
LINC
Review
2018

LINC Review

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Introduction

The latest edition of the Leipzig Interventional Course took place January 30 – February 2, 2018 at the Trade Fair Leipzig. Over the four-day programme, LINC 2018 welcomed leading experts from all over the world to showcase cutting-edge reports, lectures, lively discussions and first-time-data.

As always, live cases played a central role, with more than 90 demonstrations from leading national and international centres in Germany, Italy, Ireland, USA, France and Switzerland. What's more, the *Scrub-in with the experts symposia* saw esteemed operators exhibiting their own techniques, tips and tricks via satellite, providing an immersive experience packed with insight.

Collaboration has always been vital for LINC, and this year the meeting continued its international relationship with leading vascular courses. These were exemplified in the "@LINC" sessions, which gathered together international perspectives for the audience.

The *LINC Review* brings you highlights from LINC 2018, including new data, novel techniques, device updates, case discussions and beyond. For even more, head to http://www.leipzig-interventional-course.com to watch videos of key sessions and live cases, and to browse through the presentation archive.

The LINC 2018 organisers would like to thank all delegates and industry sponsors for their continued support, and hope to see you in Leipzig in January, 2019 for the 15th edition of LINC.

Contents

Society and association accreditation

LINC 2018 was accredited by:

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

The Swiss Society for Angiology with 31 CME points.
www.angioweb.ch

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

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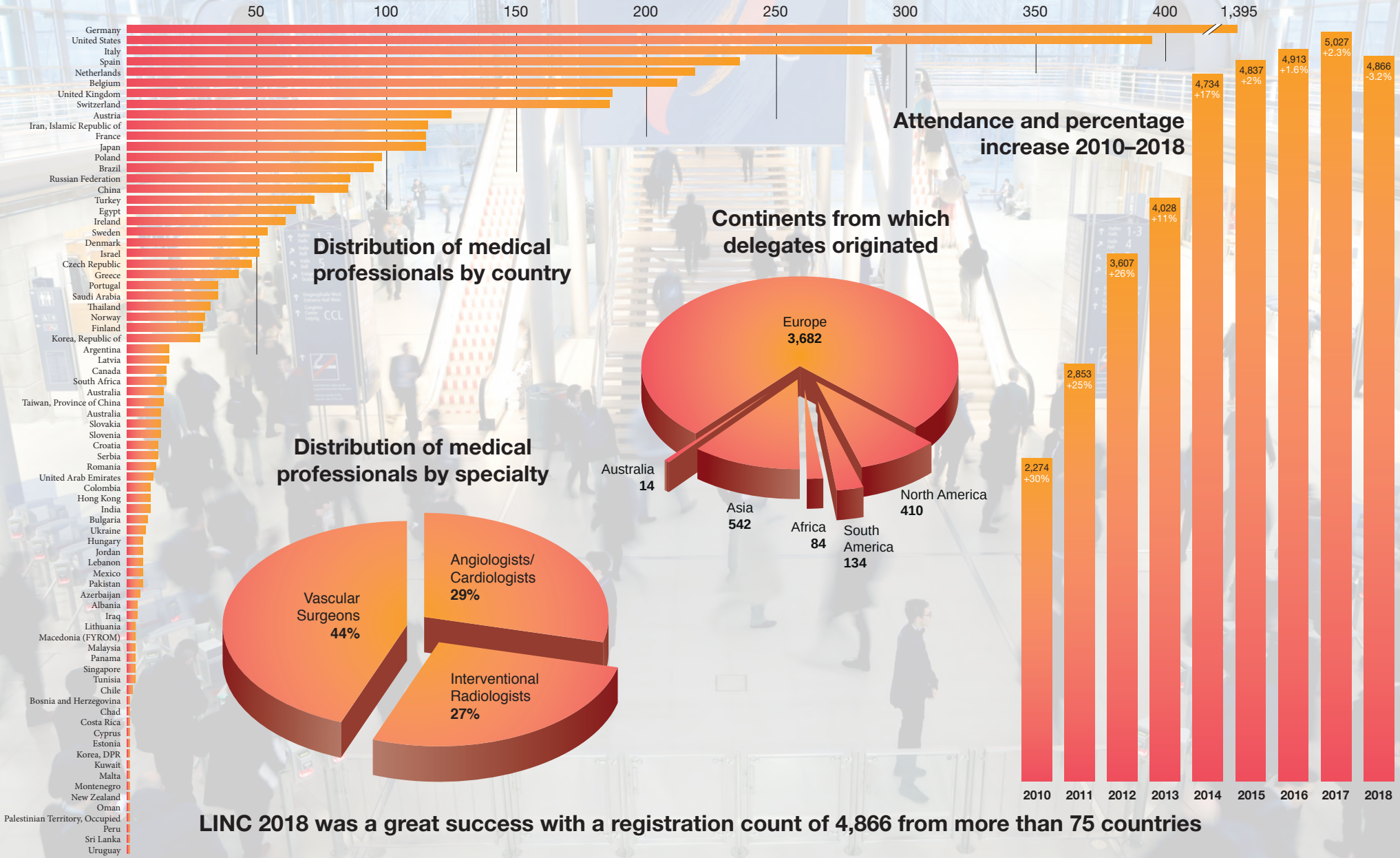
LINC in numbers



LINC 2018 was a great success with a registration count of 4,866 from more than 75 countries

One-year data from the MIMICS-2 study released

LINC 2018 featured first-time release of 12-month data from the MIMICS-2 Study, investigating the safety and effectiveness of the BioMimics 3D Stent System (Veryan Medical, UK) in femoropopliteal arteries of patients with symptomatic peripheral arterial disease.

The BioMimics 3D stent has a unique three-dimensional helical shape, designed to impart natural curvature to the diseased femoropopliteal artery, promoting swirling flow and elevating wall shear, which has a protective effect on the endothelium. The helical shape of the BioMimics 3D stent is also designed to facilitate shortening of the stented segment during knee flexion and mitigate the risk of stented segment compression causing localised strains that in a straight stent may lead to stent fracture and chronic vascular injury.

Thomas Zeller (Bad Krozingen, Germany), who is European Principal Investigator (PI) of the trial, spent a few moments explaining how the BioMimics 3D stent mimics the natural anatomical conditions of the vessel, particularly swirling flow: "This swirling flow increases the wall stress, and this increased wall shear stress has been shown to be protective against stenosis development and restenosis," he pointed out, adding that natural swirling flow may be compromised by anatomy, disease and straight stents, and he referred to animal studies that show 30% less intimal hyperplasia in animals with helical stents compared to those with straight stents (p<0.005).[1]

MIMICS-2 Study

MIMICS-2

Baseline Patient Demographics

		N= 271 Subjects
Age	Mean years ± SD (N)	68.4 ± 9.5 (271/271)
Gender	Male / Female	180 (66.4%) / 91 (33.6%)
Risk Factors	Diabetes Mellitus	45.4% (123/271)
	Hypertension	90.0% (244/271)
	Hypercholesterolemia	81.9% (222/271)
	Smoker Current / Former	80.8% (219/271)
Coronary Revascularization	Previous Percutaneous or Surgical	43.2% (117/271)
Previous Peripheral Intervention	None in target vessel	98.2% (266/271)
Rutherford Category	1	0% (0/271)
	2	26.9% (73/271)
	3	67.5% (183/271)
	4	5.2% (14/271)
	5	0.4% (1/271)
Ankle Brachial Index	Mean ± SD (N)	0.70 ± 0.20 (257/271)

Source: www.leipzig-interventional-course.com

Mimics RCT

The Mimics Study was a prospective, part-randomised study. It comprised an initial roll-in registry of 10 subjects treated with BioMimics 3D followed by a randomised assignment to treatment with BioMimics 3D or control (majority treated with LifeStent manufactured by CR Bard, USA) on a 2:1 basis for 76 subjects.

Referring briefly to the Mimics study, Professor Zeller said: "The proof of principle was established by the randomised study comparing the BioMimics 3D stent to LifeStent. Challenging lesions were included, as well as total occlusions and moderate to severe calcifications. The two-year outcomes favour the BioMimics 3D stent compared to LifeStent, which was the gold standard at the point of time of study design.

"Looking at the longer-term effects, regarding freedom from target lesion revascularisation (TLR) [at] one and two years, you can see that there is no TLR for the BioMimics 3D stent, but there is some for the LifeStent cohort." Freedom from loss of primary patency at two years was 75.6% for BioMimics 3D subjects versus 56.0% for the control group (p=0.06). "The conclusion of the initial RCT was better primary pa-

"The unique BioMimics 3D stent design provides haemodynamic and biomechanical benefits for primary and complementary stenting." ***Thomas Zeller***

tency and no stent fracture at two years by x-ray," he added.

The MIMICS-2 study

MIMICS-2 is a prospective, single-arm, multicentre clinical trial of the BioMimics 3D Stent, which has enrolled 271 subjects in 43 sites. It is an investigational device exemption (IDE) study, being conducted in the US, Germany and Japan. Co-PIs for the US and Japanese centres of the study are Timothy Sullivan (Minneapolis, USA) and Masato Nakamura (Tokyo, Japan) respectively.

MIMICS-2 aims to provide data to support premarket approval applications in US and Japan. The trial is evaluating the BioMimics 3D Stent System against the performance goals defined by VIVA Physicians, Inc. for the safety and effectiveness of nitinol stents used in the treatment of symptomatic disease of the femoropopliteal artery.

The primary safety endpoint is a composite of major adverse events (MAE) comprising death, any major amputation performed on the target limb, and clinically-driven (CD) TLR through 30 days. The primary effectiveness endpoint is primary stent patency at 12 months, and the follow-up period is three years.

Technical success was 100%, reported Professor Zeller, and freedom from MAE was 99.6% at 30 days, including death and major amputation. This surpassed the performance goal of 88%, thus the primary safety endpoint was achieved.

Twelve-month freedom from CDTLR was 88.4%, according to Kaplan-Meier survival analysis, and 12-month freedom from loss of primary patency was 81.9%. Core-lab confirmed percentage stent fracture rate was 0% in both the Mimics Study and MIMICS-2.

"MIMICS-2's primary safety and effectiveness endpoints were met," said Professor Zeller, noting that the probability of freedom from loss of primary patency at 12 months with BioMimics 3D is similar to those for drug-eluting stents or balloons. As such, he underlined that natural swirling flow is an alternative to antiproliferative drugs.

"The unique BioMimics 3D stent design provides haemodynamic and biomechanical benefits for primary and complementary stenting," he said in closing.

Reference

1. Caro CG *et al.* Intimal hyperplasia following implantation of helical-centreline and straight-centreline stents in common carotid arteries in healthy pigs: influence of intraluminal flow. J R Soc Interface. 2013 Dec 6; 10(89): 20130578.

"MIMICS-2's primary safety and effectiveness endpoints were met." ***Thomas Zeller***

LOCOMOTIVE steams ahead

Twelve-month data from the LOCOMOTIVE registry show that the VascuFlex Multi-LOC (B. Braun, Germany), a novel multiple stent delivery system (MSDS), was safe and effective in patients with peripheral arterial occlusive disease (PAOD), according to data reported for the first time at LINC 2018.

Presenting the results was Klaus Amendt (Mannheim, Germany), who was principal investigator. Specifically, the data showed that the primary patency was 85.7% overall (CLI and non-CLI patients), and target lesion revascularisation (TLR) was 9.3% overall.

Providing some context to the need for spot stenting, Professor Amendt explained that the MSDS offers spot stenting only where it is needed, therefore leaving less foreign material behind. "Over the last year we've seen that drug coated balloons [DCBs] alone do not solve the problems of long lesions," he asserted, referring to the two-year results of the Real-PTX randomised controlled trial (RCT) comparing the Zilver PTX (Cook Medical, USA) drug-eluting stent (DES) versus DCB in femoropopliteal lesions.

The MSDS (VacuFlex Multi-LOC) has six short stents (13 mm) with high radial force that can be placed in arteries wherever needed, Professor Amendt noted. "Animal studies show that there is high patency in the MSDS versus a standard long nitinol stent, and no stent fractures. Once the CE mark was approved, results were reproduced in-man. No negative effects were seen on the biomechanical properties of arterial functioning, and the lumen was stabilised even in severely calcified lesions."

This non-randomised, prospective multicentre registry (LOCOMOTIVE) is collecting all-comers data on safety and efficacy on

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"A procedural success rate of 100% was achieved." ***Klaus Amendt***

LOCOMOTIVE steams ahead

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the use of VascuFlex Multi-LOC in the common femoral to distal popliteal artery (Rutherford 2-5, Fontaine 2-4). Inclusion in the registry stipulates femoropopliteal lesions prepared with uncoated or paclitaxel (PTX)-coated DCBs, and if flow-limiting dissections, elastic recoil, or calcification occur and require stenting, then spot stenting is performed. The lesion length must accommodate the release of at least two mini-stents. Exclusion criteria were in-stent restenosis and restenosis after DCB.

Six-month target lesion revascularisation (TLR) rate was the study's primary endpoint. The six-month results showed that 176 target lesions had been treated, of which 51.1% (90/176) were TASC C/D lesions, and overall total lesion length was approximately 14.5 cm, with 97% being severely calcified. At six months, TLR rates were 5.3%, and primary patency was 90.7% overall. Analysis of procedural data showed that technical success rate was 100% (no flow-limiting dissections or residual stenosis > 30%), and nitinol stent length was reduced by 50%. Spot stenting strategy was considered safe and effective in femoropopliteal lesions.

At LINC 2018, Professor Amendt reported the 12-month results including TLR rate. Other endpoints were walking distance; ankle brachial index (ABI); color-coded duplex sonography (CCD); patency rate; change in Rutherford class; and amputation rate.

There were two groups of lesion morphology: critical limb ischaemia (CLI) patients, and non-CLI patients. Distal run off of 1 or 0 was 40% and 15% respectively in CLI patients. TASC C/D was 73.1% in the CLI patients and 41.9% in no-CLI. Total lesion length in the CLI patients was 19.0±9.5 cm; and 60% of patients had occlusions. "The length of the lesions in these patients is really challenging," said Professor Amendt.

On procedural details and device characteristics, Professor Amendt reported that there was 100% technical success in all patients, and, "with this technique we saved around 50% of lesion length being covered with a stent [0.47±0.18 across all patients]."

A total of 75.6% of all patients required pre-dilation with plain balloon. Primary patency at 12 months was 85.7% across all patients (CLI: 93.3%; non-CLI: 83.3%) compared to 90.7% at six months; TLR occurred in 9.3% (CLI: 5.0%; non-CLI: 10.9%) at 12 months compared to 5.3% at six months.

LOCOMOTIVE registry: 12-mo FU patients

Clinical outcomes

	All patients	Critical limb ischemia	No critical limb ischemia	p-value
Patients	75	20	55	-
12 months				
Target leg ABI	0.91±0.38 n=53	0.91±0.40 n=13	0.91±0.38 n=40	0.973
Rutherford shift pre vs. 12 months	2.2±1.3 n=60	2.8±1.7 n=15	2.1±1.0 n=45	0.038
Major amputations, target leg (+0)	2 (2.7%) n=75	**2 (10.0%)** n=20	0 (0.0%) n=55	**0.017**
Major amputations, contralateral leg	1 (1.3%) n=75	1 (5.0%) n=20	0 (0.0%) n=55	0.095
Death all causes (+3 in IC)	9 (12.0%) n=75	3 (15.0%) n=20	6 (10.9%) n=55	0.630
Death				
cardiac	1 (1.3%)	0 (0.0%)	1 (1.8%)	
vascular	3 (4.0%)	2 (10.0%)	1 (1.8%)	0.398
non-cardiovascular	5 (6.7%)	1 (5.0%)	4 (7.3%)	

Comments:
[1] statistical analysis not meaningful due to small patient numbers, [2] based on angiographic or sonographic data only. All categorical variables were compared with the Pearson's Chi2 test, continuous variables were analyzed with the unpaired student t-test

Source: www.leipzig-interventional-course.com

"This is quite convincing overall. We only had some additional restenosis in non-CLI patients."

Freedom from TLR was 90.7% overall (CLI: 95%; non-CLI: 89.9%). Amputations in target legs was 2.9% overall (CLI: 10.5%; non-CLI: 0%). Death from vascular means occurred in 5.3% of patients.

Pre-procedure overall ABI was 0.62 and post-procedure was 0.83 at six months ($p<0.001$ versus pre-procedure). At 12 months ABI increased to and 0.91 ($p<0.001$ vs pre-procedure).

In conclusion, Professor Amendt said that the 12-month data show that the MSDS was safe and effective in patients with PAOD. "A procedural success rate of 100% was achieved in releasing individual stent segments even in morphologically challenging lesions. No stent loss was seen, nor was there any conversion to standard stenting; TLR rates in CLI and non-CLI patients were both less than 10%, and primary patency at 12 months was 85%, while assisted primary patency was 95%."

"Over the last year we've seen that drug coated balloons alone do not solve the problems of long lesions." ***Klaus Amendt***

COMPARE trial: RANGER and IN.PACT head to head

The COMPARE prospective, multicentre randomised controlled trial (RCT) is ongoing in investigation of the Ranger drug-coated balloon (DCB; Boston Scientific, USA) versus the IN.PACT DCB (Medtronic, USA) in complex superficial femoral artery (SFA) lesions.[1]

Principal investigator Dierk Scheinert (University of Leipzig, Germany) described the study, along with the outcomes of its 12-month interim analysis: "It's very tempting to compare devices directly – this is done in almost every presentation. However, this is really the first RCT which compares two different paclitaxel-coated balloons with different coating and paclitaxel dose density for the treatment of femoropopliteal disease."

The Ranger paclitaxel-coated PTA balloon catheter possesses acetyl tri-n-butyl citrate coating, with a 2 µg/mm^2 dose of paclitaxel. The control devices were the IN.PACT Admiral or IN.PACT Pacific DCB, which possess a urea coating and convey a paclitaxel dose of 3.5 µg/mm^2.

This investigator-initiated study is sponsored by the University of Leipzig, funded by a research grant from Boston Scientific, and carried out at 15 German centres. Its phase 1 pilot study includes 150 patients, with an extension in recruitment in phase 2 of up to 414 patients for testing of the formal non-inferiority hypothesis.

Lesions are being stratified according to length, with follow-up clinical visits at six, 12 and 24 months. The study includes independent monitoring with 100% source data verification, and independent core lab for angiographic and Duplex imaging, along with a clinical events committee.

The study focuses on patients with symptomatic peripheral artery disease (PAD) of Rutherford class 2-4, with stenotic or occlusive lesions, *de novo* or restenotic lesions, excluding in-stent restenosis and severe calcification. At least one patent below-the-knee vessel supplying the foot needed to be present. Lesion lengths of up to 30 cm were included, and lesions were stratified into three groups of ≤10 cm, >10 cm and ≤20 cm, and >20 cm and ≤30 cm.

The cohort of 150 patients described in the COMPARE interim analysis were investigated with respect to the primary efficacy endpoint of 12-month patency, defined as absence of clinically-driven target lesion revascularisation CD-TLR due to symptoms and drop of ankle brachial index [ABI] of ≥20% or >0.15 when compared to post-procedure), or Duplex ultrasound-based restenosis using peak systolic velocity ratio (PVR) >2.4. The primary safety endpoint is a composite of freedom from device- and procedure-related death through 12 months post-procedure as well as freedom from both target limb major amputation and CD-TLR.

Dierk Scheinert

Secondary endpoints include: TLR rate; Duplex-defined restenosis; sustained clinical improvement (improvement in Rutherford classification of one class in amputation-free and TLR-free surviving patients); and walking

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"This is really the first RCT which compares two different paclitaxel-coated balloons." ***Dierk Scheinert***

COMPARE trial: RANGER and IN.PACT head to head

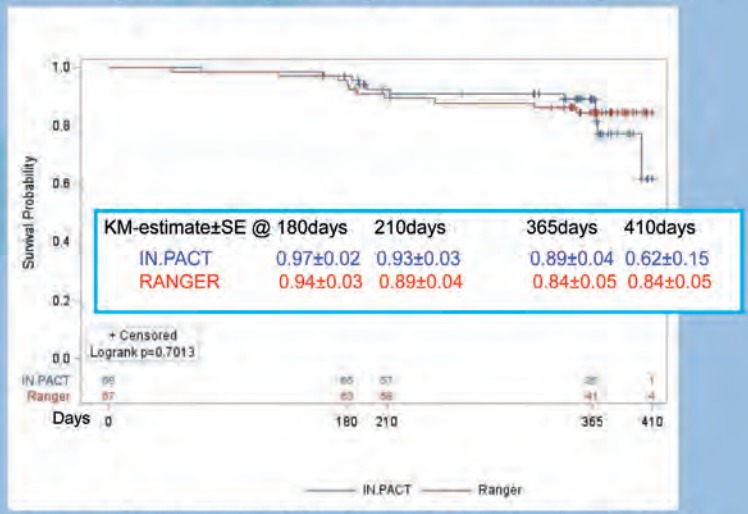
Source: LINC 2018 presentation archive (www.leipzig-interventional-course.com)

Procedural Outcomes* n=150

	RANGER DCB (n=74)	IN.PACT DCB (n=76)	p-value
Bailout stent placement	19 (25.7%)	17 (22.4%)	0.6
MVD postprocedure, mm	3.6±0.6	3.7±0.8	0.6
Diameter stenosis postprocedure, %	25.8±11.6	26.0±14.6	0.9
Residual stenosis > 30%	26 (35.1)	29 (38.2)	0.7
Dissection	70 (92.1%)	70 (94.6%)	0.7
Type A/B, n (%)	54 (77.1%)	44 (62.8)	0.1
Type C-F, n (%)	16 (22.9%)	26 (37.2%)	
Complications			
Embolic event	2 (2.7%)	1 (1.3%)	
AV-Fistel (local)	5 (6.8%)	5 (6.6%)	
Target Vessel Perforation	1 (1.4%)	1 (1.3%)	

* Per angiographic core lab assessment.
Data are given as mean±SD or number (%).

