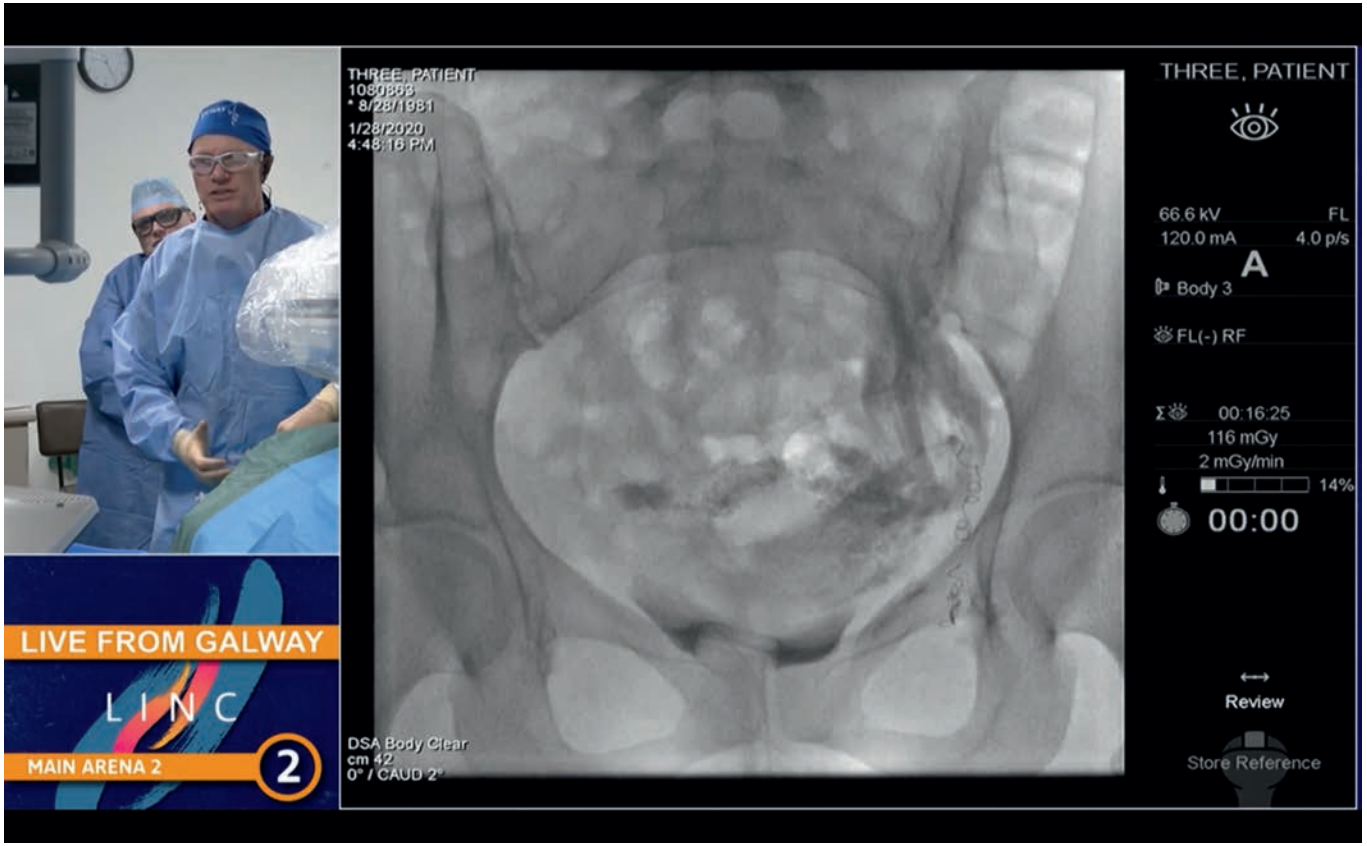
Dr O’Sullivan also emphasised the importance of clinical symptoms in diagnosing PCS: “You are not treating the picture, you are treating the patient. Our patient has appropriate symptoms for this condition. The classic for me is a woman who, when she walks into a venue, the first thing she looks for is to sit down. It is almost always gravitational, so worse at the end of the day.

*“Technically, this is very accomplishable. The biggest issue is in the diagnosis.”*

**Gerry O’Sullivan**

Patients make a sweeping motion with their hands downward, as if it is a prolapse. But often these are young women who don’t have a prolapse and who don’t have any other symptoms. You have to look for that and evaluate it.”

The patient was placed under general anaesthetic with a urethral catheter. Access was gained via the right internal jugular vein, using a 10-F, 23 cm sheath with a 5-F, 100 cm Impress Cobra catheter (Merit Medical, USA). “Our aim is to go down through the inferior vena cava into the left renal vein and down the gonadal vein, ideally into the parametrial varices, and up the right ovarian vein. If you can do that ‘loop the loop’ it is very quick, and it




Following contrast injection, left pudendal and gonadal veins were filled by foam sclerotherapy.

means you can coil from a very secure position.

"We use coils; I use non-detachable, pushable coils [MREye, Cook Medical, (USA)] for the majority of cases, and foam (Sclerovein [1%, diluted 3:1]) in the central portion. We will also take care of the pudendal varices while she is asleep, which involves typically puncturing them directly, injecting foam into the vein and possibly tumescence around that area.

"Technically, this is very accomplishable. The biggest issue is in the diagnosis."

Venography demonstrated significant cross-pelvic collaterals, as expected. Very large varices were present on the left hand side of the uterus. Additionally, IVUS was performed in order to delineate the left common iliac vein, however compression was not evident. The team's attempts to 'loop the loop' from the left to the right side via the parametrial varices proved unsuccessful. In the left gonadal and pudendal veins, as well as the right pudendal and ovarian veins, foam sclerotherapy was conducted after filling varices with contrast, and thereafter coils were placed.

Commenting on the choice of coil size, Dr O'Sullivan explained: "Compared to varicoceles, these are big veins. I don't bother using IVUS to size the coils – I find that if you just put in lots of big coils, you will get a result. I am going for big coils that aren't going to move – that is my primary objective. They will block the vein. I think getting distal is important – typically that is done with foam across the parametrial varices. At the end, we will also puncture the paralabial varices."

Asked whether he would treat May-Thurner simultaneously should it coincide with PCS, he replied: "I don't know if there is a right or wrong answer to this. But for all of the patients in whom I look for iliac vein compression and pelvic varicosities, the number that have both syndromes is relatively low. I think I've only had one in the last six months, and I probably do two of these cases per week."

He added: "Obviously if you have somebody who is post-thrombotic, it is a very different kettle of fish, because you know it has caused a big problem. But here, with pelvic vein embolisation, typically in young females, if they haven't had a previous DVT I must say I am slow to place stents. I am concerned that we could be over-treating. If I can get rid of the varices and there is no significant narrowing or wasting [of the iliac vein] then I am inclined to think they probably should not get a stent.

"We can get into the habit of thinking, 'there is a lesion – I must stent it'. I think that is wrong. We can do better than that. Clinically, you assess the patient multifactorially."

# AAA, endo or open? It's about nuance, volume & experience

A comprehensive roundup of available evidence on treating ruptured aortic abdominal aneurysms (AAAs), using either open or endovascular means, was provided by Dittmar Böckler of the department of vascular surgery at the University of Heidelberg, Germany.

"Since the first EVAR was performed ... this modality to treat ruptured aneurysms has become more and more available, and is used in many centres," he said.

He commented on the increasing numbers of hybrid open repairs and stent grafts: "EVAR became a really complementary treatment option for AAA rupture. If wisely selected, having both methods in one setting and one hospital is, I think, worthwhile. [We can] apply those two different approaches to our patients."

Comparing the two techniques should not be about which approach beats the other, positioned Professor Böckler: "It's about when to use which method." To prove this hypothesis, he has looked at available evidence including a meta-analysis, one Cochrane study and five randomised trials. "There are more than a hundred closed controlled studies if you look carefully in the literature," he added.