Primary efficacy endpoint: Patency rate*



*Patency: defined as absence of clinically driven TLR or restenosis with PVR>2.4 evaluated by duplex ultrasound scan; both per core lab assessment.

Source: LINC 2018 presentation archive (www.leipzig-interventional-course.com)

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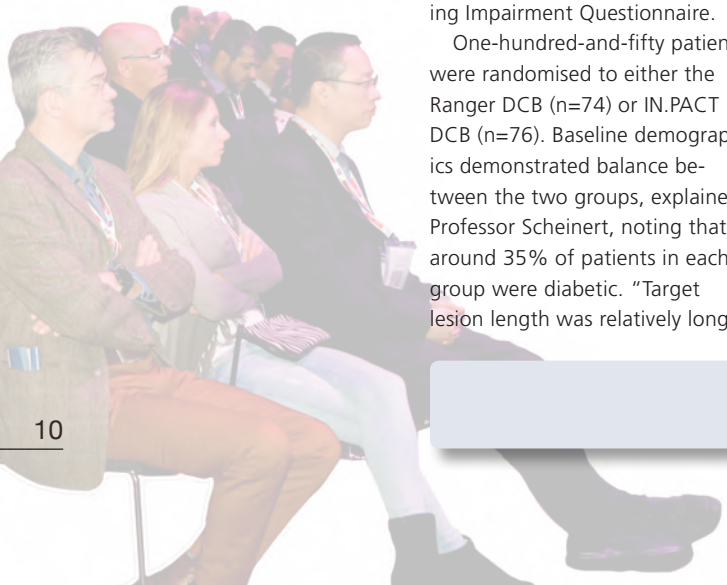
capacity assessment by the Walking Impairment Questionnaire.

One-hundred-and-fifty patients were randomised to either the Ranger DCB (n=74) or IN.PACT DCB (n=76). Baseline demographics demonstrated balance between the two groups, explained Professor Scheinert, noting that around 35% of patients in each group were diabetic. "Target lesion length was relatively long, around 12 cm, with about 40-45% total occlusions," he said. "A good number of patients [were] classified as moderately severe or severely calcified. Bail-out stent placement was around 25% in both groups."

Discussing the Kaplan-Meier curve expressing the primary endpoint in terms of the core lab-assessed primary patency rate, Professor Scheinert said: "At one year, the data are very comparable between the two groups [0.89±0.04 (IN.PACT) versus 0.84±0.05 (RANGER)].

"If you look at the end of the follow-up window, which was pre-specified as ±45 days you can see that the primary patency in the Ranger group was [0.84±0.05] compared to [0.62±0.15] in the IN.PACT group. However, the standard deviation is bigger here, probably due to the fact that we had some missing data points in terms of unreadable Duplexes. So I find these results comparable."

Summarising the significance of this head-to-head comparison, Professor Scheinert said: "The study subset was a real-world complex lesion subset with a lesion length of 12 cm and a proportion of CTOs around 40%. Excellent efficacy at one year was shown in both arms, with similar primary patency rates in the low-dose Ranger and the higher-dose IN.PACT balloon. The recruitment of the full cohort is ongoing and will likely be completed in the second quarter of 2018, so hopefully we will see results in the next couple of years."



"At one year, the data are very comparable between the two groups." ***Dierk Scheinert***

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1. Compare I Pilot Study for the Treatment of Subjects With Symptomatic Femoropopliteal Artery Disease. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT02701543 (retrieved Jan 2018).

A Phoenix rising

Speaking during a session on advanced solutions for calcified lesions and CTO, Grigorios Korosoglou (GRN Academic Teaching Hospital Weinheim, Germany) presented clinical experience with the Phoenix rotational atherectomy system (Volcano/Philips, USA/NL) for complex calcified femoropopliteal lesions.

A collaborative study between Dr Korosoglou and colleagues from GRN Hospital Weinheim, together with Internal Medicine and Angiology Practice (Hirschberg-Großsachsen) and the Fuerst Stirum Hospital Bruchsal Department of Cardiology & Angiology (Bruchsal, Germany) included 29 consecutive patients with CLI treated by Phoenix atherectomy in combination with DCB angioplasty or balloon angioplasty, with additional stenting in some cases.

While DCB angioplasty has proven effective in the femoropopliteal region relative to plain balloon angioplasty[1], heavy calcification still poses a challenge as it has been shown to be an independent predictor of restenosis[2]. This has led to the proposal that atherectomy may more effectively tackle focal calcification by resulting in luminal gain without barotrauma, which facilitates better access of antiproliferative drugs to the vessel wall and may obviate the need for stent placements or surgery.[3]

However, little data exists to date on the relative efficacy of atherectomy debulking plus DCB versus DCB alone in calcified femoropopliteal lesions. In 2013, a retrospective study of 89 patients by Zeller *et al*. found the combination of directional atherectomy plus DCB to be associated with lower rates of restenosis at 12 months of follow-up, compared to atherectomy plus plain balloon angioplasty.[4]

In 2017 Zeller *et al*. completed DEFINITIVE AR, a multicentre randomised trial to estimate the effect of directional atherectomy before DCB in 102 consecutive patients with femoropopliteal disease. Technical success was superior in the directional atherectomy plus DCB group, and pre- and post-dilatation rates were lower relative to the DCB-alone group. Thus treatment with atherectomy was considered safe. However, the study was underpowered to detect differences in rates of revascularisation after one year.[5]

Another 2017 study compared 72 patients treated between 2009 and 2015 with either DCB angioplasty alone or with directional angioplasty with anti-restenotic therapy for isolated popliteal artery stenotic disease. In this study, the combination of directional atherectomy with DCB resulted in higher primary patency rates compared to DCB alone, with statistically similar rates of bailout stenting in both groups.[6]

Speaking to *LINC Review*, Dr Korosoglou underscored that these data pertain to directional atherectomy, noting that data on the use of rotational atherectomy plus DCB remains lacking. Indeed, atherectomy systems are far from transposable, and a 2015 report from the American College of Cardiology set out the indications best suited to different atherectomy types[7].

The Phoenix was designed to reduce the risk of distal embolisation and negative vessel interaction. Integral to it is an internal screw that captures debris, with the intention of reducing the need for aspiration and interim device removal. Investigation to date into rotational atherectomy with the Phoenix system takes shape in the EASE trial, a multicentre non-randomised IDE trial conducted in across 16 countries, with a per-protocol analysis in 106 patients. Lesions included in the study were of Rutherford class 2-5, of total treated lesion length ≤10 cm, as well as possessing at least one patent tibial vessel runoff. Cases with in-stent restenosis, active infection, severe circumferential calcification or evidence of distal embolisation were excluded. Early and mid-term outcomes were published in December 2017, with six-month freedom from TLR and TVR placed at 88.0% and 86.1%, respectively. Major adverse events were experienced by 5.7% of patients through 30 days and 16.8% through six months.[8]

Grigorios Korosoglou

Asked how the particular characteristics of the Phoenix system influenced patient selection in the study he presented at LINC, Dr Korosoglou noted: "Indeed, we used the Phoenix atherectomy device mainly for the treatment of either diffuse or focal highly calcific lesions in femoropopliteal and in BTK arteries. In 2 of 29 cases, we used the device for the treatment of in-stent restenosis. We did not use the device for the treatment of thrombotic lesions or for the treatment of in-stent restenosis with thrombus.

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"We used the Phoenix atherectomy device mainly for the treatment of either diffuse or focal highly calcific lesions." ***Grigorios Korosoglou***

A Phoenix rising

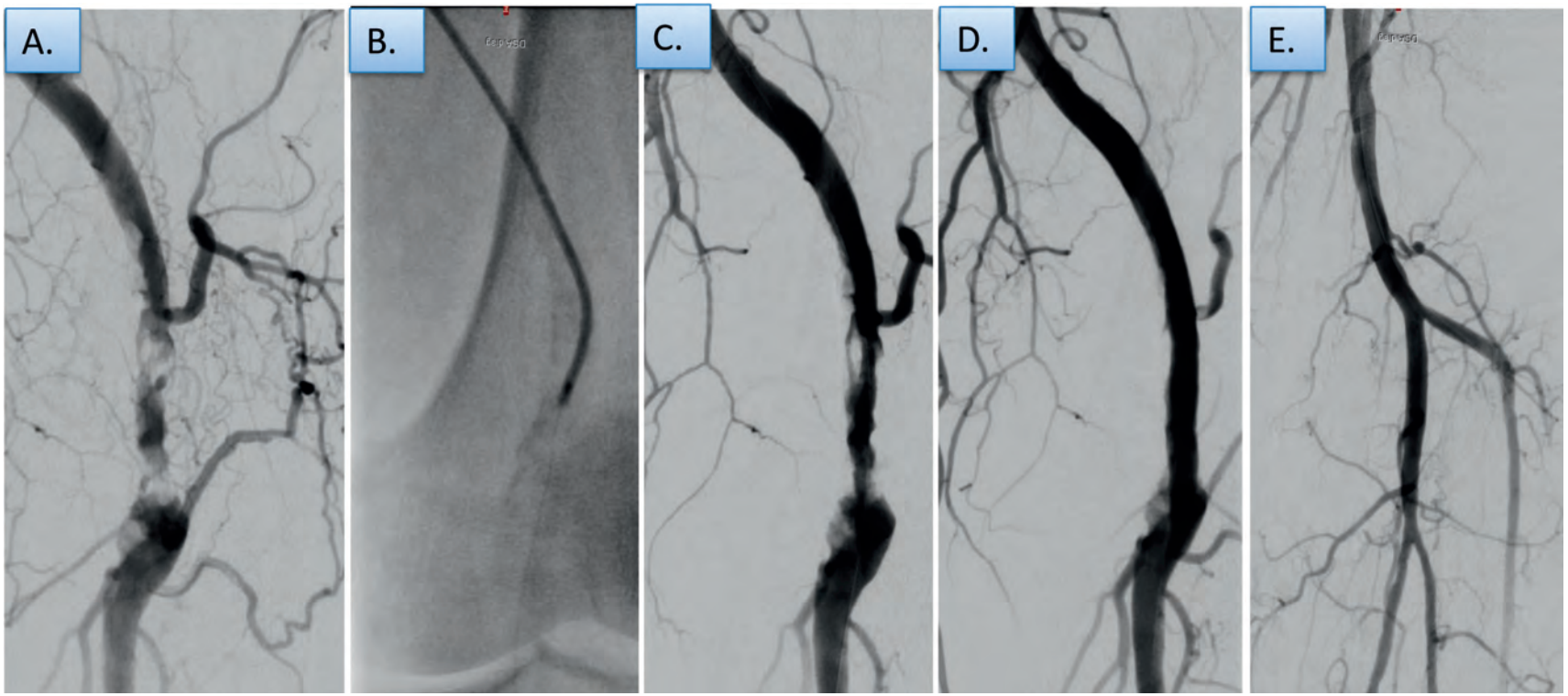

Figure courtesy of Dr Korosoglou, GRN Teaching Hospital Weinheim

Figure 1. Calcified femoropopliteal lesion (A), treated with 7F Phoenix. Full deflection of the device was used to facilitate maximal tissue removal (B). After atherectomy ~50% lumen gain is evident (C). The final result after 7.0 mm DCB at low pressure (6 atm) can be appreciated (D). Stent placement was not deemed as necessary. The outflow is shown in (E).

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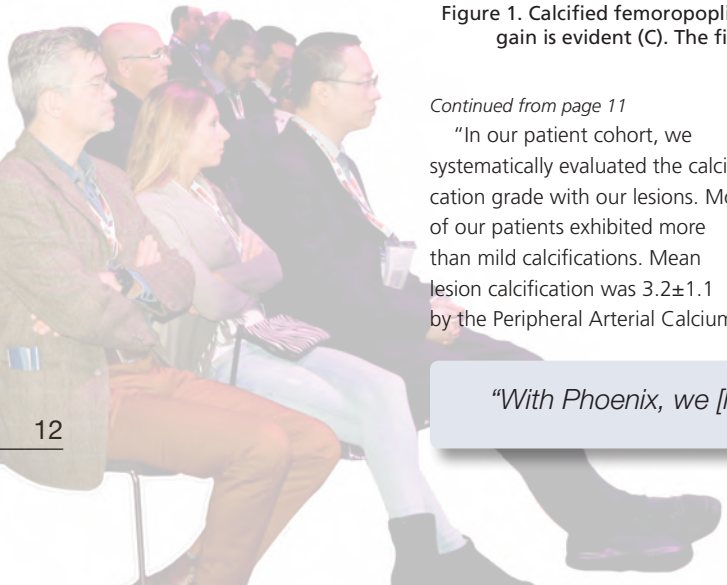
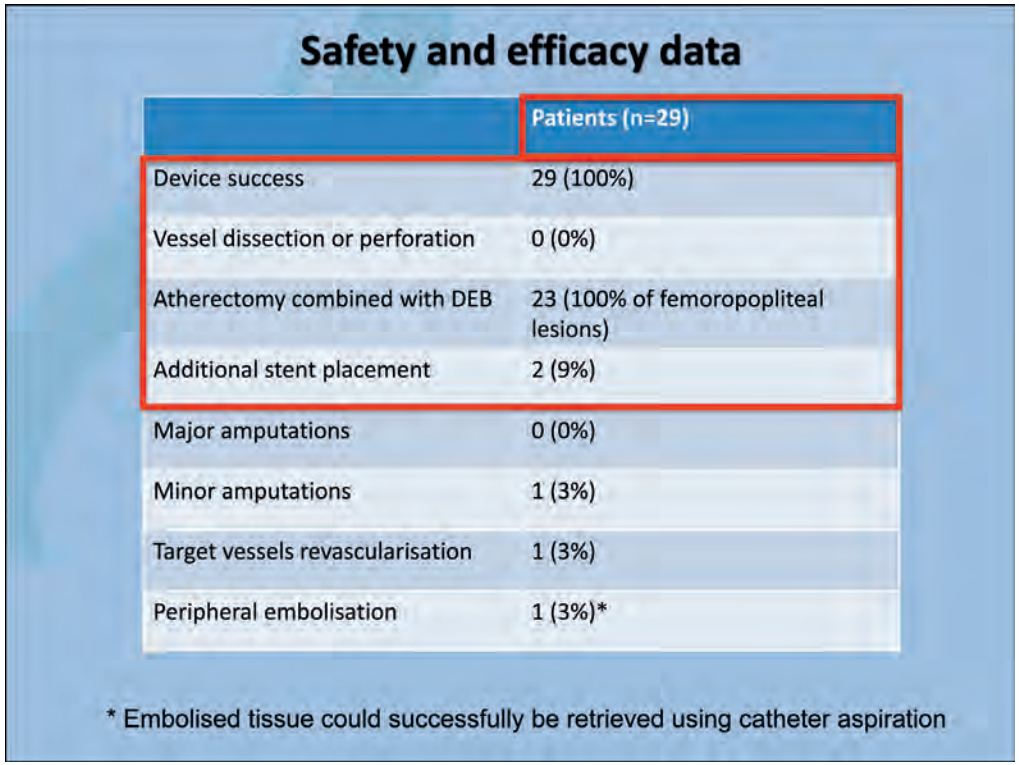
"In our patient cohort, we systematically evaluated the calcification grade with our lesions. Most of our patients exhibited more than mild calcifications. Mean lesion calcification was 3.2±1.1 by the Peripheral Arterial Calcium Scoring System [PACSS score; calcification grades 0 to 4]."

Of the 29 patients in this cohort, six had intermittent claudication, eight ischaemic rest pain without ulcerations, and the remaining 15 had ischaemic ulcerations. Mean Rutherford class was 4.5±1.0. The majority of lesions were TASC C or D. Twenty-four of 29 (83%) patients exhibited moderate or severe calcification and underwent atherectomy of the femoropopliteal (n=23) or below-the-knee (n=7) segments. Atherectomy was followed by DCB angioplasty in all 23 patients with femoropopliteal disease. Technical success of atherectomy was achieved in all patients without vascular complications. Additional stent placement was performed in only two out of 23 patients. No major amputations and one minor amputation was recorded at four weeks of clinical follow-up. TVR was performed in a single patient due to extensive dissection after DCB, which required additional stent placement.

Going on to describe his experience with the atherectomy procedure, Dr Korosoglou continued: "I

"With Phoenix, we [have not observed] any acute complications such as vessel dissection or perforation so far." **Grigorios Korosoglou**





would advocate in favour of DCB after atherectomy for femoropopliteal lesions. With Phoenix, we [have not observed] any acute complications such as vessel dissection or perforation so far. Tissue embolisation was observed in one of 29 cases (3.4%). In this case, catheter aspiration of the embolised tissue successfully prevented embolic vessel occlusion. Thus, the device seems to be safe in the hands of experienced operators."

On the topic of expertise required for the adoption of atherectomy in practice, Dr Korosoglou spoke of the learning curve, noting that he would advise others to choose a single device with which to hone their expertise rather than multiple devices. "For interventional cardiologists who perform similar procedures in coronary arteries such as rotablation, and for interventional angiologists who perform rotational thrombectomy, it should be relatively easy to quickly adopt the use of Phoenix atherectomy in clinical practice."

In his concluding remarks, Dr Korosoglou commented on where he envisions the Phoenix device, and more broadly atherectomy, fitting in amid technology today. Notably, the concept of the 'no-stent zone' has changed dramatically along with improved understanding of biomechanical concepts and their mimicry. Is it the case that both atherectomy and stenting are improving side by side, providing new options for distinct patient populations? And how do such 'competing' technologies compare? "This is definitely a 'tough one'," responded Dr Korosoglou.

"Indeed, both debulking techniques and stent technology rapidly emerged and improved side by side within the last few years. However, particularly for moving vessels segments, such as the popliteal artery, I believe that the notion to prepare the vessel with optimal debulking techniques such as Phoenix atherectomy and finalise the treatment with DCB, avoiding stent placement, would be ideal – especially for younger patients who may need reinterventions or surgical treatment in the long term. With individuals who are older, have cardiac or pulmonary comorbidities and are at high risk for surgery on the other hand, treatment with angioplasty and stent placement may be a more cost-effective and less time consuming alternative option."

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"...it should be relatively easy to quickly adopt the use of Phoenix atherectomy in clinical practice." ***Grigorios Korosoglou***

Challenges to the received wisdom of the ATTRACT trial

Erin Murphy is Director of the Venous and Lymphatic Institute at the Sanger Heart and Vascular Institute at Carolinas Healthcare System in Charlotte, North Carolina, USA. She has authored over 50 articles, serves on the editorial board for the *Journal of Endovascular Therapy* (*JEVT*) and is actively involved in ongoing clinical trials – including as US lead principle investigator for the Medtronic Abre Stent IDE trial. Dr Murphy turned her considerable expertise in vascular surgery to the ATTRACT trial, which sent ripples throughout the community when its results were published. "There are lessons to be learned," she said ahead of the LINC meeting, where she discussed the trials, its shortcomings, and lessons learned moving forward.

ATTRACT compared patients undergoing early thrombus removal with thrombolysis or pharmacomechanical thrombectomy to those managed with anticoagulation alone for the prevention of post-thrombotic syndrome (PTS) after acute proximal deep venous thrombosis (DVT). However, Dr Murphy relayed how the trial reported that early thrombus removal techniques do not lower the risk for PTS compared to anticoagulation alone, but do increase the bleeding risks. "As a stand alone statement, I believe this conclusion is misleading," she said.

"Like most people I was initially surprised and disappointed by the findings of ATTRACT. However, upon further review, there were major shortcomings of the trial that explain the failure to identify a benefit from early thrombus removal in the prevention of PTS after proximal DVT. When viewed from a broader perspective, the results provide an interesting insight into proximal DVT management."

Dr Murphy, who was not involved in the ATTRACT trial, said things have changed considerably. "Overall, the ATTRACT trial was well intended, and was designed according to best standard knowledge and practice at the time," she said. "This trial carries a great deal of weight as it was a government sponsored trial which provides level 1 data and is published in a high impact medical journal."

Because the venous field overall is relatively new, and is still being defined, any level 1 data is highly impactful, she added. "Unfortunately, there are major shortcomings in the trial, which significantly limit the ability to draw conclusions about the prevention of PTS using today's best interventional strategies," she said.


Erin Murphy

"I do not believe the ATTRACT manuscript highlighted either the most significant drawbacks of the ATTRACT trial or the most important lessons to be learned. Those regularly practicing the current best standards for DVT management, which differ from the best management strategies employed during the ATTRACT trial, simply have different outcomes."

The field of venous surgery is in its infancy, so trials are limited. "There is a lack of currently published data to demonstrate this," she said.

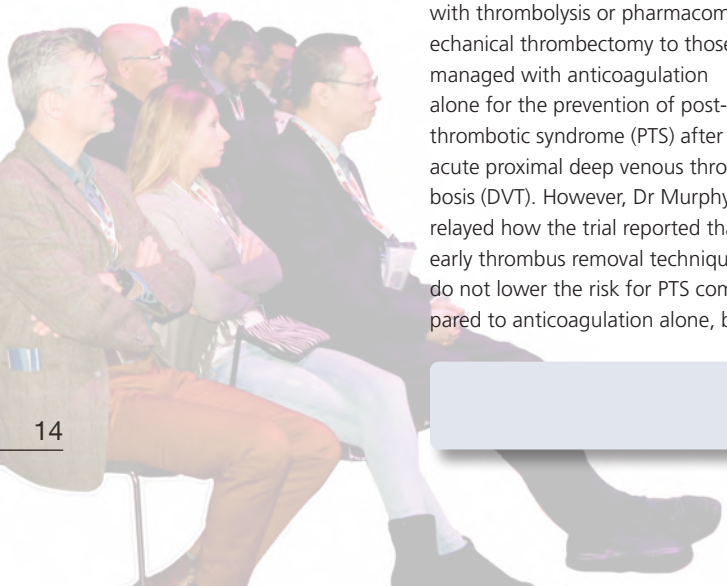
Interventional techniques have evolved beyond the techniques used in this trial, Dr Murphy emphasised: "High-volume interventionalists are experiencing more promising results than suggested by the ATTRACT trial, with regards to the ability of early intervention to both prevent and reduce the severity of postthrombotic disease for patients with iliofemoral DVT. Data demonstrating this are clearly needed."