For example, a cohort study published 11 years ago[1] collected data from over a 1,000 patients at 49 centres. The overall mortality was 21.2% and the conclusion of this paper was that EVAR showed lower procedural mortality. It reported 19.7% for EVAR versus 36.3% for open. In other words,

> *"Evidence is not for or against open versus endo. Both are complementary, especially for morphologically suitable patients."*
>
> **Dittmar Böckler**

EVAR is highly significant in what Professor Böckler calls a favourable anatomy. "But in an unfavourable anatomy what are you going to do? That's the point. There is still room for open," he reasoned.

Professor Böckler went on to note that four of the most important randomised trials showed no survival benefit when comparing EVAR and open. "They concluded that both treatment options are available and should be offered to patients," he said. The well-known IMPROVE trial agreed with the others,

showing no difference in 30-day mortality between EVAR and open[2], but in the longer term[3] there was a difference. "At three years there was a significant difference in favour of EVAR," he said, adding: "[And] women may benefit more from EVAR than men. We need complementary treatment options."

Professor Böckler looked at a meta-analysis[4] of three well-known randomised trials – AJAX, ECAR and IMPROVE, totalling 836 patients – and found no real difference in 90-day survival. Furthermore, a Cochrane review[5] looked at 30-day mortality and major complication rates. "This moderate-quality evidence suggests no difference between open and endo regarding early mortality," he added. Long-term data was not available through Cochrane review, he noted.

Strong data supporting the importance of experience, volume and protocols does exist, however, according to Professor Böckler, showing data from Matt Thompson, previously of St George's Hospital Trust (London, UK). "A low-volume capacity hospital has higher mortality, after EVAR and even after open," he said. "In a low-volume and low-bed capacity hospital, you also have a high turn-down rate – you find patients who have not been treated either open or endo."

Hospital volumes influence the method of treatment, too. "The higher the volume you have, the more likely you use endovascular techniques, so there is a biased selection of the modality you use to treat ruptured AAA," said Professor Böckler.

Surgeon volume also plays a role. A paper examining 5,972 open and 8,121 EVAR interventions[6] established that surgeons conducting low volumes of interventions saw a higher mortality rate of 8.7% compared with high-volume surgeons whose cases averaged a 3.3% mortality rate. Other papers suggest mortality varies with country and territory too.

"The question is what's the benchmark or threshold or the cut-off?" said Professor Böckler. "This is being answered by the European Society for Vascular surgery (ESVS) guidelines, with good evidence for open, but less for EVAR."

He added: "I think one of the conclusions is that volume does

matter, as does experience."

On the topic of centralisation, Professor Böckler said many papers show increased specialisation, and improved outcomes. "General surgeons have less experience, especially in endovascular techniques – they do less good than vascular surgeons," he said. As such, he recommended a management protocol for each hospital treating patients for endo and open, as well as protocols for the emergency room and in the selection of patients. "You need infrastructure. I think the hybrid operating room is required these days to treat these patients properly," he said.

*"For women, EVAR may be better, but we need open surgery in our armamentarium."*

**Dittmar Böckler**

Education and training in a teaching hospital is key, continued Professor Böckler. "Theory alone will never teach you how to swim," he said, noting that the recommended yearly caseload, published in the European guidelines, stands at a minimum of 30 repairs per year, per hospital. "If you do less than 20 you should not do it at all," he added.

Professor Böckler framed his concluding remarks: "Evidence is not for or against open versus endo. Both are complementary, especially for morphologically suitable patients. For women, EVAR may be better, but we need open surgery in our armamentarium for the treatment of AAA, and we need infrastructure and experience in high-volume centres."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# DETOUR into long lesions

## A viable alternative to open fem-pop surgery

Peter A Schneider is a vascular surgeon within the Division of Vascular and Endovascular Surgery at the University of California, San Francisco, USA. At LINC 2020, he focused on an important ongoing trial of the DETOUR System (PQ Bypass, Inc., USA) for femoropopliteal bypass. "I've been involved in a number of different methods to tackle femoropopliteal lesions and one of them is the DETOUR System," Dr Schneider told the *LINC Review*. "I think it has the potential to be the next generation for bypass."