Other kinds of data are also required, she continued: "Data demonstrating the essential role for intravascular ultrasound are paramount, because experienced operators will tell you that outcomes are strongly tied too this technology."

Isolated data for femoropopliteal DVT might also be useful too, said Dr Murphy, as the number of cases needed to prevent a case of PTS in this group is likely much higher than for iliofemoral DVT and many may not require intervention. "However, there may be some patient subgroups with isolated femoropopliteal DVT who benefit from treatment, and these data are lacking," she added.

But there is reason for optimism, she stressed. "On the upside, this trial has generated significant discussion and has motivated leaders in the field to publish their data which we can expect to start seeing as the year progresses. Thus, in the end, ATTRACT will hopefully help to move us forward as a field."

"Overall, the ATTRACT trial was well intended, and was designed according to best standard knowledge and practice at the time." ***Erin Murphy***



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Open repair a thing of the past for ruptured AAAs

Ruptured abdominal aortic aneurysms (rAAAs) were discussed by Thomas Larzon (Örebro University, Sweden), who argued that all rAAAs can be exclusively treated by endovascular aneurysm repair (EVAR) and adjunctive techniques.

Observational studies and registries comparing EVAR to open repair (OR) have suggested superiority of EVAR in the treatment of rAAAs, but randomised controlled trials have not been able to back this up.[1] That being said, as Dr Larzon has previously stated, experiences gleaned from dedicated centres, especially teaching institutions, show that it is possible to completely replace OR with EVAR by incorporating adjunctive strategies.[1]

One such adjunct is the chimney technique, whereby stents are used to create a landing zone where the main graft would ordinarily cover branch vessels. In brief, a stent is deployed into a branch vessel, parallel to another aortic stent graft.[1] "In an emergency situation, the priority must be to avoid a Type I endoleak in the easiest and fastest way," said Dr Larzon. "Our main principle is to achieve short-term efficacy (to prevent death) and the long-term result must come second. Normally there will be options later on for a secondary intervention, if needed."


Thomas Larzon

He went on to note that some of the most important considerations when planning the chimney technique are how to handle short and tortuous necks, and how to preserve both renal arteries. "Depending on the situation – e.g. is the patient in a circulatory stable situation or not – sacrificing one renal artery can be the strategy of choice," he said. "That also gives the possibility to do a double chimney with the easiest renal artery to cannulate, and the superior mesenteric artery, and that normally gives you a good sealing zone for the stent graft."

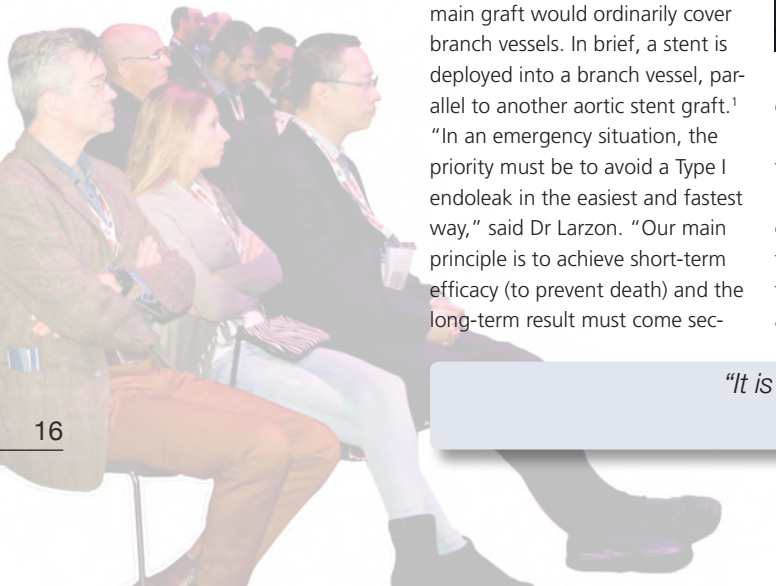
Another adjunctive technique is embolisation, and there are a range of options available. Coils, while reliable for endoleaks, can cause downstream displacement which may lead to ischaemic complications.[1] Alternatively, vascular plugs can be precisely deployed, and are a common solution in large, high-flow vessels at low risk of migration and recanalisation.[1]

"In aorto-iliac aneurysms where you have to extend into the external iliac artery, you need to seal backflow from the internal artery with some sort of embolisation method," said Dr Larzon. "In elective cases, the algorithm is that you embolise the internal artery before you place the iliac stent graft. In an emergency situation, with an unstable patient, that is not an optimal algorithm, so I would say that it is major pitfall. For Type IA endoleaks it can be hard to get coils in all of the positions needed to obtain an instant and complete seal (which is mandatory in a ruptured case)."

Indeed, in cases of tortuous or complicated anatomy, both coils and plugs can be difficult to use effectively. However, other modalities, including liquid embolic protection, could offer a solution – for example the Onyx Liquid Embolic System (Medtronic, USA), which Dr Larzon described: "A key benefit is that you do not have to manoeuvre your catheter to a precise position, rather you just place it in the area where you want embolisation to appear. While coils and plugs are well suited for spot embolisation, such as a defined vessel, liquid embolic protection can embolise an entire cavity."

Dr Larzon noted that while radiopaque material must be added to visualise liquid embolic application, a benefit of Onyx is that it has tantalum already added to the formula. This means it is easy to visualise during fluoroscopy, enabling better protection of remote embolisation in, for example, the renal arteries. However, the downside is that artefacts are created on CT angiograms.

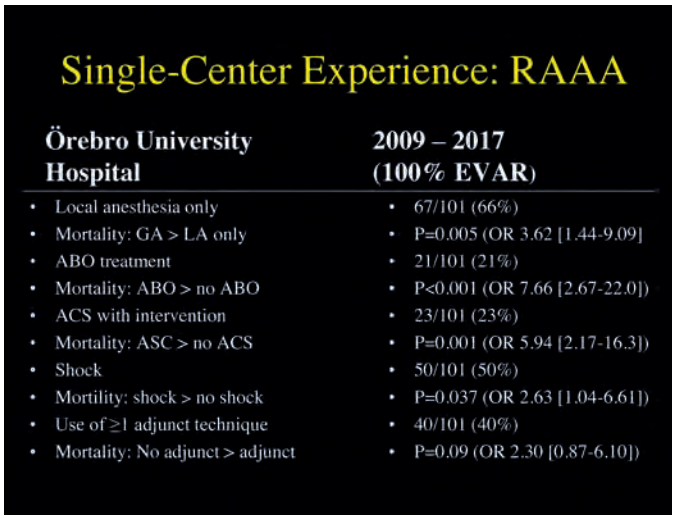
But just how applicable is Onyx in tricky situations such as Type I endoleaks? "My opinion is that liquid embolisation has great advantages in Type I endoleaks, because you can seal both the neck and the remaining cavity in a fast way, with an immediate result," reasoned Dr Larzon.



"It is very simple: if the team treat almost all elective cases with EVAR, they will probably have a much better result if they do the same when a rupture arrives." ***Thomas Larzon***

He went on to note other procedural shifts that have bolstered endovascular treatment of rAAAs, including how to deal with increased abdominal pressure without a traditional laparotomy. "We have shown that a minimally invasive approach, under local anaesthesia – where a drainage catheter is inserted into the haematoma, and is then infiltrated with a solution of blood and tPA – can effectively remove blood," he said. "We need to know more about the technique, when it is sufficient, and in which cases the traditional technique is necessary."

He also stressed that the most influenced procedural shift has been the introduction of local anaesthesia, facilitated when using a percutaneous technique. He relayed that when he started to treat rAAAs via EVAR in 2001, there was still an aim to perform procedures percutaneously. "We implemented the fascia closure technique, and it is still in use for us even though there are suture-mediated closure devices on the market, working well," he said. "However, they need the sutures to be adapted as the first step of the operation. It is a drawback which the fascia suture technique does not have."



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Dr Larzon shared the single-centre experience he has assembled over the years at Örebro University Hospital. Impressively, the last open repair of an rAAA performed at the hospital was in May 2009. However, the results were not always open-and-shut for the EVAR-only approach. "You will go through different phases," said Dr Larzon. "When I started in 2001, our results were stunning, with a 30-day mortality of 13%, compared with almost 50% for open repair. That was the reality at that time.

"However, there was a selection bias, [although] it was not cherry picking where we just treated stable patients. In fact, we had more unstable patients in the EVAR group than in the open repair group. But we did not have the adjunctive techniques at that time, and short necks – for example – were a technical limitation. Also, a 24/7 endovascular service was not possible at that time.

"The next step was when we expanded the indications, changed from a single operator to the whole team, and finally changed to the 100% EVAR strategy. The mortality rate was doubled during that period. But now we are in the third phase, where the whole team performs elective EVAR on a regular basis, have experiences of adjunctive methods, and have the skill to perform even complicated ruptured cases. Now we see that the mortality rate has started to go down again."

Dr Larzon was keen to underline that just because all rAAAs have the potential to be treated with EVAR and adjunctive techniques, that does not mean that they all will: "It is all about the skill of the team at that special day and time when you face the patient with a ruptured AAA. It is very simple: if the team treat almost all elective cases with EVAR, they will probably have a much better result if they do the same when a rupture arrives."

Speaking more generally, Dr Larzon also turned to the criticisms of EVAR. For instance, bias is a common complaint about EVAR registries, but RCTs are now also seeing their fair share of criticism. "Today it seems to be a consensus that the RCTs are also flawed," he said, adding: "My understanding of the debate is that there is a shift towards EVAR as the first line of treatment."

Framing the kinds of solutions that could help more people trust in the data, Dr Larzon emphasised the potential in creating protocols that centres can rely on. "Treatment is not just about the procedure itself, but about the whole chain: from the first call, to transportation, to emergency department setup, to procedure and then to post-procedure strategy. I am not sure that another RCT can add value."

Dr Larzon shared his concluding thoughts: "I do think that the successful implementation of ruptured aneurysm EVAR will facilitate opportunities to also implement endovascular methods in other emergency aortic diseases. I am especially thinking about acute Type A dissection, where we have a deeply established tradition for open repair. Two cultures will meet, and there will surely be occasion for controversy, but the history of EVAR has shown that you never can stop development.

"What could be better for the patient than taking the best experiences from two different worlds? And in the new world, I am convinced that endovascular methods will have a significant role."

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"What could be better for the patient than taking the best experiences from two different worlds?" ***Thomas Larzon***

Stem cell angiogenesis: showing promise

Sigrid Nikol (Asklepios Klinik St. Georg, Hamburg, Germany) presented on the current developments in cell and gene therapy during a Focus Session on 'no option' CLI patients.

Dr Nikol presented the design of the PACE study, the randomised, double-blind, multicentre, placebo-controlled, parallel-group phase III study to evaluate the efficacy, tolerability and safety of intramuscular injections of PLX-PAD (placental-derived adherent stromal cells) for the treatment of patients with critical limb ischemia (CLI) with minor tissue loss who are unsuitable for revascularization.[1] PACE is an EU-sponsored Horizon 2020 project. The study is presently in the early stages of randomisation.

Dr Nikol has previously conducted research in angiogenesis gene therapy[2], a field she has now deems "dead". "All the last trials were, as far as I know, prematurely ended. Last year there was still one large trial recruiting, but that has also been ended prematurely."

Efforts are now planted firmly in the cell therapy realm, specifically using allogeneic placental cells. While cells derived from patients themselves are likely to be more immunologically compatible, other issues have proved problematic.

Referring to work by Hill *et al*. wherein increased cardiovascular risk was associated with depletion of progenitor cells[3], Dr Nikol said: "It has been shown that cells taken from older organisms produce less growth factors, and the number of available cells is lower."

Most published work to date has been carried out using autologous cells derived from blood or bone marrow. While a 2015 meta-analysis on all available randomised, placebo-controlled[4] demonstrated no advantage of bone marrow-derived stem cell therapy on the primary outcome measures of amputation, survival, and amputation-free survival in patients with CLI, the authors concluded that more sophisticated cell therapy strategies should be explored in future randomised trials.[4] Presently, a number of trials continue to explore both autologous bone-marrow and allogeneic stem cell therapy for peripheral artery disease.

"Many colleagues still believe in autologous cells, and do not know about this 2015 meta-analysis," commented Dr Nikol. "From the scientific point of view they did not prove any benefit."

"For the PACE trial, we have very well-defined cells, coming from young, healthy women. The cells are much better than autologous cells from older organisms."

Sigrid Nikol

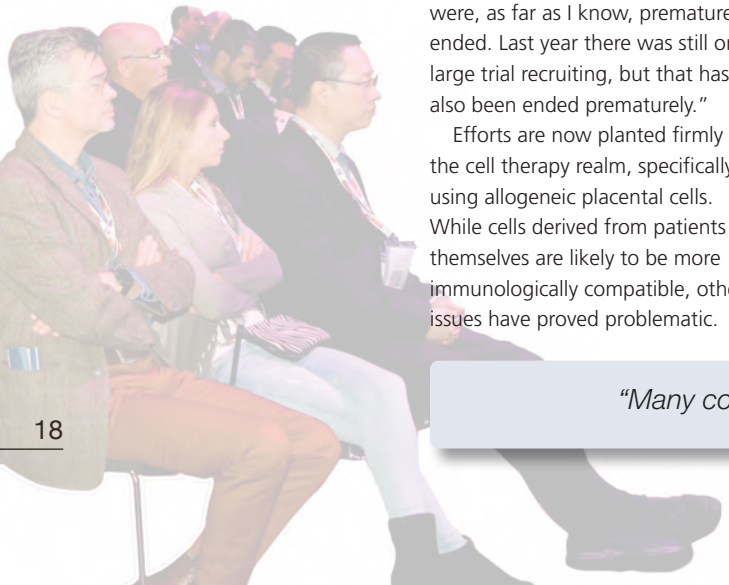
After being extracted, placental cells are grown in vitro within a proprietary platform, after which they can be frozen and stored. The fact that these cells are placenta-derived means that quantities are potentially unlimited, explained Dr Nikol, as well as allowing for quality control and greater cost-effectiveness. Despite them being allogeneic, placental cells are largely immunoprivileged, with no evidence existing of PLX-PAD specific humoral or T-cell allosensitisation.

The PACE study will evaluate patients with Rutherford 5 CLI with regard to the efficacy of PLX-PAD intramuscular injections given twice at eight-week intervals, in order to extend the duration of growth factor secretion (it is know that cells may not survive for long periods following administration).

The study is being carried out in Europe and North America, with a duration of 36 months. A total of 30 injections are made above and below the knee, anteriorly and posteriorly. Injections sites do not include the foot, explained Dr Nikol, because very little muscle occurs here, especially in CLI patients experiencing muscle atrophy as a result of ischaemia. Yet, despite patients characteristically having poor run-off to the foot, it is known from animal studies that growth factors effectively permeate systemically throughout tissues to the extent of reaching the contralateral leg as well as the foot ipsilaterally.

The primary endpoint of PACE is amputation-free survival, and a number of secondary efficacy and exploratory endpoints will also be investigated[1]. Asked whether proving efficacy in a cohort of such sick patients might be confounded by their comorbidities, Dr Nikol noted that previous work in angiogenesis gene therapy for claudication had failed, forcing the question as to whether this might be too early a disease stage to demonstrate a benefit.

In order to address this, Dr Nikol and others are currently investigating the treatment of intermittent claudication with placenta-derived



"Many colleagues still believe in autologous cells, and do not know about this 2015 meta-analysis." ***Sigrid Nikol***

Laboratory production of placental cell products with the proprietary bioreactor system.

stem cells, in a multinational phase II trial (n=172)[5]. This study is now in the follow-up phase, with first findings expected to emerge later this year: "The proper evaluation of the trial has to be awaited, so I would just give as my impression that generally there are hints that the repetitive therapy with cells is better than just a single therapy, which goes along with the preclinical data."

"We always felt that early therapy would probably be better, because it takes a lot of time for collaterals to grow. We know from pig experiments that it takes several months – and these were very young pigs. But the older the organism, with cell doubling being lower, the longer it takes. It may well be that, if we start with angiogenesis at too late a stage, it is just too late.

"This is why you see that in the PACE study only Rutherford 5 patients with stable ulcers were allowed. We feel that if we allow Rutherford 6 with large ulcers, or big problems with gangrene or uncontrolled infection, that angiogenesis would come too late. Then we would get confounding results, too many amputations and too many deaths."

Exploratory endpoints in the PACE study look at contralateral leg effects, as well as wound healing, pain and quality of life endpoints. In addition, a mechanism of action sub-study will be carried out, investigating immunologic reactions as well as cytokine and mRNA expression. "The good thing about the EU project is that we have on the one side, the clinical assessments. On the other hand we have the Brandenburg Centre for Regenerative Therapies in Berlin, where they do all the investigations regarding all kinds of mechanisms.

"They do sequencing of the cells, looking at whether the cells from the different placentas are different. They also look at what kind of immunological reactions the cells cause. Also, how does the body react against them? It goes both ways. It is known that these cells do have effects on inflammation. On the other hand, what does the body do to these cells? They are allogeneic (derived from another body) and normally rejection happens. We know that these cells do survive for some time and don't cause severe rejection reactions, but probably they do cause a little bit of rejection. This is being investigated with immunological tests.

"It has to do a lot with mechanisms too. Whenever we present clinical data people ask for mechanisms. How does it work and how does the body react? Not everything you can translate from mice to men. I just learned that in Japan, therapies can be approved based just on animal experiment. But, at least in the West, it is also required to test on humans because the reaction, and the dosing, may be different."

"We have very well-defined cells, coming from young, healthy women…much better than autologous cells from older organisms." ***Sigrid Nikol***

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Know when not to stent in acute DVT

Live from Galway University Hospital, Ireland, Gerry O'Sullivan presented a case of extensive iliofemoral DVT with concomitant popliteal and calf vein thrombosis, alongside Mahmood Al Hajriy (Royal Hospital, Oman). While the procedure was not carried out live, it was presented by Dr O'Sullivan as a learning opportunity given the challenges that may be associated with less-than-ideal cases of acute DVT such as those with delayed presentation of more than six weeks.

"This is a really good learning case," said Dr O'Sullivan. "It shows what to do when things aren't perfect. In an ideal world we will always get patients with acute DVT of under 14 days…they will all be fit and active and young, and we will treat them with a single-session device and they will be home the next day.

"In reality, not many patients are like that. Most of the cases you get are delayed – delayed presentation, or the medical people won't refer them, and they actually don't come to you often until after three weeks. Anything over three to four weeks is not an ideal time to treat, because thrombolysis does not have the same action (the fibrinogen receptor sites shut off). This case exemplifies a few different angles of that."

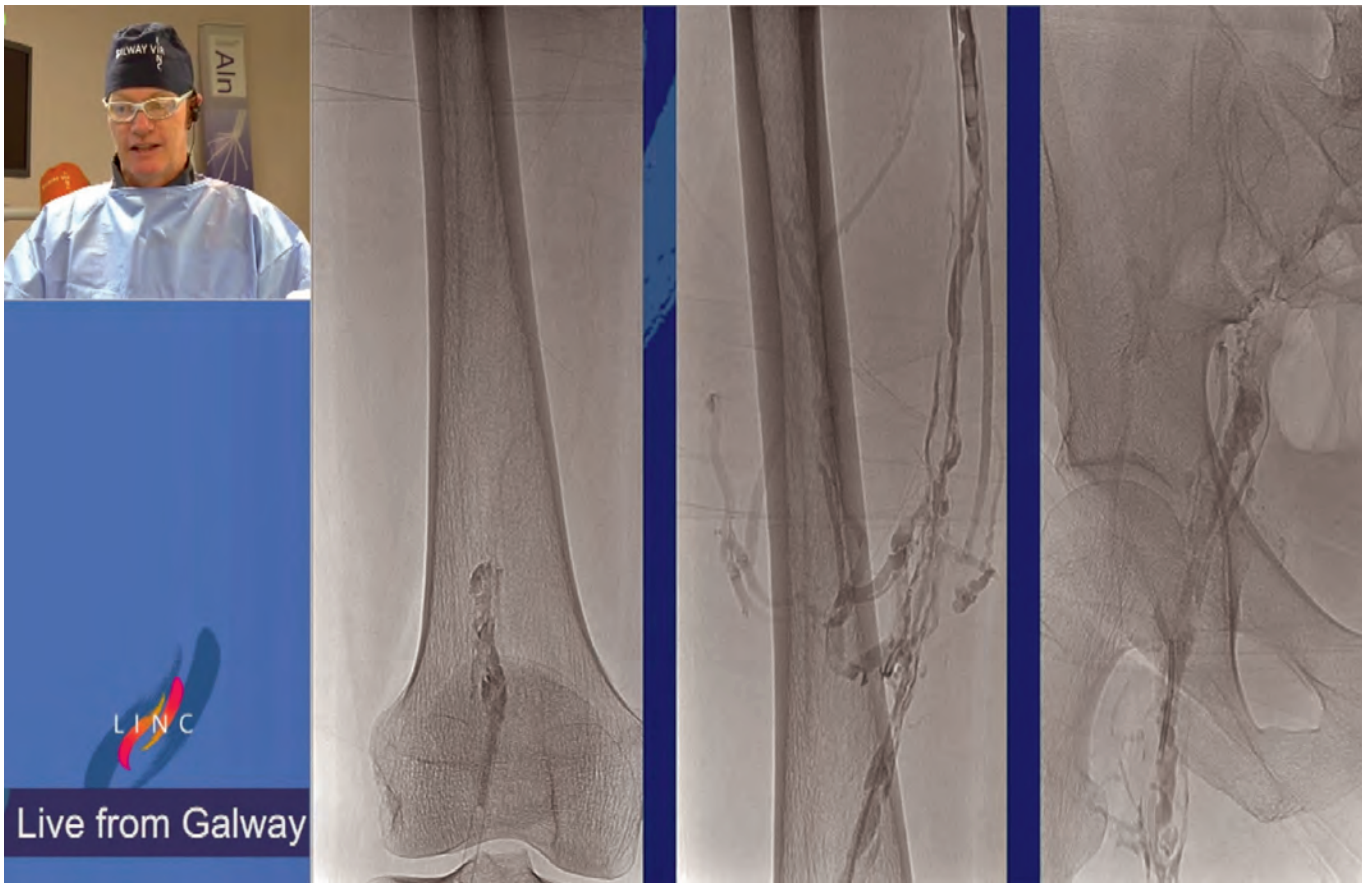

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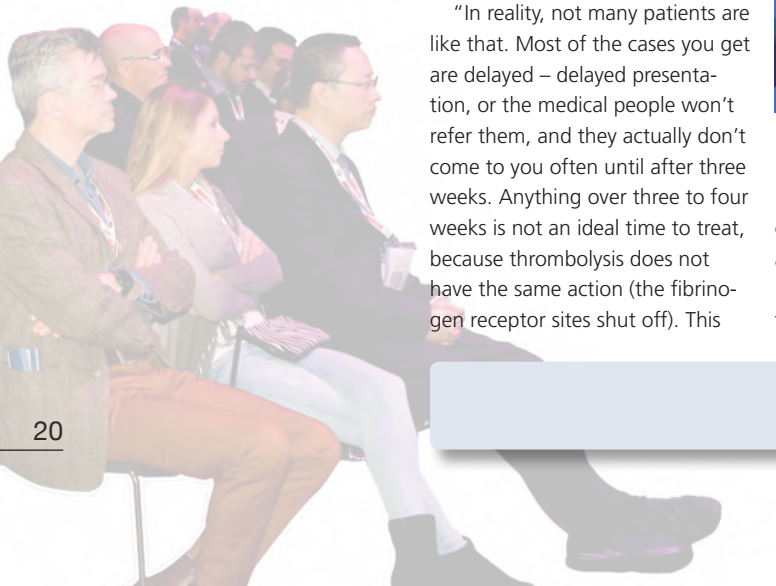
Figure 1. The patient's extensive DVT included a thrombosed popliteal, scarred femoral and common femoral veins, and absence of flow in the iliac vein. Thrombus was also evident through the mid-calf.