The DETOUR System, under fluoroscopic guidance, deploys a series of stent grafts from the popliteal artery into the femoral vein, and from the femoral vein into the superficial femoral artery (SFA) in a continuous, overlapping fashion through two independent anastomoses.[1] The intended result is a large lumen, endograft bypass that delivers unobstructed, pulsatile flow from the SFA ostium to the popliteal artery.[1]

Important to realise, added Dr Schneider, is that the PQ Bypass system does not compete with endovascular solutions: "This is not just another endovascular procedure – you are going after lesions that have never been considered for endovascular treatment before. It's competing with femoropopliteal bypass – which is an important aspect of open vascular surgery."

During his presentation, Dr Schneider talked about the latest investigational device exemption (IDE) study of the DETOUR System, dubbed the US IDE DETOUR II Clinical Trial, recruiting across 37 sites in the US, Germany, Poland and Latvia.* As is standard for IDE trials, the study is bound by strict guidelines, including the minimum number of patients to be included. The primary endpoint is patency at one year. Secondary endpoints are focused on follow-up for deep vein integrity, noted Dr Schneider. "It's making nice progress," he said, relaying that more than half of the enrolment is now complete.

Importantly, what makes this trial an exception is that the average lesion length is 35 to 40 cm. "In that sense, this is dramatically different from other types of endovascular procedures where the lesions are typically much shorter. This has never been undertaken previously with any kind of endovascular procedure. You can see why this is a special trial."

*"This is not just another endovascular procedure – you are going after lesions that have never been considered for endovascular treatment before."*

**Peter A Schneider**

Importantly, many different specialties have embraced the DETOUR procedure, added Dr Schneider. "It's not just vascular surgeons, it's also interventional cardiologists, interventional radiologists and angiologists."

Having several specialties involved hastens the evolution and refinement of the procedure, continued Dr Schneider: "Procedures get to the right patients a little quicker if there are multiple specialties collaborating on the development of it. I think that's the case here, which is a good thing.

"Whenever we have a new procedure, we have a developmental timeframe during which we can really get used to the practice. This being a multistep procedure, it took a little time, but now it's routine for these cases to be done in two hours or less." That duration competes favourably with open bypass patients, noted Dr Schneider, with patients typically being treated as outpatients.

Grzegorz Halena from the Medical University of Gdansk (Poland) and Dainis Krievins from the Pauls Stradins Clinical University Hospital, the University of Latvia (Riga, Latvia) were instrumental in developing this procedure, Dr Schneider went on: "They found out what works, what was most expeditious and what needs to be done to

make it successful. They have both been terrific to really push this forward from a clinical standpoint."

Should the device be FDA approved, Dr Schneider foresees a change in the way bypasses are approached worldwide. "There's still a substantial number of lower extremity surgical bypasses done in the United States, as well as in other countries, and I think that those numbers will decrease because some of those patients will go on and have a bypass with the DETOUR System," he said. "I can picture a situation where DETOUR could be good enough to really replace open bypass in a lot of patients, or it could be used in patients that need a fem-pop bypass, but just can't because of other risk factors."

*"This is a procedure that's really extending what we can do with endovascular therapies."*

**Peter A Schneider**

Certainly there may be a new set of patients who could receive the DETOUR System that would not previously have qualified for open surgery. That includes the kind of critical in-patient who may have been put forward for amputation because an open bypass would be too risky. So, on the one hand it could potentially compete directly with the established procedure, but on the other hand it may broaden the scope of patients who may be treated because in the past, for a 35 or 40 cm lesion, there would be limited options, said Dr Schneider.

Other patient groups might also see additional benefits from DETOUR II, he noted. As an IDE study, it's directed towards claudication, but the procedure may also be of benefit to critical limb ischaemia patients, he added.

"This is a procedure that's really extending what we can do with endovascular therapies. DETOUR II is taking on longer lesions than have ever been approached by endovascular means," concluded Dr Schneider.

* As of January, 2020.

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# Long lesions do not mean reduced patency with spot stenting

Spot stenting is efficient in long and complex femoropopliteal lesions as evidenced by findings from the LOCOMOTIVE registry study in patients treated with VascuFlex® Multi-LOC spot stenting system.

Data from the registry were presented at a B. Braun-sponsored symposium at LINC 2020, alongside the reporting of experience with the company's new VascuFlex® 2-LOC/3-LOC spot stenting system that was launched during the congress.