The patient was a 50-year-old female with no past relevant history or medication. She initially presented in March 2017 with acute DVT. Thrombolysis was attempted on day 10 of symptoms. An inferior vena cava (IVC) filter was placed due to pulmonary embolism, although the patient unfortunately developed acute anaphylactic reaction to contrast leading to hypotensive shock on the table. After resuscitation, the procedure was abandoned, and the patient

"As the experts have shown me, the whole game is the in-flow." **Gerry O'Sullivan**



was given anticoagulation.

Around six weeks later, the patient returned with severe swelling of the left leg (without ulceration) and was in a great deal of pain. "This was precisely the wrong time to intervene," commented Dr O'Sullivan. The patient was found to have a patent IVC, but occlusion from the common femoral vein down to the mid-calf, including the profunda femoris. The popliteal vein was also thrombosed. (Figure 1).

"The US ACCESS PTS trial would suggest that you can treat these patient aggressively with the EkoSonic Endovascular System [EKOS, USA – a BTG International group company] catheter-directed thrombolysis[1]. I must say, I haven't a great deal of experience in that.

"This was an intelligent woman, who was taking her anticoagulation and wearing her [compression] stocking. Because she was between six weeks and six months, I didn't really *want* to do anything. But her leg was very painful. So she falls into an unusual category where it is worthwhile treating."

The team carried out a technique of simultaneous antegrade and retrograde vascular access to the popliteal vein – the 'criss-cross' technique – as recently described by O'Sullivan and others (2018). In this technique, antegrade popliteal venous access is gained according to the usual technique using duplex ultrasound (DUS) guidance, and thrombolysis or thrombectomy is then performed. Then, a retrograde sheath is placed under DUS guidance, a tibial vein is selectively catheterised, and again thrombolysis or thrombectomy is performed.[2]

In the present case, thrombectomy was performed using Penumbra Continuous Aspiration Mechanical Thrombectomy 3 (CAT3) and 8 (Penumbra, USA). "Within about 30 minutes, [the patient] had less pain in the leg. That was really gratifying," said Dr O'Sullivan.

Following this, catheter-directed thrombolysis was performed for 48 hours, which partially resolved the extent of thrombosis. Angioplasty was then carried out, with aggressive ballooning of the common femoral vein. Despite unresolved poor in-flow, the leg was much improved clinically, noted Dr O'Sullivan. "This is a situation that I have been in many times. And this is why I don't treat people generally between six weeks and six months, because you end up with what I would call 'a dog's dinner'. There is no good in-flow, and no defined profunda femoris vein. The femoral vein is clearly scarred. There is no iliac. My experience in these patients is that if you stent them when there is no defined in-flow from below, everything will thrombose in a matter of days. Then you are in a much worse situation."

As such, the patient did not undergo immediate stenting, but went under anticoagulation and returned after six months. In this way, explained Dr O'Sullivan, a dominant in-flow would establish itself.

After six months, the patient returned. She underwent MR venography indicating normal IVC, but signs of classic iliac vein compression syndrome on the left side, with "obliteration" of the left common iliac vein, scarring of the (very small) left external iliac vein, with synechiae running through the left external iliac vein. "There is nothing unexpected in all of this," said Dr O'Sullivan.

"As the experts have shown me – Michael Lichtenberg, Rick de Graaf, Stephen Black, and Nils Kucher – the whole game is the in-flow. This is where it all begins and ends. You need to decide on your in-flow, and you need to decide which vein you are going to access."

Noting the presence of scarring at the mouth of the profunda visible on MR venogram, and the important implication this has in venous recanalisation (where the principle is to stent from healthy to healthy vessel), he continued: "You need to get the in-flow right if you expect your stent to stay open. Every person I know who does this intervention agrees that stents are essential. Balloon angioplasty on its own is a waste of time. That is not because I like using stents, but they are an essential tool, I think everyone would agree, for venous intervention."

The team proceeded with stenting. The team planned at outset to enter with right internal jugular vein access with a 10-F sheath and 45-cm hockey-stick catheter. A CXI (Cook Medical, USA) would be used to cross the lesion from above, followed by a hydrophilic guidewire. Dr O'Sullivan noted the importance of oblique views to determine the best path during lesion crossing, followed by ultrasound of the left groin if necessary, to see if the profunda femoris vein is visible for access. This would be followed by high pressure predilatation ballooning with a 16-mm Atlas (CR Bard, USA) in the common iliac vein. Stenting would be carried out in the common iliac and common femoral veins, followed by post-dilatation ballooning.

Stressing the importance of IVUS guidance during this intervention, Dr O'Sullivan said: "I used to think that you could get away without IVUS, but I was wrong. You must do IVUS, if you are in a serious venous programme."

The critical aspects after the intervention, he continued, are the use of pneumatic compression boots, class 2 thigh-high stockings, colour Doppler ultrasound on day 1, 30 and 90, and full anticoagulation for six months before review.

Following the principle of stenting from healthy to healthy vessel, IVUS was used to identify the dominant in-flow vessel. Complete occlusion of common iliac and external iliac veins was apparent. Through the May-Thurner point, extensive scarring was visible in the common femoral vein, together with a lip of scarred synechiae sitting across the mouth of the profunda femoris. For these reasons, the profunda femoris was the dominant vessel, and so ballooned at high pressure using a 16-mm Atlas. Then, a 14x140 mm Zilver Vena stent (Cook Medical)

Continued on page 22

"Stents are essential. Balloon angioplasty on its own is a waste of time." ***Gerry O'Sullivan***

Know when not to stent in acute DVT

Source: www.leipzig-interventional-course.com

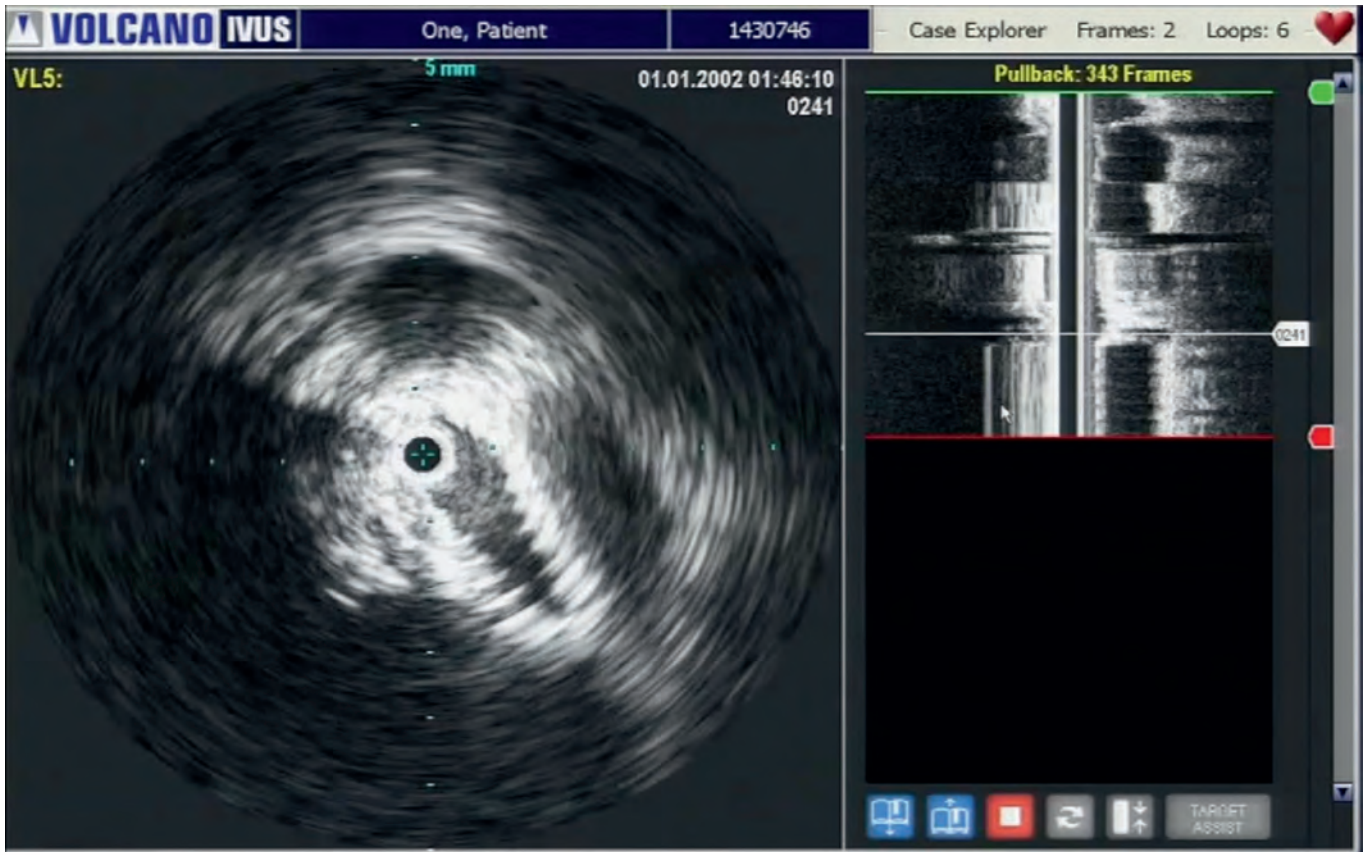


Figure 2. IVUS clearly showed compression of the Veniti Vici Venous Stent placed in the left common iliac vein.

Continued from page 21

– selected for its flexibility – was placed, terminating at healthy profunda vein, and ballooned aggressively to 14 mm.

"You might say that this is ridiculous – that you can't stent beyond the inguinal ligament," said Dr O'Sullivan, "But unless you are going back to normal vein you are wasting your time. This is not like arteries – you can't spot stent and then expect the arterial 160 mmHg of pressure to push through. Here, you need in-line flow through a normal repaved vein."

The high radial force 16x120 mm Veniti Vici Venous Stent (Veniti Inc., USA; distributed by Boston Scientific, USA) was selected at the left common iliac vein. However, its placement did not go according to plan, as Dr O'Sullivan explained: "When you are placing this stent, there is risk of contralateral iliac vein thrombosis. But a far bigger risk is not covering the causative lesion. Those of us that have made as many mistakes as I have, have been caught out both ways. But today, I made the mistake of landing the stent too low."

Although the stent result looked acceptable on fluoroscopy, IVUS showed it to be seriously compressed (Figure 2). At the lower end of the stent, a 30-mm gap was evident between the just-placed Vici Venous and the Zilver Vena stent. In order to cover this gap, a 16x90 mm Wallstent (Boston Scientific) was implanted. Then a 16x60 mm Vici Venous was implanted at the stenosed left common iliac segment. This, despite all intermediate issues, resulted in perfect in-line flow, as confirmed by IVUS and fluoroscopy. "Compared to what we had to start with, that is a really good result," said Dr O'Sullivan in closing.

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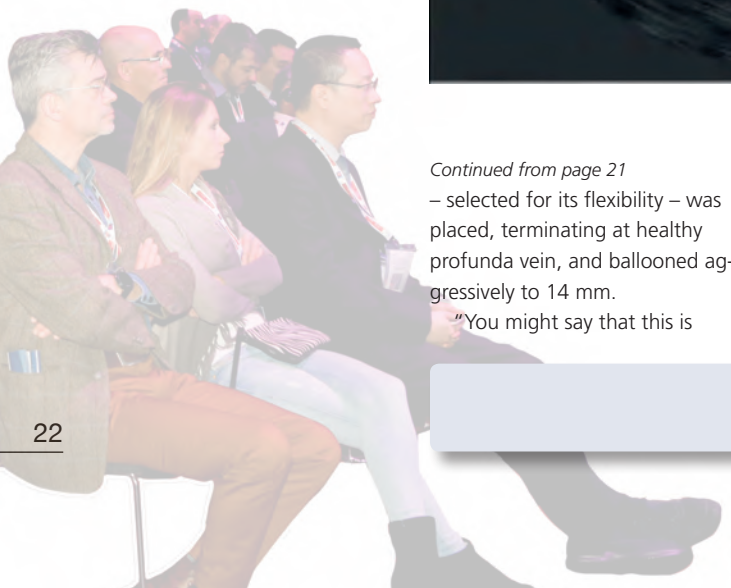
"You must do IVUS, if you are in a serious venous programme." ***Gerry O'Sullivan***



‘Astonishing’ results of Luminor in fempop artery

The Luminor drug-coated balloon (DCB) took centre stage at the iVascular symposium with results from two major trials reported.

Introducing the Global Expert Exchange Forum session, Koen Deloose (AZ Sint Blasius Dendermonde, Belgium) relayed how the programme would encompass both data on the use of Luminor in the superficial femoral artery (SFA) before moving to the below-the-knee (BTK) area. At the symposium, data from the Angiolite drug-eluting stent (DES) and iVolution self-expandable stent were also presented to finally discuss the best solution. “With the SFA we know that we have the treatment possibility of DCBs, but also of modern nitinol stents. It’ll be interesting to hear what works best in which indication,” said Dr Deloose.

Luminor is a paclitaxel-coated balloon specifically designed for dilatation of stenosis located in the iliac, femoral, iliofemoral, popliteal, infrapopliteal and renal arteries, as well as for the treatment of obstructive lesions of arteriovenous fistulas, whether original or artificial. It is also indicated for stent post-dilatation in the peripheral vascular system.

Koen Deloose

Ulf Teichgräber

It is available with 0.014”, 0.018” and 0.035” guidewire compatibility, providing the most completed DCB of the market.

It is designed to have crossing capability, optimised shape with short shoulders and short inflation time (only one minute). The DCB itself is coated with paclitaxel (3 µg/mm^2) and uses a unique nano technology coating known as TransferTech™ that ensures uniform delivery to the vessel wall and minimised drug loss during navigation.

First to the podium was Professor Ulf Teichgräber (University Hospital Jena, Germany), who discussed the six-months results of the EFFPAC trial. This is a multicentre, randomised controlled trial (RCT) to assess the effectiveness of paclitaxel-coated Luminor balloon catheter versus uncoated balloon catheter (plain old balloon angioplasty; POBA) in the SFA and popliteal arteries to prevent vessel restenosis or re-occlusion.

“What is so special about Luminor is the unique nano-coating technology that is ultra-thin and uniform,” said Professor Teichgräber, principal investigator of the study. “But does the theory translate into trial results?” he added.

The EFFPAC trial, held across 11 sites in Germany, pre-dilated all patients with POBA as per protocol, then a second angiography was carried out prior to randomisation. The primary efficacy endpoint was late lumen loss (LLL); with secondary endpoint set at freedom from target lesion revascularisation/target vessel revascularisation (TLR/TVR), patency, change of ankle brachial index (ABI), Rutherford stage, and quality of life. The primary safety endpoints were major and minor amputation rate of the index limb, and mortality independent of cause.

Of the 171 patients randomised 1:1 to POBA or Luminor, 77 and 76 reached six-month follow-up, respectively, and were entered into the analysis. “A total of 37-41% had diabetes with nearly 80% having claudication,” reported Professor Teichgräber. “Lesion lengths in both groups were approximately 6 cm, and total occlusion rate was 20% and 25% in the Luminor and POBA arms respectively. Vessel preparation was performed in both groups, dissection rate was nearly 40% in both groups, and bailout stenting was relatively low at 15-18%.”

Professor Teichgräber emphasised that the results were “quite astonishing.” Late lumen loss was 0.14 mm [CI: -0.38; 0.67] in the Luminor group versus 1.06 mm [CI: 0.54; 1.59] in the POBA group. “This was the best result compared to trials with a similar study design,” he said, adding that it is also the first balloon to show clinical benefit according to improvement of three Rutherford stages at

Continued on page 24

“Compared to other similar trials, these results are by far the best at six months.” ***Ulf Teichgräber***

‘Astonishing’ results of Luminor in fempop artery

Continued from page 23

six months.

Clinical improvement in walking distance was seen using Luminor, and Professor Teichgräber added that the TLR rate was also “surprising”, at 1.3% versus 17.1% in the Luminor versus POBA groups, respectively. “Compared to other similar trials, these results are by far the best at six months.”

Patency at six months was 94.7% and 75.0% in the Luminor and POBA arms respectively (relative risk: 1.26; p<0.001). “Again, compared to other trials, it is the best at the moment,” asserted Professor Teichgräber. “Luminor also showed no adverse events at six months, including minor and major amputations

“The Luminor DCB shows high clinical effectiveness and safety in inhibiting restenosis compared to POBA. The innovative coating matters and is shown not only in the patency, LLL and TLR data, but also in an improvement of the Rutherford stage.”

Vicente Riambau

Peter Goverde

Marc Bosiers

12-month Luminor registry data

Vicente Riambau (Hospital Clínic of Barcelona, Spain) shared the Spanish experience with the Luminor DCB, by reporting results of the LUMINOR Registry, which is an observational, prospective, multicentre study with single-arm treatment for stenotic or occlusive lesions, or in-stent stenosis of the femoropopliteal and BTK vessels.

“Real world experience with Luminor DCB is highly positive in terms of safety and effectiveness, even in patients with very poor clinical and anatomical conditions,” said Professor Riambau. “Its extra low crossing profile combined with TransferTech, the iVascular proprietary technology for drug release, have demonstrated Luminor DCB efficacy in several clinical studies,” remarked Professor Riambau.

The primary endpoints of the study comprise primary patency, defined as freedom from >50% restenosis as indicated by duplex ultrasound peak systolic velocity ratio (PSVR) <3 in the target vessel with no re-intervention, and freedom of serious adverse events defined as death, major amputation and TLR during a 12-month follow-up period.

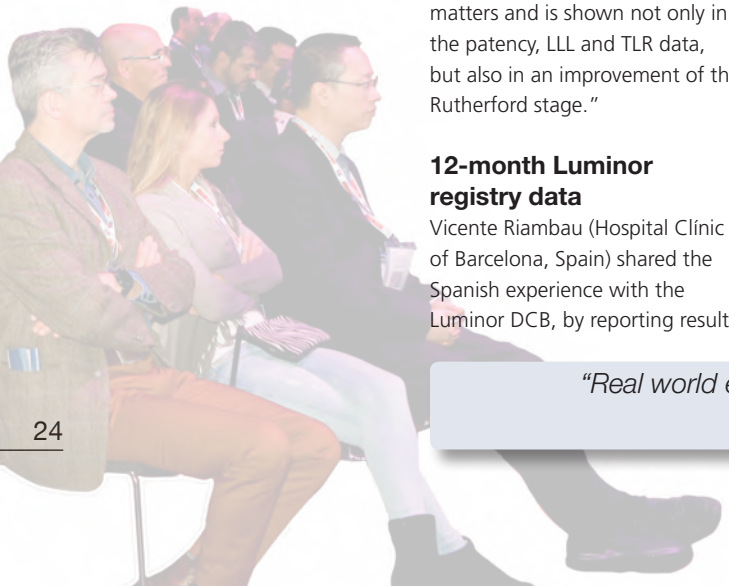
A total of 207 validated Rutherford 2-5 cases were recruited during a 15-month period.

Referring to patients with critical limb ischaemia (CLI) alone (n=148), 72% had diabetes, 30% had chronic renal failure, and 84% were Rutherford class 5, reported Professor Riambau. A total of 180 lesions of mean length 77.4 mm were included, with 54% totally occluded, 46% with stenosis, 49% sited BTK, and 56.7% severely calcified.

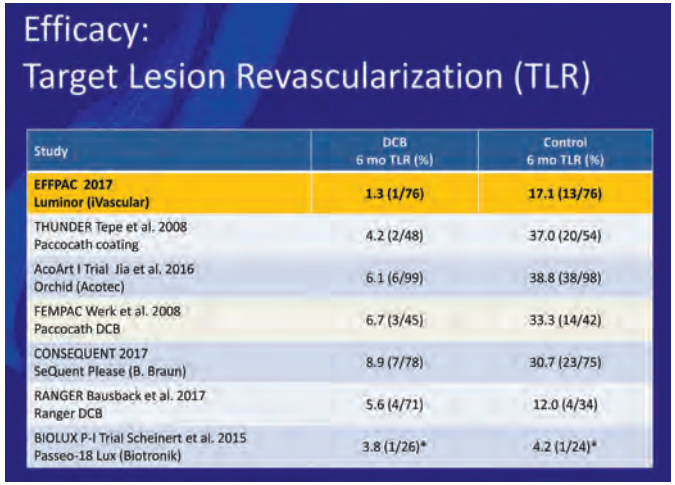
In the CLI group, 30-day follow-up showed a 3.4% all-cause mortality; 2.0% major amputations; and TLR of 1.7%. At one-year follow-up, primary patency was 87.7%, one-year survival was 85.1%, freedom from amputation was 84.7%, and freedom from TLR was 92.1%.

Looking at BTK cases alone, one-year interim results showed 85.9% primary patency, 88.2% survival (primary patency), freedom from major amputation of 79.0%, and freedom from TLR of 89.6%.

“Real world experience with Luminor DCB is highly positive in terms of safety and effectiveness, even in patients with very poor clinical and anatomical conditions.” ***Vicente Riambau***



Source: iVascular



Angiolite BTK six-month data

Peter Goverde (ZNA Vascular Clinic in Antwerp, Belgium) also presented results at the symposium, in his talk entitled, 'Is there still any space left for drug eluting stent (DES with sirolimus) in the BTK area?'

Angiolite BTK is one of only four DES on the market with the indication to treat BTK arteries, but of note, it has the strongest radial force. The results presented by Professor Goverde referred to the six-month data of the Angiolite BTK trial.

This trial was a safety and feasibility study with Angiolite BTK as a bailout in BTK procedures in a prospective, single centre, real-world study of 50 patients with Rutherford-Becker lesions of 4-6. Primary endpoints were safety and feasibility using the Angiolite BTK DES and absence of clinically driven TLR at 12 months.

Interim results showed that primary patency was 88% at six months. "Use of Angiolite BTK is safe and feasible but follow-up work needs to confirm advantages. There appears to be a positive effect on revascularisation and wound healing," he concluded.

iVolution

Finally, Marc Bosiers (St. Blasius Hospital in Dendermonde, Belgium) reported 12-month data of the EVOLUTION trial of the iVolution stent. The prospective, non-randomised, multi-centre study investigated the efficacy of the self-expanding iVolution nitinol stent for treatment of femoropopliteal stenotic or occlusive lesions. This stent is the most flexible stent on the market, with a great radial force. It also has a high nitinol quality, without inclusions* that are known as a factor of stent rupture.

The primary endpoint was primary patency at 12 months, defined as freedom from >50% restenosis. A total of 120 patients received treatment and at 12 months 86.3% showed primary patency, 88.0% showed freedom from TLR.

"The final results show that the iVolution stent is a very effective treatment for femoropopliteal TASC A and B lesions," concluded Dr Bosiers.

Closing the session

Wrapping-up the proceedings, Dr Deloose thanked all the speakers and concluded that all the outcomes, using an iVascular DCB or a stent, are highly significant and the chosen treatment depends on the case.

* Publication under review, data on file at iVascular SLU

"Use of Angiolite BTK is safe and feasible … There appears to be a positive effect on revascularisation and wound healing." ***Peter Goverde***

Retrograde puncture below the knee: a growing trend

Retrograde tibial puncture has changed the algorithm for crossing tibial lesions in CLI, said Peter Schneider (Kaiser Foundation Hospital, Honolulu, Hawaii) to delegates at LINC 2018. Dr Schneider described this new algorithm, as well as some of the data that reflect its growing support among the interventional community.

The concept of retrograde tibial puncture, he explained, has been popularised by the Leipzig group. Crossing tibial occlusions endovascularly must be reliable in order to treat CLI patients. As shown by Graziani *et al*. (2007) in a study of diabetic patients, 66% of below-the-knee lesions were occlusions, 50% of which were >10 cm[1].

"The old paradigm – at least in our practice – was to do everything we could antegrade, and if we still couldn't, there was the potential to try again or to do a bypass," commented Dr Schneider. "Our new algorithm is to go directly to retrograde, by tibial or pedal puncture."

There are several rationales for this, he explained: "The branches and collaterals take off with a caudal angle from above, and the wire often gets lost in any potential tributary or collateral. Second, the distal end of the occlusion is often softer than the proximal end, and we learned this by doing, for example, iliac and sometimes superficial femoral artery [SFA] occlusions. Thirdly, it turns out that tibial or pedal puncture is much safer than I thought it would be."

Dr Schneider also spoke about clinical issues, noting that he typically applies the retrograde approach for CTOs reconstituting in the popliteal or tibial arteries, where there is reconstitution of the vessel with enough true lumen working room to engage the lesion. He added: "The more experience we have, the less distance we seem to require – really just a few centimetres. And what we have done now is to set a time limit on the antegrade approach – for us it is about five minutes, but for others it may be different."

He noted that there are other methods of approaching from 'the other direction' in addition to retrograde. These include pedal loop, trans-collateral, and direct puncture of the occlusion. Going on to describe technical aspects of the retrograde approach, he said: "With a long sheath placed quite distal in the popliteal artery, there are multiple potential sites for puncture on any of the three tibial vessels. All three are suitable. We typically use a sheathless approach – that is, a micropuncture followed by a V18 [Boston Scientific, USA] or a Command 18 [Abbott Vascular, USA]. And if we need support it is typically with a CTO catheter.

Peter Schneider

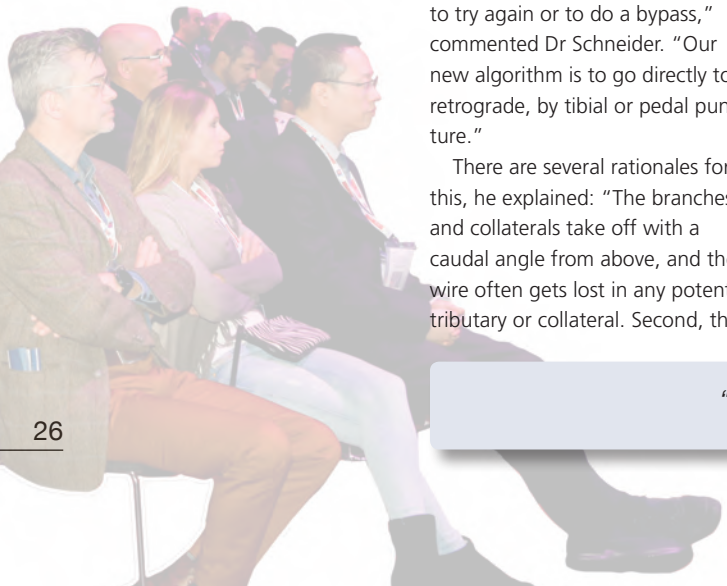
"We use a sheath in less than 10% of cases, but a 3 or 4 Fr sheath is typically adequate. We pass the wire from retrograde, externalise the wire, and then treat from the antegrade direction. The other thing of note when you are doing a pedal puncture is that passage through the anterior tibial or the posterior tibial can be really enhanced by either dorsiflexion or plantar flexion of the foot to make it straighter."

On the topic of guidance, Dr Schneider recommended either ultrasound or fluoroscopy. While ultrasound is the mainstay at outset in his practice, he noted that fluoroscopic guidance may be advantageous for heavy calcification.

He then cited the PRIME CLI study[2], which looked at ultrasound-guided access outcomes among patients with CLI, including 649 procedures at 896 sites. In a comparison of access site, with respect to number of attempts, time to access and access success, rates in the posterior and anterior tibial sites were found to be comparable to those in the common femoral in this large cohort.

Dr Schneider also cited the Leipzig experience[3], which included 343 limbs over 14 months where intention to cross was antegrade. Failure to cross antegrade occurred in 17.8% of cases, and success with the retrograde approach was achieved in 86.3% of these.

He also cited a number of smaller studies. The University of Virginia experience[4] – featuring 99 patients treated with a retrograde tibial and pedal access – demonstrated an 89% technical success rate along with 8% complication rate. El-Sayed *et al*.[5] (2016) reported that, of patients treated with retrograde access, 57% of access sites were the dorsalis pedis, and that adverse limb events and perioperative deaths significantly bettered objective performance goals. In the same year Chou *et al*.[6] compared an antegrade approach versus a bidirectional ante-



"Our new algorithm is to go directly to retrograde, by tibial or pedal puncture." ***Peter Schneider***

Source: www.leipzig-interventional-course.com

Figure 1. Despite an overall low complication rate in retrograde below-the-knee puncture, Dr Schneider highlighted a case of reocclusion one year following a successful recanalisation of the posterior tibial artery in this patient.

grade and retrograde approach, showing that patency was the same in both groups.

Retrograde access is not without its complications, however. Dr Schneider described a single case of a long segment posterior tibial occlusion that was approached both antegrade and retrograde.

"When the patient came back with a new lesion a year later, we could see that the entire posterior tibial had occluded. The complication risk is low, but also we have to monitor these patients and understand their eventual outcome." (Figure 1)

"This technique is becoming more widely practiced," said Dr Schneider in his concluding statement. "It appears safe and effective. However, we need a little bit more data to monitor and understand the outcome of the distal vessels that are punctured."

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"We have…set a time limit on the antegrade approach – for us it is about five minutes." ***Peter Schneider***

Contego's latest offerings in endovascular surgery

Ravish Sachar, MD, FACC, is Founder and CEO of Contego Medical, based in Raleigh, North Carolina, United States. In addition to his role at Contego, he is Physician-in-Chief of the North Carolina Heart and Vascular Hospital. He trained at Columbia Presbyterian Medical Center and The Cleveland Clinic, and his clinical interests include carotid artery stenting, acute stroke intervention, peripheral vascular intervention, and critical limb ischaemia (CLI). Dr Sachar is an extensively published researcher, and frequently presents at medical conferences, as well as directing several teaching programmes on carotid artery disease and peripheral vascular disease. He is also the Co-Managing Director of Rex Health Ventures, a hospital-based VC fund focusing on the healthcare space.

Contego Medical is a medical device company developing innovations in the field of endovascular medicine – peripheral and cardiovascular. Central to the company's success is their Integrated Embolic Protection (IEP™) technology, the core benefit of which is the integration of embolic protection onto the same catheter as the treatment portion (i.e. balloon or stent). The company holds 33 issued or pending patents.

LINC Review spoke to Dr Sachar to find out more about his perspectives from LINC 2018, and the role that Contego devices have in the endovascular arena.

Overall, from your perspective as a physician and entrepreneur, what were the greatest takeaways from data presented at LINC?

I am heartened by the continuous innovation that is occurring in our industry, which has resulted in dramatically increased options for patients over the last decade. This year's LINC meeting continued the tradition of showcasing the latest of these advances. One particular theme of note was that we are starting to see more long-term data comparing different treatment strategies. For example, we saw long-term follow-up data comparing the Medtronic In.Pact Admiral DCB to the Cook Zilver DES. We also saw preliminary data from the COMPARE Trial, a head-to-head randomised trial comparing the Medtronic In.Pact Admiral balloon to Boston Scientific's Ranger Balloon.

Of note, which key Contego products were featured at this year's LINC?

Contego's products were noted in two types of presentations at LINC. Our commercial devices – the Paladin® Carotid Post-Dilation Balloon with Integrated Embolic Protection and the Vanguard IEP® Peripheral Balloon Angioplasty System with Integrated Embolic Protection were featured in multiple talks and live cases, which demonstrated how physicians are integrating these products into their standard practice. At the same time, we had the opportunity to showcase our newer innovations, specifically the Neuroguard IEP® Carotid Stent System which generated a high level of interest in novel devices, specifically with the potential to dramatically impact the approach to carotid stenting.

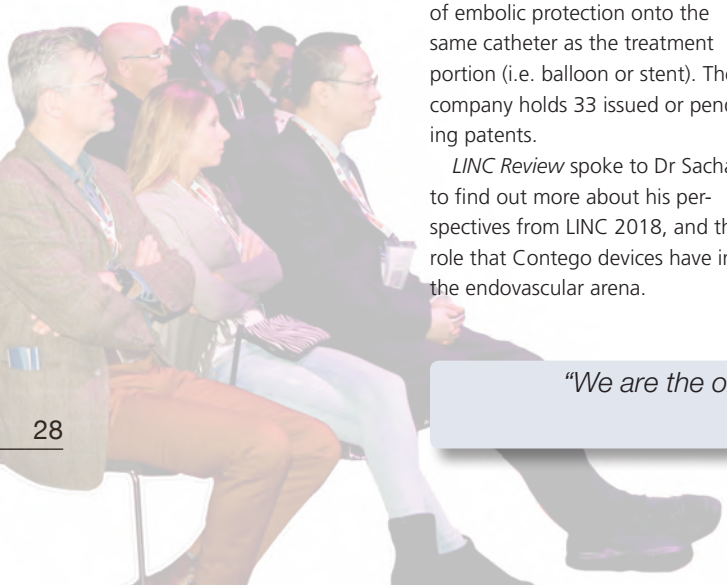
What do you think are the greatest opportunities for improvement in endovascular care, and how might new technologies address these needs over the next few years?

In the field of carotid artery stenting, the advent of embolic protection has allowed physicians to deploy stents without risk of major strokes. However, for various technical reasons, existing technologies are not optimised, and do not adequately address the concerns of peri-procedural minor strokes. The next generation of embolic protection devices and systems are specifically focused on this clinical unmet need and will provide the interventionalist with an improved set of tools to perform endovascular procedures both faster and more easily, with enhanced safety and efficacy.

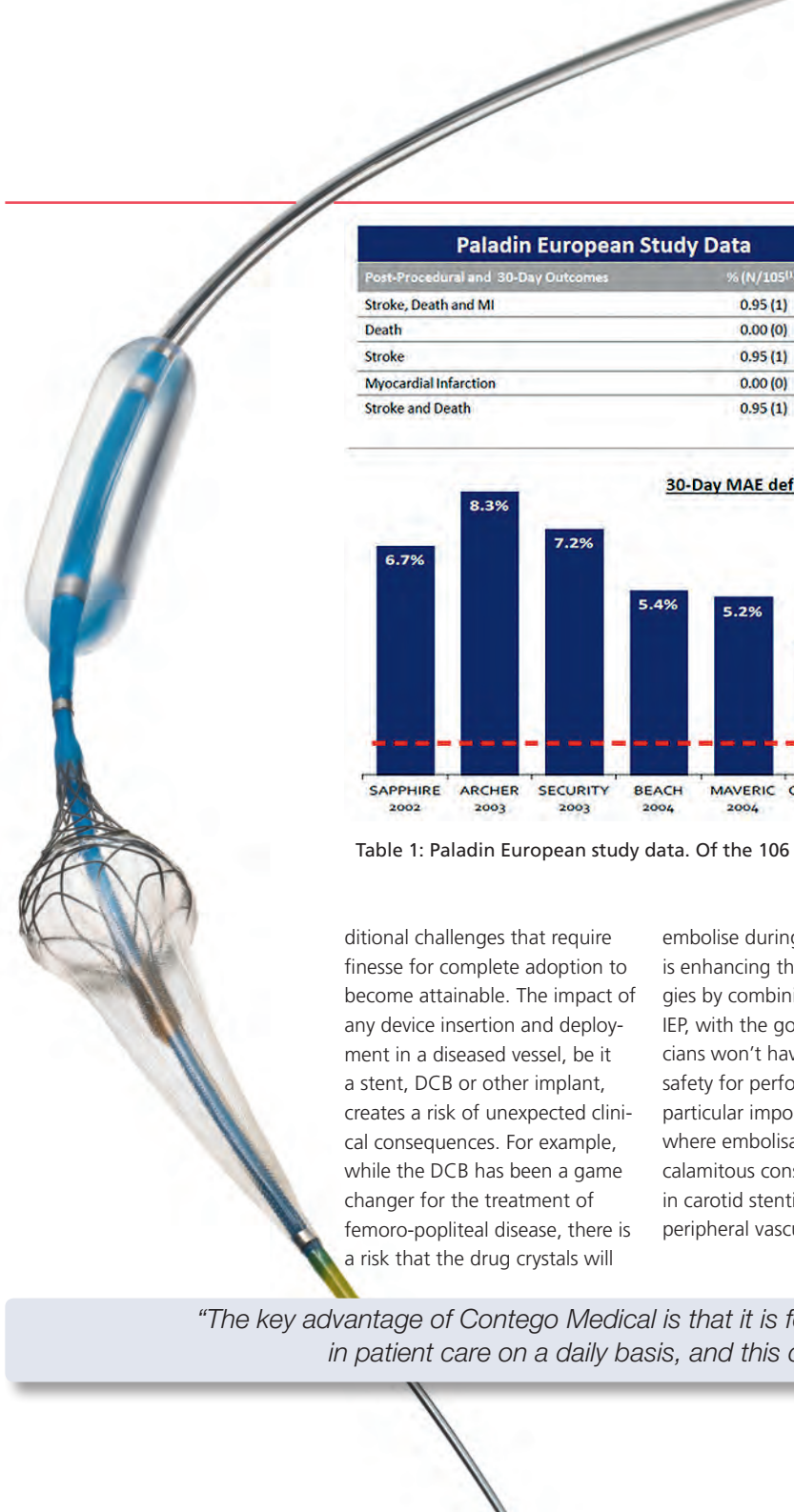
In the field of lower extremity vascular disease, head to-head comparisons of anti-restenotic therapies as well as vessel preparation strategies will shape how we approach patients with complex femoro-popliteal disease. Improvements in drug delivery strategies should result in improved patency in infrapopliteal vessels among patients with CLI.

More specifically, what impact will Contego devices have in satisfying these unmet needs?

As newer and more advanced technologies become available, they typically carry with them ad-



"We are the only company to have developed a proprietary technology that incorporates filter-based embolic protection directly onto the treatment device." ***Ravish Sachar***



Paladin European Study Data	
Post-Procedural and 30-Day Outcomes	% (N/105[1])
Stroke, Death and MI	0.95 (1)
Death	0.00 (0)
Stroke	0.95 (1)
Myocardial Infarction	0.00 (0)
Stroke and Death	0.95 (1)

- 106 subjects enrolled at 5 sites in Germany
- 99% Technical Success
- No Deaths, strokes, MI or other Major Adverse Events (MAE) through discharge
- 1 stroke at day 12 due to non-compliance with medications, complete recovery

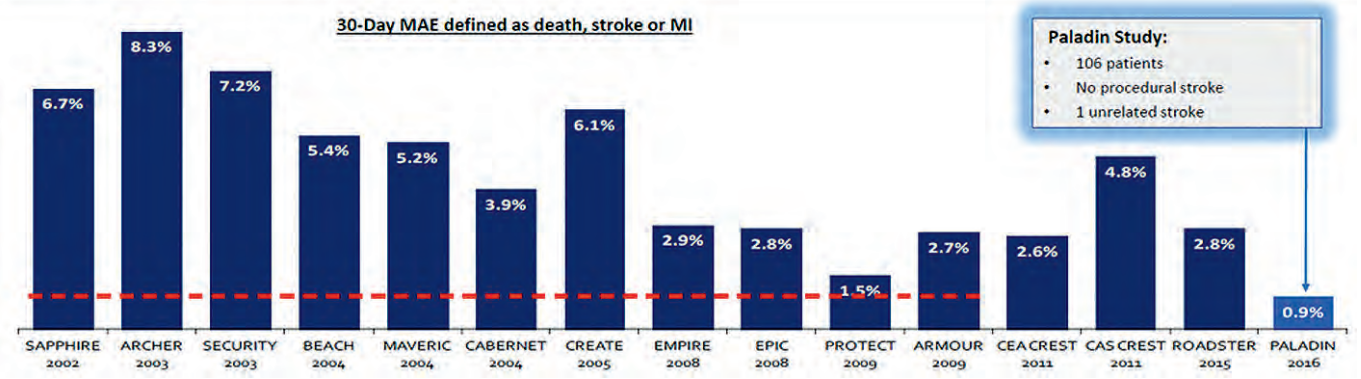


Table 1: Paladin European study data. Of the 106 subjects enrolled, one subject withdrew consent following discharge, and 105 were eligible for follow-up at 30 days. Reproduced with permission from Contego Medical.

ditional challenges that require finesse for complete adoption to become attainable. The impact of any device insertion and deployment in a diseased vessel, be it a stent, DCB or other implant, creates a risk of unexpected clinical consequences. For example, while the DCB has been a game changer for the treatment of femoro-popliteal disease, there is a risk that the drug crystals will embolise during delivery. Contego is enhancing these new technologies by combining treatment and IEP, with the goal that physicians won't have to compromise safety for performance. This is of particular importance in situations where embolisation can result in calamitous consequences, such as in carotid stenting or in high-risk peripheral vascular patients.

What is the key differentiating factor of Contego's IEP technology?

The key advantage of Contego Medical is that it is founded by physicians who experience the unmet needs in patient care on a daily basis, and this drives our innovation process. We are the only company to have developed a proprietary technology that incorporates filter-based embolic protection directly onto the treatment device. Additionally, our filters and devices are designed specifically for the needs of each target anatomy, creating seamless protection while maximising performance. For example, in the Paladin and Neuroguard IEP devices for carotid stenting, we employ a 40-µm filter to capture microemboli before traveling into

Continued on page 30

"The key advantage of Contego Medical is that it is founded by physicians who experience the unmet needs in patient care on a daily basis, and this drives our innovation process." ***Ravish Sachar***

Contego's latest offerings in endovascular surgery

Continued from page 29

the delicate neurovasculature. With the Vanguard IEP we use a filter with a larger pore size to allow for continuous blood flow, while capturing macro-emboli that can lead to prolonged procedures and possible limb loss. As these filters are on the same catheter as the treatment device, and deploy in a single step, Contego's devices are simple to use and do not add complexity to the overall procedure.