The latest analysis clearly demonstrated that there is no longer any correlation between long lesions and reduced patency.

Presenting the data were three experts with extensive experience with the B. Braun spot-stenting devices. Klaus Amendt (Diakonissenkrankenhaus Mannheim, Germany) reported results of the LOCOMOTIVE EXTENDED study; Gunnar Tepe, Professor of Radiology (Klinikum Rosenheim, Germany) also presented further insights and sub-group analyses of the LOCOMOTIVE EXTENDED study; and Erwin Blessing (SRH-Klinikum Karlsbad-Langensteinbach, Germany) took delegates through a case study using the new VascuFlex 2-LOC/3-LOC.

A live case was presented by Ralf Langhoff (Sankt Gertrauden-Krankenhaus, Berlin) of a femoropopliteal artery stenosis.

Erwin Blessing

Gunnar Tepe

Klaus Amendt

VascuFlex® Multi-LOC and the new VascuFlex® 2-LOC/3-LOC are particularly suitable for spot stenting in challenging lesions including major dissections and calcified, stenotic, or fibrotic lesions where there is some early narrowing of the artery or recoil, despite intervention with a balloon. VascuFlex® Multi-LOC is comprised of six short stents of 13 mm in length loaded onto one 6-F multiple stent delivery system separated by spacers of 5 mm length, each of which can be delivered in different places in the vessel. Diameters range from 5 to 8 mm, and of note, the radial force and compression resistance are very high and comparable to standard nitinol stents. Once a stent is at the required location, a single-hand wheel mechanism releases the individual stent.

Peripheral spot-stenting is growing in popularity, not least because full coverage of a lesion is associated with relatively high restenosis, risk of stent fracture that might harm vessel wall integrity. Even with drug eluting stents (DES), patency rates decrease over time due to permanent trauma from the chronic outward force of common oversized nitinol stents.

## LOCOMOTIVE EXTENDED study

Dr Amendt provided an overview of the LOCOMOTIVE EXTENDED study. "The programme started in 2015 and it is the first step in evaluating VascuFlex® Multi-LOC as a specific spot stenting device to treat long and complex femoropopliteal lesions with less metal."

The registry is collecting safety and efficacy data on all procedures with VascuFlex® Multi-LOC used on all patients being treated for *de novo* and restenotic lesions of common femoral to distal popliteal arteries with Rutherford class 2 to 5 or Fontaine stage 2-4 disease.

Overall, the patient cohort in the LOCOMOTIVE study was relatively challenging with 49% of patients having diabetes mellitus, 87% with hypertension and 72% with hypercholesterolemia. "Also, lesion morphologies were interesting with mean lesion length of 16 cm, a high grade of calcification (86%) and lesion locations from the proximal superficial femoral artery (SFA) down to the P3 segment," remarked Dr Amendt.

Inclusion requires that patients have a stenosis or an occlusion of the SFA, popliteal artery (P1-3), and a redo lesion length suitable for release of at least two stents spaced at least 5 mm apart. Other requirements include a reference diameter of 4 to 7 mm; distal runoff in at least one vessel in the foot as well as collaterals that supply adequate blood flow to the foot; and severe calcification after subintimal percutaneous transluminal angioplasty (PTA).

Vessels were prepared with uncoated and/or drug-

coated balloons (DCBs) prior to spot-stenting if flow-limiting dissections, elastic recoil, or recoil caused by calcification occurred.

Dr Amendt highlighted that, in particular, the LOCOMOTIVE EXTENDED study allowed the researchers to investigate the spot stenting approach in a wide range of real-world patients and to perform several sub-group analyses.

Sharing the latest clinical results of the LOCOMOTIVE EXTENDED study, Dr Amendt said they were very promising in this challenging patient-cohort. "With a 81.8% primary unassisted patency and a 88.4% freedom from target lesion revascularisation (fTLR) we see this approach as a valid option to treat femoropopliteal lesions. The clinical outcome after 12 months was promising too, concerning persistent benefit in walking capacity, Rutherford Classification Shift and ankle-brachial pressure index (ABI)," he reported.

Asked what key insights endovascular interventionists should note with respect to the LOCOMOTIVE EXTENDED analysis, Dr Amendt drew attention to spot stenting working very well in long and complex SFA lesions. "Dedicated spot stenting devices like the VascuFlex® Multi-LOC or the new VascuFlex® 2-LOC/3-LOC are very good tools to handle these lesions," he said, adding that, "even without combination with drug eluting devices, they demonstrate persistent morphological and clinical results in these severely diseased high-risk patients. Together these results show that the intention to 'leave as little as possible behind' can be realised by this spot stenting."

*"[VascuFlex® 2-LOC/3-LOC] offers an easy-to-use tool with several diameters and lengths."*

**Erwin Blessing**

Professor Tepe expanded on insights from the LOCOMOTIVE EXTENDED study, providing clinical data about spot stenting in over 300 patients. The size of the database enables several sub-group analyses to further investigate the potentials and limits of spot stenting in the femoropopliteal segment, he said.

"In the LOCOMOTIVE EXTENDED study we assessed subgroups for the performance of spot stenting in combination with DCBs in different lesions setups," he explained.

Professor Tepe reviewed the key findings. "In the lesion length sub-group, we were able to show that spot stenting is able to overcome the negative correlation between long lesions and reduced patency," he said, emphasising the information that delegates had been waiting to hear.

Another sub-group combined the clinical outcome of plain old balloon angioplasty (POBA)/ DCB treatment with spot stenting in short and long lesions. "This analysis has led to the impression that spot stenting performs very well in long SFA lesions in combination with a DCB treatment with 94.3% fTLR at 12 months," he pointed out.

"Based on our registry findings, spot stenting seems to be a valid option with a very promising clinical outcome especially for those patients with challenging lesions," he said. "The 'leave as little as possible behind' approach works very well in long and complex SFA lesions. Dedicated spot stenting devices like the VascuFlex® Multi-LOC or the new VascuFlex® 2-LOC/3-LOC are very good tools to handle these lesions."

## VascuFlex 2-LOC/3-LOC in a long and complex fempop lesion

Professor Blessing discussed a case study of VascuFlex® 2-LOC/3-LOC in a long and complex femoropopliteal lesion, but he began by establishing that there was a need for alternatives to DCBs in treating these long and complex lesions.

"Long and complex lesions in the femoropopliteal segment remain challenging. Despite the use of DCBs with a very acceptable patency rate, they do come with a high bail-out stent rate," he pointed out. "This means that stents cannot be fully avoided in 4 out of 10 patients." Indications for bail-out stenting are either flow-limiting dissections or residual stenosis after lesion preparation.

But he highlighted that the question remained as to whether it was necessary to cover the entire segment with a full metal jacket or place short stents only where needed - spot stenting. "Some data from the literature support the concept of spot stenting rather than long lesion coverage. VascuFlex® 2-LOC/3-LOC offers a helpful tool to the interventionalist to easily deliver two or three short stents to cover short dissections/ segments of residual stenosis," remarked Professor Blessing.

VascuFlex® 2-LOC/3-LOC combines spot stenting with procedural advantages and causes less acute and chronic trauma due to less material on vessel wall. Made for femoropopliteal lesions, it has an open cell design for optimal vessel deposition with two or three stents on one device. It measures 5-8 mm in diameter, 30-40 mm in length, and shaft length is 80 cm or 130 cm.

Turning to the case study, Professor Blessing discussed a 62-year-old male with diabetes type 2 and arterial hypertension, who had a very complex lesion (Rutherford 3) with a <20 cm occlusion in the femoropopliteal segment. "After lesion preparation involving long inflation with a regular balloon followed by DCB angioplasty, flow limiting dissections needed to be covered with short stents. VascuFlex® 3-LOC stents were placed to cover dissected segments with an excellent final result," he recounted.

In conclusion, Professor Blessing summed up his thoughts on using the novel VascuFlex® 2-LOC/3-LOC. "It offers an easy-to-use tool with several diameters and lengths available, with either two or three already remounted stents on one delivery system. It helps to reduce intervention time, there's no need to use two or three separate delivery systems."

He drew comparison with the VascuFlex® Multi-LOC device. "The 2-LOC and 3-LOC stents are firstly, longer and secondly, have open-cell design stents as most of the stents in the femoropopliteal segment."