At LINC we saw data on Paladin, an introduction to Vanguard IEP, and a sneak preview of Neuroguard IEP. Is the plan to continue to develop your pipeline?

We are always looking for new opportunities to improve the safety profile and reduce the complexity of endovascular procedures. Unlike most smaller device companies, we have a steady pipeline of devices in development and commercialisation planned over the next five years. These are targeted for multiple treatment applications and vascular beds.

Results relating to the Paladin system presented at LINC 2018 included an initial clinical study (Paladin European Study Data & Comparison of MAE Across CAS Studies)[1]. The results demonstrate lower stroke rates as compared to all other published carotid artery stenting studies of > 100 patients (Table 1). Of a total of 106 patients that enrolled in the trial, there were no signs of procedural stroke. Another comparison study of MRI data across four other competing technologies, with case size of approximate 25 to 40 people, has shown significantly optimistic results. The incidence size and new lesions on MRI of patients treated with the Paladin device were an order of magnitude lower than previously reported clinical trials.

What can we look forward to from Contego Medical at the 2019 Leipzig Interventional Course?

LINC provides a great opportunity for us to speak with other leading physicians and showcase our latest innovations, both via the exhibition and the clinical programme. In 2019, we will have completed the PERFORMANCE I Trial for Neuroguard IEP, and will present final results. We also anticipate having a CE mark with full commercialisation well underway. The ENTRAP Study data for Vanguard IEP will also likely be part of the clinical presentations. Depending on timing for our other endeavours, we may have additional peripheral vascular devices, the early experience of which we will hopefully be able to share with the audience.

Prevalence of endovascular diseases increases with the aging population[2] and is believed to be associated with a high risk of CV morbidity[3].

The current standard of care in the EV and CV markets results in incomplete embolic protection in a large number of patients. Evidence demonstrates that embolisation can occur with every intervention[4] and clinical consequences cannot be predicted.

Contego's product technology addresses specific areas of vascular procedures namely carotid artery stenting, coronary artery disease and peripheral artery disease, substantially increasing emboli capture rate, thereby improving efficacy of procedure as well as enhanced safety.

Contego's technology also provides seamless integration of the treatment device and anatomically-specific embolic protection on the same catheter, optimising performance, simplicity and safety for multiple vascular beds.

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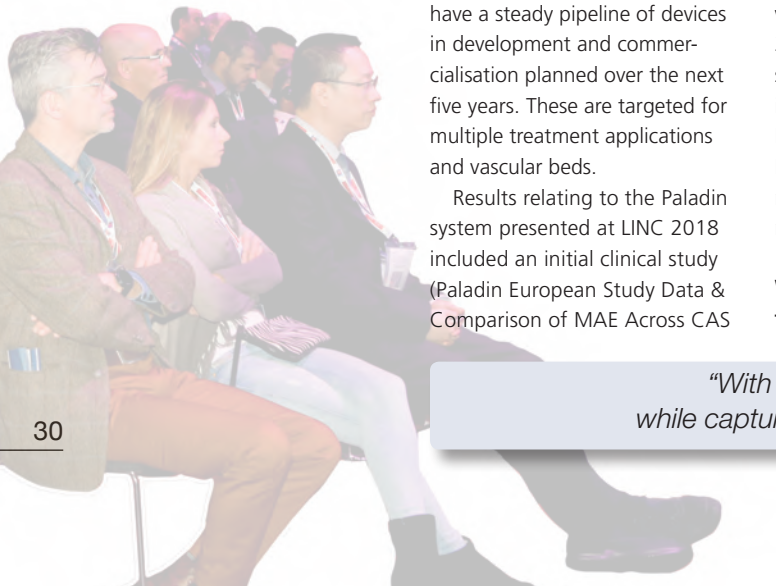

"With the Vanguard IEP we use a filter with a larger pore size to allow for continuous blood flow, while capturing macro-emboli that can lead to prolonged procedures and possible limb loss." ***Ravish Sachar***

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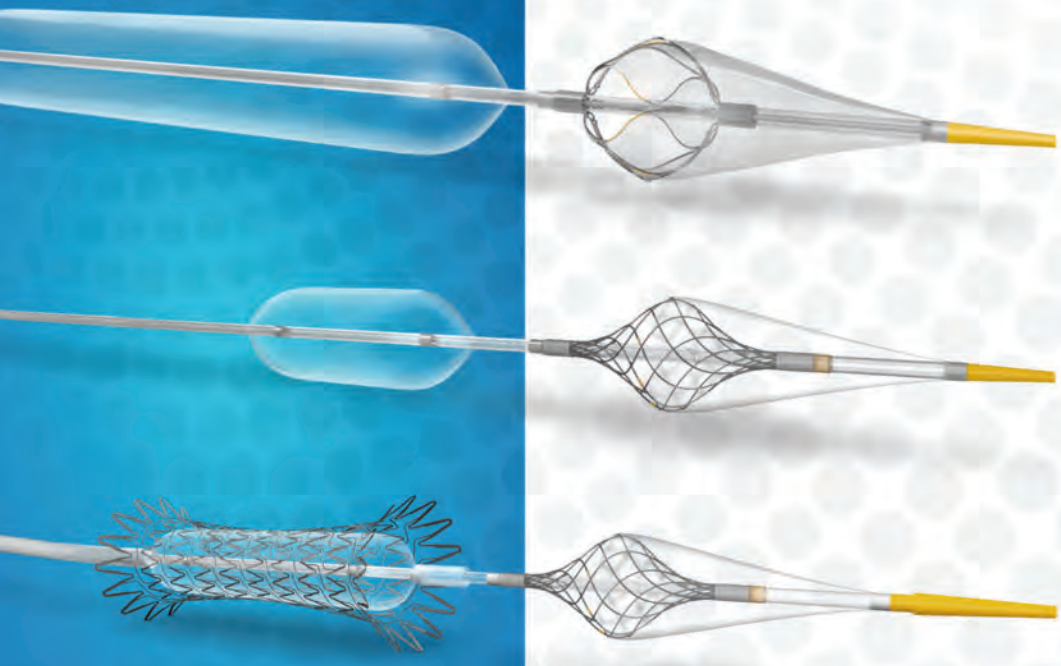

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MDT-2113 (IN.PACT Admiral DCB) 'consistent and durable'

LINC 2018's roster of 'First time data release' sessions saw two-year follow-up results of a Japanese trial evaluating the safety and efficacy of the MDT-2113 (IN.PACT drug-coated balloon (DCB), Medtronic, USA) for the interventional treatment of *de novo* and non-stented restenotic lesions in the superficial femoral artery (SFA) and proximal popliteal artery (PPA).

The prospective, multicentre, randomised trial pitched the DCB against standard percutaneous transluminal angioplasty (PTA), randomising 2:1, respectively. 100 subjects (DCB=68, PTA=32) were enrolled at 11 sites in Japan.

Presenting the results of the trial's treatment of atherosclerotic lesions in the SFA/PPA was Osamu Iida, from Kansai Rosai Hospital in Amagasaki, Japan. "These are the first reported outcomes from an independently-adjudicated randomised, single-blind trial evaluating a DCB in Japanese patients through two years," he told the LINC audience.

The primary effectiveness endpoints were: primary patency at 12 months, defined as freedom from clinically-driven target lesion revascularisation (CD-TLR), and freedom from restenosis as determined by duplex ultrasound-derived PSVR ≤2.4.

Primary safety endpoints were freedom from device- and procedure-related death through 30 days, and freedom from target limb major amputations and clinically driven target vessel revascularisation (CD-TVR) within 12 months post index procedure.

The key inclusion criteria in the trial were: Rutherford 2,3 and 4 lesions in the SFA and /or PPA, single *de novo* or non-stented restenotic lesions (70-99% occluded with total length ≥4 cm, and ≤20 cm, 100% occluded total length ≤10 cm, combination and tandem lesions allowed if criteria above met, lesion gap ≤3 cm and evidence of

"Results demonstrate a consistent and durable treatment effect of the MDT-2113 DCB in a more complex patient demographic than typically seen in other DCB pivotal trials." ***Osamu Iida***

adequate distal run-off through the foot).

The key exclusion criteria were: Rutherford 5 and 6, stroke or STE-MI ≤3 months prior to enrolment, chronic renal insufficiency, contralateral SFA/PPA disease requiring treatment at index procedure, any major surgical procedure or intervention performed or planned ≤30 days of index and unsuccessful lesion crossing.

In terms of key patient demographics he highlighted, the age in years was 73.3±7.4 (n=68) in the DCB group versus 74.2±6.1 (n=32) in the PTA group (p=0.539). There was a slightly higher diabetes mellitus presence in the DCB group (58.8% versus 56.3%).

The baseline lesion characteristics included 91.2% *de novo* lesions in the DCB group and 100% in the PTA group. Other values for the DCB/PTA arms (respectively) included: 8.8% versus 0% restenotic lesions; 1.5% versus 3.1% proximal popliteal involvement; lesion length 9.15±5.85 versus 8.89±6.0 cm; 16.2% versus 15.6% total occlusions; 7.4% versus 9.4% severe calcifications.

In terms of procedural characteristics, 100% underwent pre-dilatation in both groups, with post-dilatation rates of 23.5%

and 18.8% in the DCB and PTA arms, respectively. Use of index procedural IVUS was 39.7% versus 25.0%, and provisional stenting was 4.4% versus 3.1%.

"The MDT-2113 DCB had a primary patency rate of 79.8% compared to 46.9% in PTA. CD-TLR was 9.1% in the MDT-2113 DCB group compared to 20.7% in PTA," said Dr Iida.

He added: "The data are consistent with the superior treatment effect seen in the IN.PACT SFA DCB trials."

In terms of the primary safety outcomes at two years, he shared that 30-day device and procedure-related deaths were zero in both groups, as was target limb major amputation, and thrombi. CD-TVR was 15.1% in the DCB group and 24.1% in the PTA group. At 24 months the major adverse event rate was 0.6% in the MDT group and 20.7% in the PTA group. The all-cause death rate was 6.1% in the MDT group and 3.4% in the PTA group. The thrombosis rate in both groups was zero.

"Results demonstrate a consistent and durable treatment effect of the MDT-2113 DCB in a more complex patient demographic than typically seen in other DCB pivotal trials," Dr Iida said in closing.

"...data are consistent with the superior treatment effect seen in the IN.PACT SFA DCB trials." ***Osamu Iida***

Live case exhibits Shockwave's Lithoplasty balloon

From University Hospital Leipzig's department of angiology, Andrej Schmidt and Matthias Ulrich led a live case to treat a severely calcified right superficial femoral artery (SFA) stenosis using the Shockwave Peripheral Intravascular Lithotripsy (IVL) system (Shockwave Medical Inc., USA).

The patient, a 72-year-old male, had severe claudication of the right calf with a walking capacity of 40 m, and right ankle brachial index of 0.47 (Rutherford Class 3). In December 2017 he underwent percutaneous transluminal angioplasty (PTA) of the left SFA. Prior to that, in August 2016, he was diagnosed with coronary artery disease, myocardial infarction and ischaemic cardiomyopathy (with ejection fraction 47%). A pacemaker had also been implanted in May 2016. He was a former smoker with arterial hypertension.

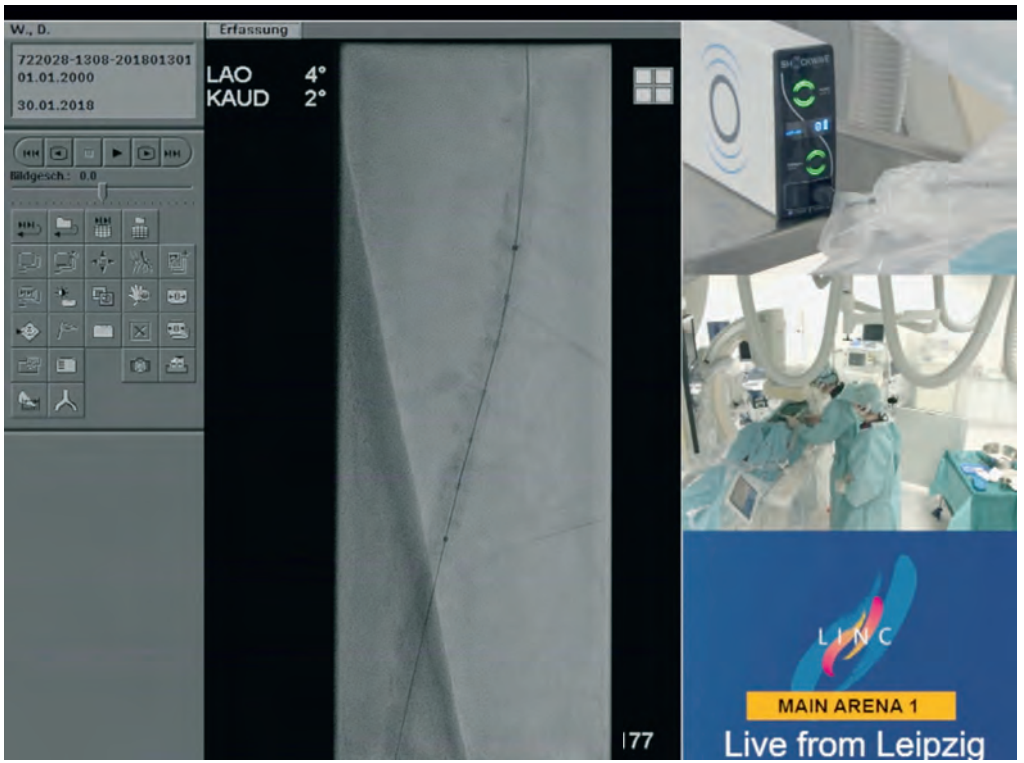
Angiography revealed extensive calcium and high-grade stenosis in the mid-SFA, with a relatively short chronic total occlusion (CTO) and extreme calcification in its distal portion.

The procedure consisted of left groin retrograde access and cross-over approach.The operators discussed recanalisation strategy: angioplasty would be carried out using a 6.0 x 60-mm Lithoplasty balloon (Shockwave Medical) followed by a 6.0 x 80-mm Luminor drug-coated balloon (DCB; iVascular, Spain).

The Shockwave IVL system, explained Dr Ulrich, consists of a sonic pressure wave emitted circumferentially at a frequency of 1 pulse/second. "It will crack the calcium in this area," he said.

Returning to angiographic images, Dr Schmidt continued: "This SFA has one calcified stenosis after the other, all relatively focal and all rather circumferentially calcified. In this regard this is a nice case for endovascular lithotripsy treatment. Of course, there are many eccentric plaques. It should (at least theoretically and from what I have seen) be especially effective in the circumferential calcification."

Once the lithotripsy balloon was positioned using the catheter's proximal and distal markers, fluoroscopy confirmed its positioning within the area of circumferential calcium, and a sub-nominal inflation at 4 atm was carried out in order to occlude blood flow. This was followed by lithotripsy pulse emission at 1 Hz, and dilation to reference vessel diameter (in this case 6 atm). A total of six 30-second cycles is possible with a single balloon, commented Dr Schmidt – totalling 180 shocks. While inflating the lithotripsy balloon, Dr Schmidt commented on balloon sizing: "This artery is 5.5 mm. The outcome from the studies is that you have to oversize the balloon a little bit, therefore we chose the 6-mm."



Source: www.leipzig-interventional-course.com

Figure 1. Positioning the lithoplasty balloon in the distal SFA.

From the panel, Thomas Zeller commented: "The general recommendation is to inflate the balloon after the shockwave emission for at least 1 minute at 6 atm. But your strategy is to follow the Shockwave Lithoplasty with DCB. Do you believe that it is necessary to inflate the balloon for 1 minute?"

Dr Schmidt replied: "We are stubbornly sticking to the protocol that has been used by the [DISRUPT PAD 2] study[1]. But you are right – that time could be saved for the post-dilatation of the DCB. I wanted to inflate it once, because

"This was impressive…It is a relatively perfect lesion for [lithotripsy]." **Andrej Schmidt**

Source: www.leipzig-interventional-course.com

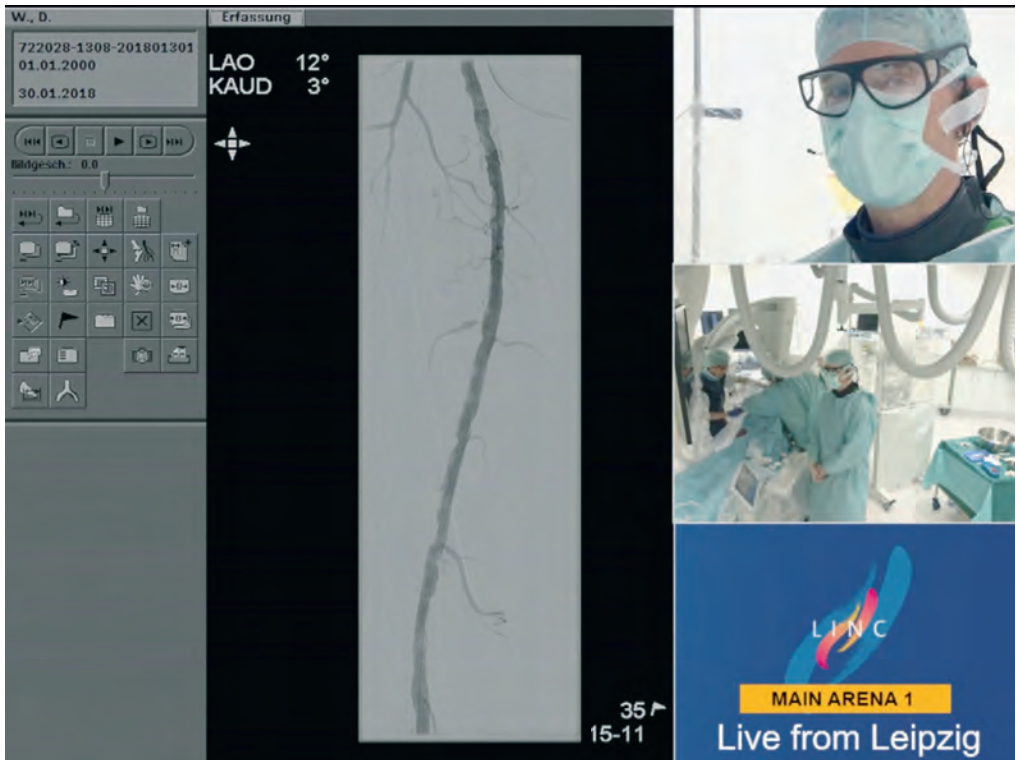


Figure 2. The final result.

I wanted to be sure that there is not an eccentric plaque [visible] in another angulation."

Indeed this was the case, and the balloon was lowered slightly and re-inflated. Dr Schmidt then asked Professor Zeller, who was principle investigator for DISRUPT PAD 2, about his experience and impression of Lithoplasty in eccentric and concentric calcification. "Definitely we have seen the best outcomes in concentric lesions," Professor Zeller replied. "That makes sense from the theoretical aspect. It works by emitting the energy concentrically. It should work selectively in calcified tissue. If you have an eccentric lesion within an area of mainly healthy vessel, nothing will happen. Part of the energy will be emitted in an area where it is not very effective."

Dr Schmidt agreed: "This was impressive … It is a relatively perfect lesion for [lithotripsy]. We have other lesions here that need to be treated with the balloon."

Session chair Ramon Varcoe then asked whether the underlying motivation of lithotripsy was to change the compliance of the vessel wall, or to assist with drug delivery into the wall. "Of course, the data are non-existent yet on what would be the best here, whether to follow with a DCB," responded Dr Schmidt, adding that vessel preparation may pave the way for greater DCB efficacy, but that further study needs to be carried out.

"One of the things we've learned from the DISRUPT series is some great results at one month, given the complexity of the lesions," added panel member Andrew Holden. "But there was restenosis – not at worrying levels, but certainly there was a need to improve the durability with a DCB. DISRUPT PAD 3[2] is going to be very important for answering that question.

"It is also important that you are being very careful particularly in those resistant areas of focal stenosis, to try and position the central source, and be prepared to re-treat. In retrospective review, we see that the mode of failure is at points that didn't receive enough energy. You are obviously well aware of that with your repositioning. You have to be persistent with that, to try to optimise the result."

The lithotripsy procedure was continued in this fashion, along the duration of the extensively calcified SFA both proximally and distally. DCB were then inflated along its length, achieving full expansion. Commenting on the final result, Dr Schmidt said: "It's really quite nice. We are quite happy with this case."

DISRUPT PAD 3 is a prospective, multicentre, single blind, randomised (1:1) study of Lithoplasty treatment used in combination with DCB versus standard balloon angioplasty used in combination with DCB to treat moderate and severely calcified femoropopliteal arteries. The trial was initiated in February 2017, and aims to recruit a total of 334 participants at 45 sites in Europe, the United States and New Zealand. Completion is planned for 2020.[2]

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"Definitely we have seen the best outcomes in concentric lesions… [Lithoplasty] should work selectively in calcified tissue." ***Thomas Zeller***

SITE@LINC: cracking controversial issues and unmet

SITE@LINC returned with its distinctive open debate format, this time on new concepts and concerns in EVAR and TEVAR. The objective, explained SITE (International Symposium on Endovascular Therapeutics) President Vicente Riambau (Cardio-Vascular Institute Hospital Clinic, University of Barcelona, Spain) to *LINC Review*, was to identify the current limitations and propose future directions within these two treatment areas.

These themes were opened up by free discussion and guided by a script of hot talking points, he explained. "We selected an expert panel to discuss, together with the audience, some controversial issues as well as some unmet needs in TEVAR and EVAR. The SITE@LINC session is a taste of the flavour of the SITEupdate."

One of these issues is of course durability in EVAR and TEVAR. The now-familiar results of large scale randomised trials such as EVAR I and II, and DREAM (Dutch Randomised Endovascular Aortic Management), demonstrated significantly lower operative mortality than open surgical repair but increased rates of graft-related complications and secondary interventions[1-3]. "Most of the topics are related to this issue," said Dr Riambau.

"The latest results coming from the old randomised trials are punishing the performance of EVAR[4]. Reinterventions are the main drawback for endovascular repair of the aorta. So we should seriously demonstrate that the new technology and the new endograft generations are improving the previous limitations. Then we would need more data in order to argue these improvements."

On this theme, what influence have advances in technique and post-operative care had, given that we now hold a greater understanding of migration, rupture, infections and type I and II endoleaks? "Early improvements are not enough. We would need long-term data to be compared with the previous trials. New endografts should fix the major limitations like migration, material fatigue or type II endoleaks. But in fixing those problems, we should avoid creating new ones."

Moving into new spheres in EVAR and TEVAR – hostile anatomies, reinterventions, and so on – brings with it new unmet challenges. Hostile anatomies, explained Dr Riambau, should be avoided in low volume centres: "It is not a good idea to push too much the envelope using regular endografts outside the instructions for use. There are (and there will be) new technologies, and probably more skills demanded, more dedicated to hostile anatomies. We should centralise hostile anatomies, but this is a very sensitive issue too."

Noting some of the other unmet needs that were on the agenda for SITE@LINC this year, Dr Riambau cited stroke and EVAR, and the question of whether cerebral protection devices are needed. Also under discussion was the sac-filling concept for the prevention of type II endoleaks in EVAR, and whether post-implant syndrome should be considered a real concern[5,6]. Endograft stiffness and its implications in heart attacks[7], endovascular treatment of aortic arch pathology, and adjuvant techniques (e.g. petticoat, candy plugs) as solutions in type B dissection were also debated.

On the evolution of education and training, as well as healthcare systems as a whole, Dr Riambau commented: "In order to teach about endovascular techniques we should identify centres of excellence. Simulation should be part of the educational programmes, but case volume with systematic case planning is key for the new endovascular specialists.

"The biggest concern for any public health system is the budget. Prices should be clearly justified. Cost-effectiveness should be very well documented. Early efficacy is not enough to justify the high price of new technology. Physicians should also be aware about health economics and put that parameter in the decision making process."

SITE held its biennial update on March 9, 2018 at the University of Barcelona's School of Medicine. SITEupdate runs during non-symposium years and is focussed towards an expert audience with a characteristic brainstorming format. The meeting, organised by the Endovascular Foundation, sees faculty of the School of Medicine review unmet needs in key clinical areas along with an international audience whose expertise lies within endovascular procedures, bioengineering, industry management, technological evaluation, and health management administration. This year, the meeting focused on aortic repair and lower limb revascularisation, with the objective of identifying current limitations and proposing future directions.

"SITEupdate is based on a fresh formula – and is a useful expert event," commented Dr Riambau. "This format has had a very good acceptance by all the participants. They like the formula. Rather than talk about what we know, we prefer to go beyond the classical presentations of 'good and impressive results', and talk about what we do not know but need to know. That means that we will discover the unmet needs and will try to imagine the potential solutions together – industry and physicians. It is a summit to foresee the future endovascular world following a strategy similar to a multilateral advisory board."

Asked how broad the discussion usually is, given that so many different disciplines and sectors are involved, Dr Riambau responded: "In only one day, we focussed our discussions on two main topics: endovascular treatment of the aorta (during the morning sessions), and unmet needs in lower limb revascularisation (during the afternoon sessions).

"This year, we had a unique opportunity to discuss and understand the new scenario depicted by the new Eucomed/MedTECH regulations. Key questions were

"The SITE@LINC session is a taste of the flavour of the SITEupdate." ***Vicente Riambau***

needs

Vicente Riambau

answered by the experts. We analysed the potential implications for future endovascular meetings and for future continuous endovascular education and training."

SITEupdate 2018 also hosted a pre-meeting workshop for young specialists, providing the best new talent to the expert audience. This workshop is offered by Endovascular Foundation to the SITE Young Talents (young international specialists). Up to 15 Young Talents are selected by the Co-Directors of SITEupdate 2018 from a list of applicants, who can register online. "Expert faculty members offer practical lectures as well as some case discussions," noted Dr Riambau. "SITE Young Talents are invited to the networking dinner, together with the all senior participants and faculty members. Additionally, they are also invited to attend and participate during the discussions of the next day when the SITEupdate is running."

Also on the programme was a 'confidential session' wherein key companies come forward to discuss new avenues: "In these sessions, companies can share their projects or pipelines with the audience. Of course, the competitors are invited to leave the room. Specific confidential agreements will be provided to be signed and returned to the related companies for their files."

Concluding his thoughts on the value of SITE, Dr Riambau said: "I believe that SITEupdate is a good meeting to identify where there is a lack of evidence, and unmet needs, to be overcome by future investigations. Physicians can start useful and translational research, industry can focalise its efforts, and health managers can understand the endovascular benefits. In this way, we as physicians, together with the industry partners, engineers and health managers, can improve endovascular therapy in terms of safety and effectiveness."

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"The latest results coming from the old randomised trials are punishing the performance of EVAR." ***Vicente Riambau***

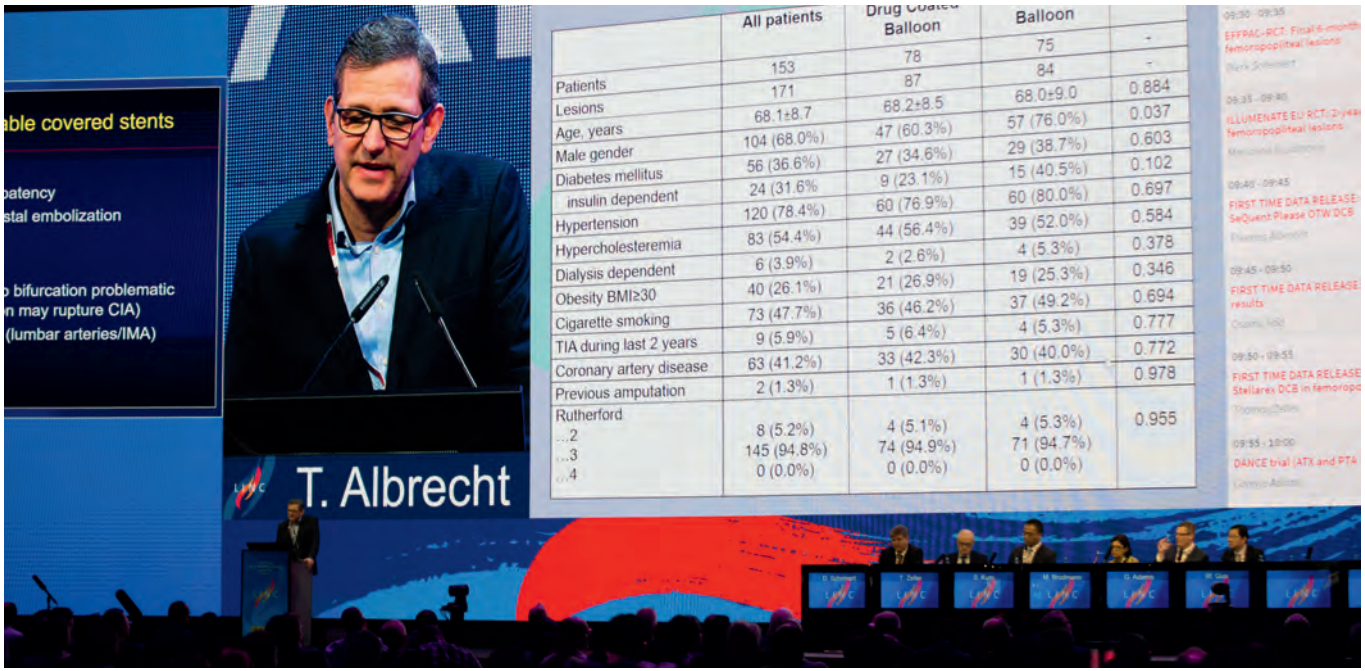
Two-year results from the CONSEQUENT trial

New 24-month results from the CONSEQUENT trial have shown sustained clinical benefits, Thomas Albrecht, an interventional radiologist from Berlin, Germany, announced at LINC.

Dr Albrecht relayed that CONSEQUENT, which had set out to assess the safety and efficacy of the Sequent Please OTW paclitaxel-coated balloon (B Braun, Germany) in treatment of fempop lesions, had continued to meet several primary endpoints over the two years. The trial is of particular interest because it included patients with longer lesions (mean 13.2 cm) than in any other previously published DCB study in a Caucasian patient population.

The CONSEQUENT study included 153 patients that had been randomised 1:1 to receive treatment with SeQuent or plain balloon (POBA) and followed up after six, 12 and 24 months.

Speaking in more detail about the demographics and comorbidities of the patients studied, he said that relatively standard inclusion criteria was used, except that lesion lengths were allowed to be up to 27 cm. Other inclusion criteria included *de novo* or restenosis post POBA in SFA



	All patients	Drug Coated Balloon	Balloon	
Patients	153	78	75	-
Lesions	171	87	84	-
Age, years	68.1±8.7	68.2±8.5	68.0±9.0	0.884
Male gender	104 (68.0%)	47 (60.3%)	57 (76.0%)	0.037
Diabetes mellitus	56 (36.6%)	27 (34.6%)	29 (38.7%)	0.603
insulin dependent	24 (31.6%	9 (23.1%)	15 (40.5%)	0.102
Hypertension	120 (78.4%)	60 (76.9%)	60 (80.0%)	0.697
Hypercholesteremia	83 (54.4%)	44 (56.4%)	39 (52.0%)	0.584
Dialysis dependent	6 (3.9%)	2 (2.6%)	4 (5.3%)	0.378
Obesity BMI≥30	40 (26.1%)	21 (26.9%)	19 (25.3%)	0.346
Cigarette smoking	73 (47.7%)	36 (46.2%)	37 (49.2%)	0.694
TIA during last 2 years	9 (5.9%)	5 (6.4%)	4 (5.3%)	0.777
Coronary artery disease	63 (41.2%)	33 (42.3%)	30 (40.0%)	0.772
Previous amputation	2 (1.3%)	1 (1.3%)	1 (1.3%)	0.978
Rutherford …2 …3 …4	8 (5.2%) 145 (94.8%) 0 (0.0%)	4 (5.1%) 74 (94.9%) 0 (0.0%)	4 (5.3%) 71 (94.7%) 0 (0.0%)	0.955

or P1/P2 segments, Rutherford 2-5, reference vessel diameters 4.0 to 7.0 mm, lesion lengths 4 to 27 cm, diameter stenosis pre-procedure of ≥70%, as well as adequate run-off with ≥1 vessel to the foot.

Chronic total occlusions were not allowed if they were longer than 10 cm. Other exclusions were restenosis post stent or DCB, and ≥2 lesions in any target vessel.

"The demographics and comorbidities of the patients were pretty much a standard population, with equally balanced distribution between the two groups," explained Dr Albrecht.

"On lesion details, I just want to point out two things here: we had a 25% rate of TASC C or D lesions, and the usual lengths were relatively long at 13 cm. This compares favourably, i.e. the lesions were longer than in previously published DCB trials. Predilatation was only mandatory for total occlusions, and the bail-out stent rate was 16% – again fairly equally balanced between the two groups."

Dr Albrecht shared the results with the LINC audience. Late lumen loss [LLL] was one of the primary endpoints that was significantly lower in the DCB group: 0.35 mm versus 0.72 mm (p=0.006). There were also lower clinically driven 24-month TLR rates (all cause) for the DCB group: 19% versus 40.6% (p=0.007), he said.

He added that 24-month patency was significantly higher in the DCB vs POBA patients: 72.3% versus 48.3% (p=0.006). Patients in the DCB group were also able to walk further at 23 months: 172 versus 52 metres, (p=0.001). "SeQuent Please OTW delivers sustained clinical outcomes in patients with long lesions up to 24 months," he concluded.

"SeQuent Please OTW delivers sustained clinical outcomes in patients with long lesions up to 24 months." ***Thomas Albrecht***

Perspectives from JET laid bare

The JET@LINC session featured a range of presentations from Japanese perspectives. The Japan Endovascular Treatment Conference (JET) has become the largest conference on peripheral vascular intervention in Japan, and the number of participants has increased to more than 2,000 in recent years.

First up to speak during the session was Yasutaka Yamauchi, a cardiologist and director of the Cardiovascular center at Takatsu General Hospital in Kawasaki. He has been interested in endovascular therapy (EVT) for around 15 years, and specialises in lower limb EVT, specifically body surface echo-guided EVT. "Together with my boss, Dr Miyamoto, we perform about 500 EVTs in one year in our hospital," he said.

He focussed on aortoiliac lesions, in particular. "Aortoiliac (AI) lesions have become widespread, as the first-line treatments advance technologically, especially stent placements," he said.

Dr Yamauchi used the session to talk about the first multicentre prospective study of its kind in the AI arena in the world: OMOTENASHI (An Observational prospective Multicenter registry study on Outcomes of peripheral

"Based on the results of the prospective multicentre study, I strongly believe that EVT in the AI arena is definitely a comprehensive first-line treatment." ***Yasutaka Yamauchi***

arTErial disease patieNts treated by AngioplaSty tHerapy in aortolliac artery). The study has looked at the treatment of aortoiliac artery disease using stent placement in over a thousand patients in 64 hospitals throughout Japan over two years.

Such a study was necessary given existing research, he said. "Papers on multicentre retrospective research have been made, but most peripheral arterial disease (PAD) patients who actually required AI-EVT had multiple diseases and lesions," he explained. One example has been reported by Dr Soga.[1]

"Moreover, in a study that looked at outcomes of patency and restenosis, we found out that if we do not try to evaluate patency periodically, restenosis will be overlooked," continued Dr Yamauchi. "If we simply analyse with Kaplan-Meier curves, the patency rate is evaluated higher. There is a risk in retrospective research."

That's why such a large-scale prospective study was required to confirm the findings. "There were no worldwide prospective studies on this lesion," said Dr Yamauchi. OMOTENASHI is the first multicentre prospective study globally, as a result. "Real-world clinical cases were enrolled and the actual clinical outcome will become clearer," said Dr Yamauchi. "It is interesting to be able to know the natural history of the outflow lesions or the contralateral limb lesions from a prospective study."

Dr Yamauchi talked about the initial success rates and data from the registry, dating from April 2014 to April 2016. "The safety and efficacy of AI EVT was feasible," he said.

The plan is to publish the one-year results, and then follow the study until three years after EVT, he explained. "For now, I will talk mainly about the safety and the six-month outcomes of real-world AI artery lesions with EVT," he said. "Our next step is to analyse independent predictors of primary patency for one year and three years."

What's also been interesting, said Dr Yamauchi, is the sub-analyses made possible from this data. For instance, the research team has already looked at specific OMOTENASHI results concerning the prevalence of polyvascular disease with AI artery disease, which were presented at last year's meeting.

There have been several other interesting topics to research, he said. "The usage rate of IVUS was high – about 70% in Japan," he said. "We will consider its effectiveness in sub-analysis." Other ongoing research includes looking at initial, one-year and three-year results after subintimal versus intraluminal approaches for AI occlusion treated with stent placement; the clinical indication and acute clinical outcomes of EVT for AI artery disease of haemodialysis patients; and the assessment strategies for EVT of CTO lesions of AI arteries. Finally, the team will look at the prevalence of depressive disorders and, specifically, the impact of EVT on depressive disorders for patients with AI artery disease.

On the whole, however, the outcomes were very positive for these stent placements, said Dr Yamauchi. "Based on the results of the prospective multicentre study, I strongly believe that EVT in the AI arena is definitely a comprehensive first-line treatment," he said in closing.

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"If we simply analyse with Kaplan-Meier curves, the patency rate is evaluated higher. There is a risk in retrospective research." ***Yasutaka Yamauchi***

CX@LINC: CO_2 flushing tackling TEVAR stroke risk

CX@LINC showcased aortic endovascular techniques presented at the Charing Cross meeting last year, which was accented by video presentations and engaging audience discussion.

Tilo Kölbel (University Medical Center Hamburg - Eppendorf, Germany) joined panel members with a presentation of tips and tricks in aortic arch interventions, with a focus on stroke prevention. Dr Kölbel has previously published work on the prevention of air embolism by carbon dioxide flushing during thoracic endovascular aortic repair (TEVAR) procedures.

Speaking to *LINC Review*, he explained how air embolism has been an underappreciated issue in TEVAR, and why CO_2 makes for an improved flushing option.

Tilo Kölbel and the CX@LINC panel

TEVAR has proven to be a superior treatment modality compared to open repair in all outcomes measures but stroke, he said. "I have always wondered why more research has not been focused on that topic, which seems to be the Achilles' heel in TEVAR. I am surprised that we still don't understand what the causes of stroke are, and that we are still led by a number of misconceptions we have been taught from the early teachers – that stroke is solely caused by catheter and wire manipulation. That is why I am fascinated in looking at other potential sources."

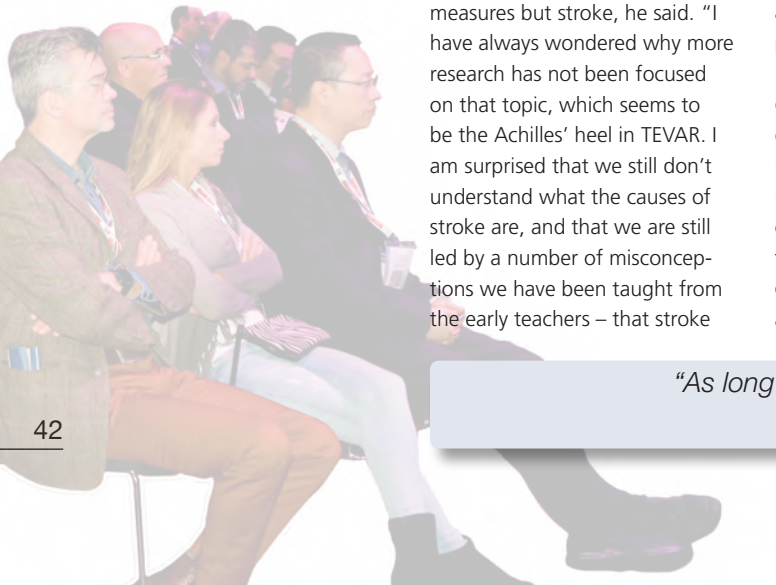
The notion that cerebral emboli generated during TEVAR procedures are solid in nature, comprising atherosclerotic or thrombotic material dislodged during mechanical manipulation of devices and tools, may be incomplete. As observed by Inci *et al*. in 2016[1], air is frequently trapped within the excluded aneurysm sac during EVAR, presumably trapped within the folds of the stent graft, suggesting that air is introduced into the vasculature in a similar way in TEVAR.

TEVAR devices are flushed with saline prior to introduction, but the process does not definitively preclude air entry into the vasculature. Since the supraaortic vessels provide a passage for air bubbles to reach cerebral vessels, the risk of cerebral injury related to air entry at this aortic level is far greater than with air introduced during EVAR.[2]

"Looking into the literature available regarding cerebral injury related to the introduction of gas into cerebral arteries, I am convinced that we should focus more on preventing this," said Dr Kölbel. "One of the injury mechanisms related to gas allowed into the cerebral arteries is the simple obstruction of the vessels, causing ischaemia. But it also has been shown in several experiments that even gas bubbles that are so small that they can be passed (below 5 µm) can cause damage by the way they pass the capillaries and change the blood-brain barrier. They can significantly impact cerebral function.

"While this is all known, it is not really focused on during endovascular techniques because we

"As long as we continue to improve our techniques, reducing stroke and optimising patient selection, endovascular options for arch repair will supersede surgical ones." ***Tilo Kölbel***



are used to focusing on the more positive parts of modern minimally invasive treatments and not on the side-effects."

In 2016, Dr Kölbel and colleagues described the technique of CO_2 flushing, applying the technique in a small patient cohort. CO_2 is more soluble than ambient air in saline, he explained, so flushing the stent graft with CO_2 prior to saline flushing ought to reduce the volume of gas entering the brain. In this study, 36 patients underwent branched or fenestrated arch or ascending TEVAR in this way, with one patient (with a highly calcified arch) experiencing a minor stroke.[2]

More recently, the group published the results of bench tests demonstrating that CO_2 flushing before saline flushing significantly reduces the volume of gas released following deployment relative to saline flushing alone (0.79 vs 0.51 ml, p=0.005).[3] "I am very convinced the reason is that the CO_2 goes into solution in the flushing liquids, just as CO_2 goes into solution in a bottle of soda. We are working on techniques to get that amount down further."

While this work elaborates on existing evidence of risk factors for cerebral infarction, it prompts discussion of a broader issue – that of its assessment, as Dr Kölbel explained: "I think that we are not focusing enough on assessing the negative outcomes of our treatment. What we report today on neurologic outcomes is usually the clinical, neurologically evident stroke. This is a rare outcome (around 5%), so if you want to study the impact of a new technique or an improvement in embolisation risk it would be very hard. And it is a rough and imprecise outcome measure of cerebral damage because usually it is judged by the treating clinicians, and not always by a neurologist. If you would have patients after TEVAR examined by a neurologist, the stroke rate would more likely be around 10%.

"In order to understand better what is happening in the brain during and after our procedures, we need a better outcome measure, which has been found in the structural heart space. There, physicians use MR lesions which show smaller but not always clinically-evident damage to the brain. In TAVI and EVAR this is present in about 80% of cases. We can measure the volume and numbers of MR lesions, and this would allow us to understand what we are doing and whether we can improve outcomes."