This evidence suggests that with the VascuFlex® Multi-LOC and the VascuFlex® 2-LOC/3-LOC means that vascular interventionalists now have more options to treat their patients leaving as little as possible behind.

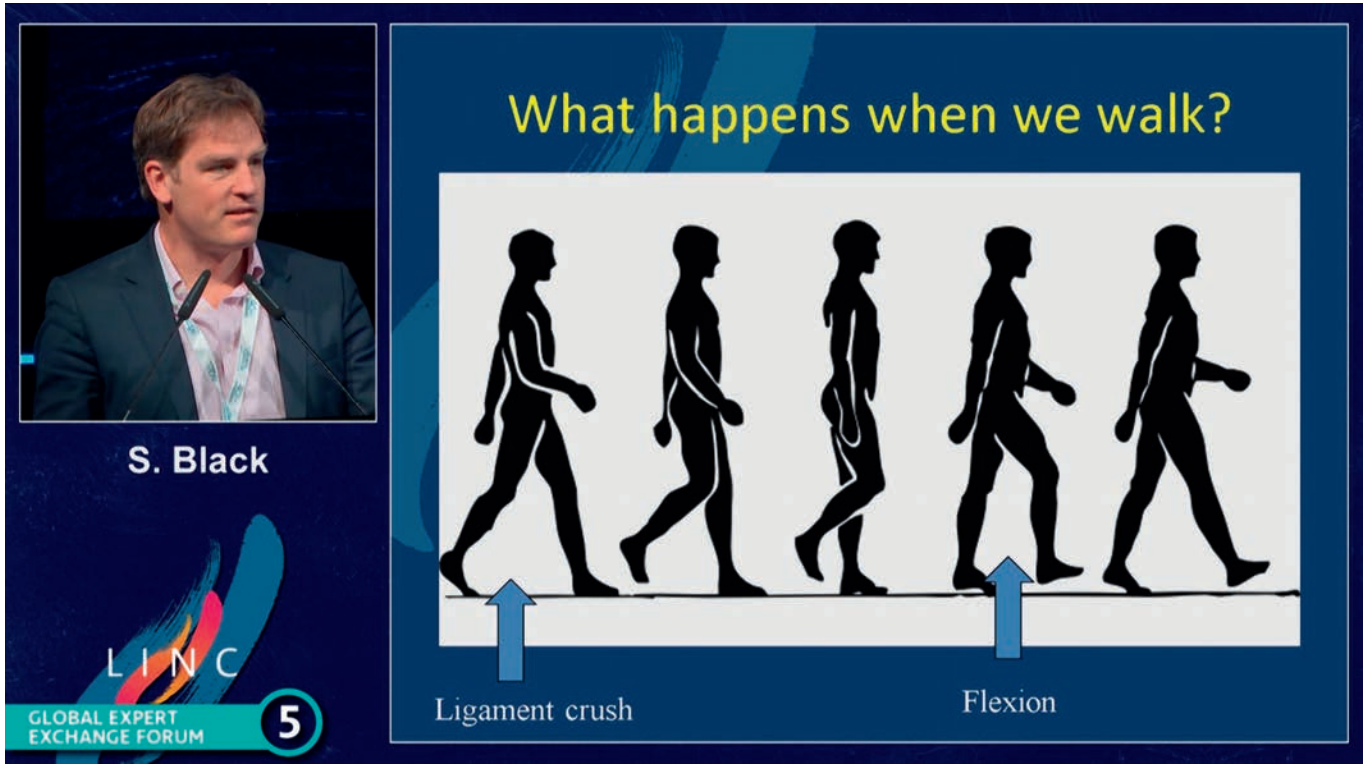
# Venous stenting is given the bench test

Data on 50-year durability testing with venous stents was presented for the first time by Stephen Black, a consultant vascular surgeon and reader in venous surgery at Guy's and St Thomas's hospitals and King's College Hospital, London, UK.

Setting the scene, Mr Black relayed that venous stents had not been durability tested for historical reasons. "Part of the problem was that a lot of the bench-model testing started from expectations we had for arterial patients," he said. "All the original bench-model testing was designed to simulate what an arterial patient did."

The problem, however, was that the demographics of both patient sets were starkly different. "The same level of activity in an elderly population cannot be expected from venous patients, who are younger and fitter," he said.

Other factors related to venous stenting were never considered when stents emerged, e.g. the Vici Venous Stent from Boston Scientific (USA). "We did not have an expectation that stents would go below the ligament," said Mr Black. Indeed, previous guidance from the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) suggested that stenting below the ligament should not be considered.




Mr Black recommended a paper looking at cadaveric modelling of the stent below the ligament by Christopher Cheng *et al*.[1] It looks at the various stages of walking, and the forces placed on the stent. "It shows the trailing leg where you get ligament crush with hyperextension, when the ligament is crushing the stent against the pubic ramus," he said. At other stages of walking, force loading changes, e.g. flexion rotation and axial loading of the stent as a walker comes into flexion.

*"What's going to determine an outcome is not failure of the stent, if we use them right – it's the failure in ourselves to implant stents."*

**Stephen Black**

What this shows is that there has been very little in the way of data focusing on stenting below the ligament, because bench testing has focused so much on arterial stenting. "The bench-testing approach for venous stenting has fallen short," said Mr Black.

Bench testing for arterial patients also assumes a certain lifetime of the stent and patient. But the assumed lifetime of an arterial stent differs quite considerably from the lifetime of the average venous patient, who may be in their 30s. As such, Mr Black said many of his patients ask if their stent will last 50 years – a difficult question to answer because of the available evidence, and exactly why it is so important to carry out modelling for stents. "Therefore, we probably need to be moving towards testing this in a bench model fashion to prove to ourselves that we can do this,"

said Mr Black.

His group has considered several main activities including walking, stair climbing and sit-to-stand. "Each of these activities have slightly different stresses on a stent," he said. "You can model the changes in hip angle based on cadaveric modelling to estimate how many times a year somebody will do them."

Any stress from walking must be put through a million cycles, stair climbing around 25,000 cycles and sit-to-stand 48,000 cycles per year, he explained: "This is how you extrapolate the bench-model testing which a stent will need. And we want to take that out to 50 years to really give us the assurance and certainty that the stents are going to last for that long."

Mr Black explained the way in which his group tested 12 stents. With cadaveric modelling of different positions, using data from four cadavers with a reference angle being the hip, a 3D reconstruction of the model can be made. "If you look at walking, stair climbing and sitting, you can see what the vein curvatures are going to do and then you can create a model for stress points based on that," he said. "You can get 3D reconstructions of what models will look like from the CT imaging of the cadavers and you can see the change from the leg at 0°, and when the leg is coming into forced hip flexion."

*"The bench-testing approach for venous stenting has fallen short."*

**Stephen Black**

The model tests beyond boundaries that the human body can move to make absolutely sure that the stent can withstand the high degree of angulation that occurs at multiple points.

The group applied this bench-testing approach, looking at different deformation mode, including torsion (twisting, bending, lateral compression and axial compression) and end-to-end compression of the stent. The group also looked at crush resistance, i.e. point compression of the artery on the stent itself.

"The model can simulate, say, bending, and then accelerates the cycles that the stent is put through multiple times in a much quicker fashion," said Mr Black. "If you take this data into computerised modelling – finite element analysis – you can model when the stents were going to break … You can understand the extreme conditions those stents work in."

He added that modelling showed no fractures: "The stent, which in this case was the Abre Venous Stent (Medtronic, Ireland), has the ability to withstand 50 years of worst-case deformation without fracturing," he stressed. "The results give us a pretty good confidence that these stents will last in our patients."

He warned, however, that the success of the stent is not just down to its durability: "What's going to determine an outcome is not failure of the stent, if we use them right – it's the failure in ourselves to implant stents in the appropriate patients and in the right way," he said.

Mr Black noted that the study is a step towards benchmark testing of venous stents. "Hopefully as we learn more about failure modes, we can introduce more aspects into this testing to understand failure of stents more appropriately," he said.

"This will provide assurance to both our patients and ourselves that the stent will last a lifetime, [as long as we] do a proper job of implantation," concluded Mr Black.

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