Commenting more generally on the future of endovascular procedures in the aortic arch, especially with the development of recent-generation arch grafts such as the three-inner branch graft[4], Dr Kölbel said: "It is a very interesting development that we see in arch procedures.

"When working close with cardiologists and cardiac surgeons, we find a lot of pathologies in the aortic arch, especially after type A repair; which are either not taken care of or are treated with open surgery. Inner branch arch endografts offer a less invasive treatment option for patients who would otherwise not be treated or treated in a more invasive way.

"In our practice, I see a significant increase in the number of patients we are treating each year. Last year we treated 20 of these cases. The patients show very good outcomes, because they are repaired from the remote access site – without opening the chest and without needing cardiopulmonary bypass. As long as we continue to improve our techniques, reducing stroke and optimising patient selection, endovascular options for arch repair will supersede surgical ones in the near future."

In his concluding remarks, Dr Kölbel commented on the format of the CX@LINC session: "It is built on edited aortic cases from Charing Cross, which was extremely well attended last year. The audience at Charing Cross enjoyed a lot the opportunity to see these 15-minute presentations – you could really go in depth into the technical details of these procedures.

"I have seen, from this audience participation at Charing Cross as well as at Aortic Live, that there is a huge interest in using live cases to better understand complex endo techniques. It is no longer about simply putting a thoracic tube graft in. These branches require a lot of small steps and subtle techniques that are difficult to explain in presentations or in papers, but very easy to explain in images and movies. That is where live cases and video presentations have their place. They can illustrate well for an educated audience how certain steps of procedures are done.

"A live case is also the most honest way, because the audience is watching in live time: nobody can say that it is very easy and quick, because they are really following the procedural steps and can witness what kind of pathology is treated. When live cases are performed by experienced operators who can operate and speak at the same time (thereby not compromising the safety of the patient), it really helps everyone get the most out of the experience. People at Charing Cross and Aortic Live have been enjoying that. Roger Greenhalgh has announced that this year's Charing Cross symposium will continue with this successful format – and Aortic Live will again include a significant number of both open and endovascular live cases, to give audience members the opportunity to see and compare both techniques."

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"We are used to focusing on the more positive parts of modern minimally invasive treatments and not on the side-effects." ***Tilo Kölbel***

Updates on the use of ultrasound-enhanced catheter-

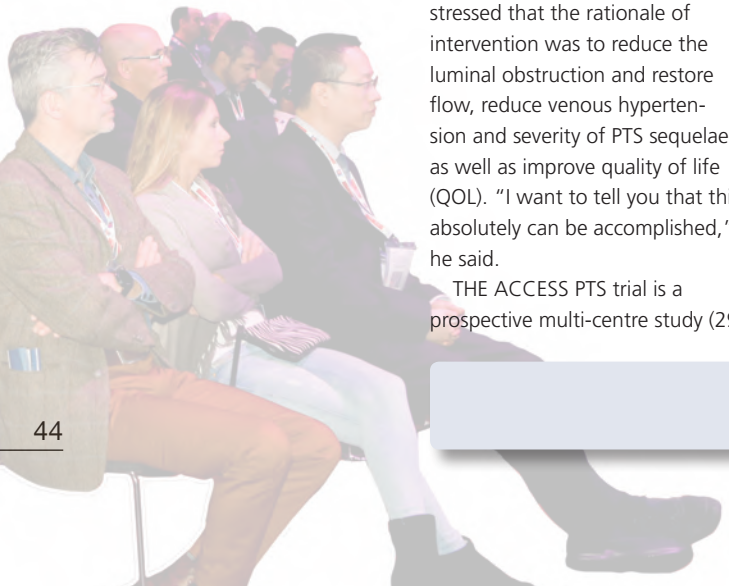
The EkoSonic™ Endovascular System with Acoustic Pulse Thrombolysis™ (EKOS Corporation, a BTG International group company) was placed under the spotlight at LINC 2018, with a number of invited experts stepping up to share their perspectives on the technology, and its use. The unique device uses targeted ultrasonic waves in conjunction with drug therapy to combat clots.

First to speak in the session was Mark Garcia (Vascular and Interventional Associates of Delaware, Endovascular Consultants, LLC, Wilmington, DE, USA) who spoke about the ACCESS PTS trial (Accelerated Thrombolysis for Post-Thrombotic Syndrome [PTS] Using the EKOS System).

Dr Garcia began by outlining some of the current challenges in delivering care for PTS. He stressed that the rationale of intervention was to reduce the luminal obstruction and restore flow, reduce venous hypertension and severity of PTS sequelae, as well as improve quality of life (QOL). "I want to tell you that this absolutely can be accomplished," he said.

THE ACCESS PTS trial is a prospective multi-centre study (29 sites) of patients with PTS for six months or more, with proven DVT. 1,216 patients were screened, 81 patients were enrolled, and 78 treated. Seventy percent of patients were males, the mean age of the clot was 13 months and mean age of patient was 54.6 years. Seventy-seven limbs were evaluable.

The ACCESS PTS protocol included weight-based enoxaparin pre-procedure (1 mg/kg BID) for 48 hours, appropriate access to obtain complete direct in-line flow from the ankle back to the heart, crossing of the occlusion using standard techniques/devices, EKOS lysis at 0.5-1.0 mg/hour overnight, and follow-up with PTA ± pelvic stenting (to lesser trochanter as needed). Patients were discharged on enoxaparin 1 mg/kg BID for one month, and compression stockings.



"There is hope for PTS patients who have failed standard-of-care therapy." ***Mark Garcia***

directed thrombolysis in treating PTS and PE

They were then transitioned to an oral agent at one month. Exercise was initiated at two to three days post-treatment, and patients were then followed-up with duplex ultrasound at 30,90,180, and 365 days.

Of the 78 patients treated, there was one major bleed (resulting in death at 32 days due to multi-organ failure), three recurrent DVTs (3.8%), and one pulmonary embolism at 30 days (1.3%, 0 during hospitalisation).

Dr Garcia concluded that ACCESS PTS is a statistically significant study: the primary endpoint was a four-point reduction in Villalta scores in 50% of patients at 30 days; this was achieved in 67% of patients (p=0.003; CI 95%).

"There was also a mean improvement in Villalta scores of 47.9% from a baseline of 15.5 (severe PTS) to 8 (mild PTS) at 365 days," said Dr Garcia. "VCSS scores improved 42.3%, from 12 to 7 from baseline to 365 days, and perhaps the most important result – the VEINES-QOL score – what the patients tell you – improved by 36.2 % at 365 days."

He added: "When you look at the hospitalisation data (68% didn't need ICU stay) the nice thing we are seeing here is that patients don't have to go to the ICU, they typically stay in a vascular bed and the mean hospital stay length was 3.4 days."

Dr Garcia concluded: "For patients suffering from chronic veno-occlusive disease and PTS, endovascular intervention using USCDT [ultrasound-enhanced catheter-directed thrombolysis] with PTA is a safe and effective treatment for recanalising chronic venous occlusions and the improvement is still seen after 365 days.

"There is hope for PTS patients who have failed standard-of-care therapy."

Keith Sterling, an interventional radiologist at Inova Alexandria Hospital, VA, USA, described the OPTALYSE PE trial, which has set out to explore the use of the EkoSonic Endovascular System in reducing recombinant tissue plasminogen activator (rtPA) dose for treatment of acute submassive pulmonary embolisms (PE).

Patients between 18-75 years of age with CT-angiography (CTA) evidence of proximal (unilateral or bilateral) PE were enrolled. Acute PEs (symptoms ≤14 days) and submassive PEs (right- to left-ventricular diameter [RV/LV] ratio ≥ 0.9, hemodynamically stable) were included. Patients were randomised to one of four treatment groups depending on treatment duration (TD), total dose of rtPA and infusion rate: 1) TD 2 hours, dose 4/8 mg, rate 2 mg/h/catheter; 2) TD 4, dose 4/8, rate 1; 3) TD 6, dose 6/12, rate 1; 4) TD 6, dose 12/24, rate 2.

Dr Sterling said: "The PE [CTA] results showed in all four dose regimens a statistically significant decrease in the RV/LV change at 48 hours, of anything between 23 and 26%, which is similar to what was seen in SEATTLE II and ULTIMA."

A statistically significant dose response was also seen; at 365 days the mean RV/LV ratio was in the 0.7 range for all cohorts. "At the one-year mark patients had normal

Continued on page 46

"Lower dose, shorter-duration USCDT appears to be as effective as the regimens employed in other USCDT studies." ***Keith Sterling***

Updates on the use of USCDT in treating PTS and PE

Continued from page 45

RV/LV ratio," said Dr Sterling. "For a six-minute walk test we saw an improvement at 30 days and at one year. There were also improvements in the PEmb-QOL [Pulmonary embolism specific quality of life] at one year, no matter what the dose regimen. PROMIS- PF scores also showed improvement."

Dr Sterling noted that there was a 2% mortality and confirmed recurrent PE in 2% of cases. Four patients had major bleeding and, of those, two received systemic rtPA after the trial ended.

"Lower dose, shorter-duration USCDT appears to be as effective as the regimens employed in other USCDT studies," said Dr Sterling. "Reduced dose and treatment duration with rtPA definitely minimises risk of major bleeding. There is very low long-term mortality and improved quality of life."

Dr Sterling stressed that the potential of USCDT lies in its use for patients with relative contraindication to lytic therapy. "I think you can change the duration, and be comfortable that you are going to be as effective as what we have seen at higher doses and potentially avoid an ICU stay," he said.

Nima Hatam, from University Hospital, Aachen, Germany, gave a surgeon's perspective on PE in his presentation, comparing the risks versus benefits of surgical pulmonary embolectomy (SPE) versus ultrasound accelerated thrombolysis(USAT).

He told the audience: "You have good results when you have good cardiac patient selection, and that's the main problem for us cardiac surgeons, because the traditional indications for cardiac surgery in pulmonary embolism were patients who were on the verge of crashing or in haemodynamic collapse."

However, Dr Hatam said a meta-analysis published last year[1] reviewing seven decades of results on SPE, including 1,500 patients and 56 studies, showed that since 2000, in-hospital mortality has more than halved, and this was due to improvements in surgery and imaging.

"As a surgeon I'd be very happy with the results, but I have some concerns, especially regarding the right ventricle, which is already strained and stressed by acute afterload stress, which it is not designed for," he said. "Then the surgeon comes along and opens the chest and pericardium and puts the poor heart on cardio-pulmonary cardiac bypass and exposes it to the operating room air, heat, hypothermia and eventually inflammation," said Dr Hatam.

"As a surgeon I'd love to have a procedure for PE which has fast RV recovery, is minimally invasive (closed chest), and with quick access and low bleeding complications. That is where USAT comes in."

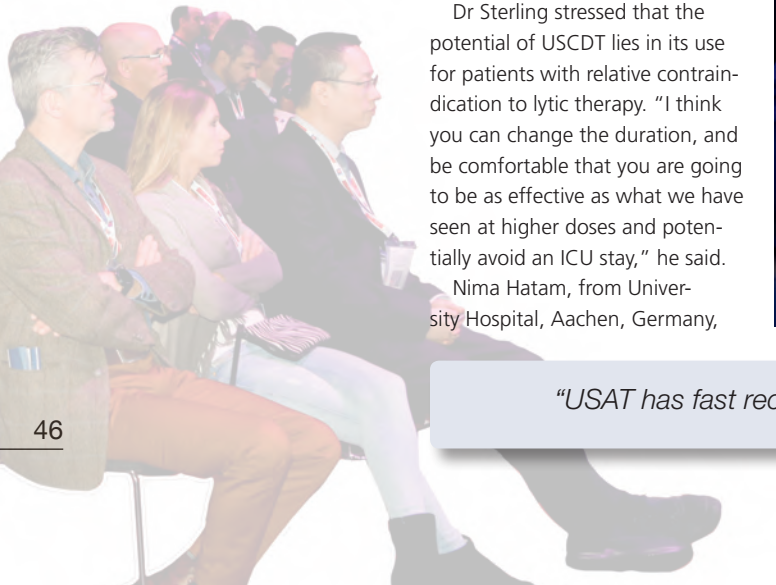
He relayed that the ULTIMA[2] and SEATTLE II[3] trials both confirmed USAT was superior to anticoagulation alone, with very quick recovery of RV dysfunction and very low rates of major bleeding complications.

Dr Hatam then discussed three patient cases with early post-operative massive PEs treated between June and October 2017, using the OPTALYSE PE protocol, which he described as a "revelation."

He went on: "We decided against surgical embolectomy and systemic thrombolysis, but we decided to put in two EKOS catheters for six hours with1 mg/h/catheter rtPA with a total dose of 12 mg," said Dr Hatam. This was one of the OPTALYSE protocols.

The unpublished results from these cases showed R/LV ratio was significantly reduced and there was also significant improvement in RV STR, as well as no major bleeding complications.

He concluded: "USAT has fast recovery in a closed chest setting with quick access, and almost no bleeding complications. Proper studies are now needed to assess the outcomes of SPE and USAT."



"USAT has fast recovery in a closed chest setting with quick access, and almost no bleeding complications." ***Nima Hatam***

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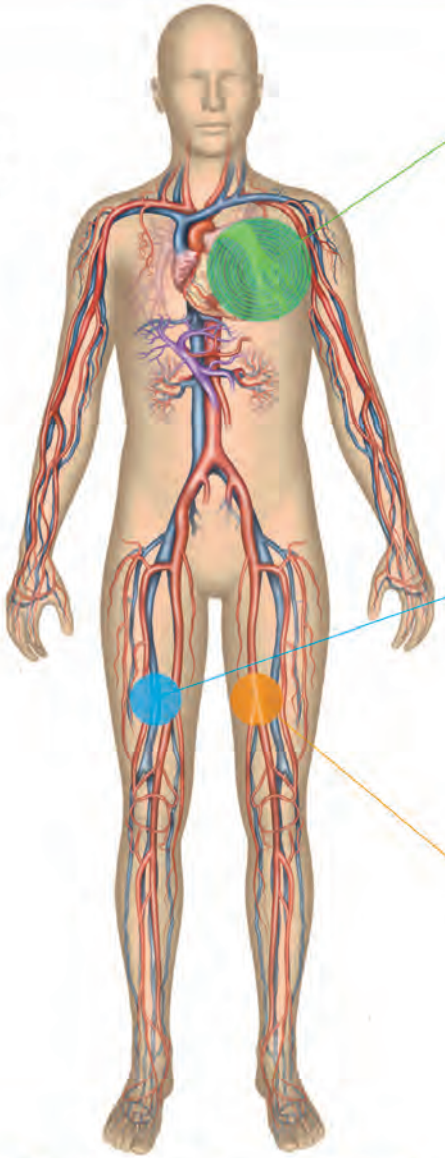

Pulmonary Embolism

- Reduces RV/LV ratio by 25% on average[1]
- Reduces PA pressures by 28% (at 48 hours)[1]
- 76% less thrombolytic drug dosage than standard treatment[1]
- At one year:
  - Mortality 2%[2]
  - Recurrence 2%[2]
  - Major bleeding 3%[2]

Deep Vein Thrombosis

- 50% of DVT patients have PE[3]
- Removes thrombus more completely compared to CDT[4]
- Reduces post-thrombotic syndrome[5]

Arterial Occlusion

- Lower 30-day amputation rate[6]
- Lower bleeding rates when compared to CDT[6]
- Higher complete dissolution rate of thrombus[6]

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INTERVENTIONAL VASCULAR | BTG

New data: Lutonix long lesions study

First time data on two-year outcomes of the Lutonix long lesion study were presented by its co-principal investigator Martin Banyai (Cantonal Hospital Lucerne, Switzerland), during a session that brought together a number of late breaking releases.

The study is a single-arm, prospective study of 118 patients with symptomatic peripheral vascular disease, who were enrolled at 14 European sites. The aim of the trial was to assess the efficacy and safety of the Lutonix drug-coated balloon (DCB; CR Bard, USA) at 12 and 24 months in treating *de novo* atherosclerotic and restenotic lesions of the superficial femoral artery (SFA) and popliteal artery of at least 14 cm in length.

"The conduct of the trial followed the same rigorous characteristics such as independent angiographic and duplex ultrasound Core Lab evaluation and 100% source data monitoring as in the LEVANT trials," Dr Banyaai told delegates. "Clinical events were assessed by a clinical event committee."

LEVANT I and II (Lutonix Paclitaxel-Coated Balloon for the Prevention of Femoropopliteal Restenosis) were randomised investigations into the safety and efficacy of the low-dose Lutonix balloon. LEVANT II, which randomised 476 patients with symptomatic intermittent claudication or ischaemic rest pain and angiographically significant atherosclerotic lesions to the Lutonix DCB or standard balloon angioplasty, found significantly improved primary patency with DCB at one year.[1,2]

In the long lesion study, following recruitment and baseline angiography, patients received balloon predilatation with a balloon approximately 1 mm smaller in diameter than the reference vessel. Upon obtaining a sufficient initial angiographic result, the Lutonix DCB was applied for at least 30 seconds for the purposes of avoiding angiographic mismatch and assuring a safety margin of at 5 mm at both ends of the lesion. Bail-out stenting was performed as angiographically necessary.

"Follow-up was very rigorous," continued Dr Banyai, "And comprised clinical, haemodynamic and ultrasound examination at one, six, 12 and 24 months. Most of the patients suffered from claudication, but only about 5% of the patients suffered from ischaemic rest pain."

77.1% of subjects has TASC C lesions, and 22.0% TASC D. A mean lesion length of 21.3 cm was

treated with a mean of number of 2.2 Lutonix balloons. The longest lesion treated was 45 cm. Chronic total occlusion (CTO) occurred in 52.1% of cases. A high proportion of calcium added to the complexity of the treated lesions, noted Dr Banyai, with 88.1% of lesions being calcified, and over 20% severely calcified (as confirmed by angiographic Core Lab).

Kaplan-Meier estimates of freedom from primary safety events – a composite of freedom from all-cause peri-procedural death and freedom from index limb amputation (above or below the ankle) and index limb reintervention – at

"The conduct of the trial followed the same rigorous characteristics…as in the LEVANT trials." ***Martin Banyai***

Source: www.leipzig-interventional-course.com

Lutonix Long Lesion vs. Zilver PTX

Kaplan- Meier Freedom From	Long Lesion Study (Mean length 212.5±68.3mm / Range 100.0, 450.0)	Zilver PTX (Lesion length range >140-240mm)
TLR (12 months)	87.4%	75.6%
TLR (24 months)	75.6%	71.3%

one year was 82.3%, and at two years 70.5%. "The safety profile of the Lutonix DCB in the long lesion trial was almost identical to the DCB arm of the LEVANT II trial," commented Dr Banyai. "The treated length however was 3.5 times longer than in the long lesion trial."

Kaplan-Meier estimates of freedom from target vessel revascularisation (TVR) were 97% at six months, decreasing to 87.4% at 12 months, and 75.6% at 24 months of follow-up. At two years an improvement of at least one Rutherford category relative to baseline could be observed in approximately 80% of patients, with over 60% of patients improving by at least two categories. Furthermore, improved ankle brachial index was observed in approximately 35% of treated subjects at two years.

Comparing these results to those in a demographically similar cohort treated with Zilver PTX, Dr Banyai noted: "In the long lesion trial, a higher proportion of patients were affected by decreased renal function. The percentage of calcification and the proportion of severe calcification of the lesions were in a very close range in both trials.

"Bearing in mind the difference concerning the trial design, the Kaplan estimate of freedom from TLR at 12 and now 24 months is at least as high, or even higher, compared to drug-eluting stenting of femoropopliteal lesions with the Zilver PTX stent."

Dr Banyai concluded: "The treatment of long and calcified femoropopliteal lesions with the Lutonix balloon is very satisfying, with results now up to two years of follow-up. The safety profile consists of high freedom from TLR, low vascular complication rate and a very low rate of amputation."

"The treatment of long and calcified femoropopliteal lesions with the Lutonix balloon is very satisfying." ***Martin Banyai***

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Spot-stenting promises to undress the full metal jacket

Preliminary data tell us that spot stenting is superior to long, full stent coverage in terms of durability of procedure in femoropopliteal lesions. Such was the opinion advanced by experts at a B. Braun-sponsored symposium, with delegates in the Technical Forum keen to hear the latest news about spot stenting.

Often after treatment of an occlusion in the femoropopliteal artery, long and complex lesions can remain, which conventional practice dictates should be treated with a long, full stent. However, a closer look reveals some focal re-coils and dissections, which might be better treated with spot stents. This marked change in practice was the focus of the symposium's sub-session titled *Spot-stenting: it's time to undress the full metal jacket*.

"Multiple short stents might overcome the limitations of a full metal jacket," remarked Thomas Zeller, (University Heart-Center, Freiburg-Bad Krozingen, Germany) who was one of three speakers on the podium. He was joined by Peter Goverde (University of Antwerp & Gand-Antwerp Area, Belgium); and Gunnar Tepe, (RoMed Klinikum Rosenheim, Germany). The session also included a live case with the SeQuent® Please OTW and VascuFlex® Multi-LOC presented by Dr Sven Bräunlich.

Coverage of long lesions challenge stenting success

It was the FESTO trial[1] in 2005 that showed reduced patency due to stent fractures predominantly close to hinge and flex points in the femoropopliteal artery. The development of nitinol (nickel-titanium) stents with their helical cell design aimed at mimicking arterial movement demonstrated improved data in terms of patency and stent fracture but failure still arose as a result of chronic trauma of the vessel wall, vessel-to-stent interaction due to arterial motion including torsion, compression, and distention, and pulsatile distension. Trials of drug-eluting stents (DES) generated positive results, but only in short and medium length lesions, which meant long lesions required another solution.

The use of drug-coated balloons (DCBs) is supported in these long lesions according to the CONSEQUENT trial (NCT01970579). This trial was designed to assess the safety and efficacy of the paclitaxel-coated balloon catheter SeQuent® Please OTW DCB (over the wire drug-coated

"The idea of DCB therapy is to leave nothing behind, but this is not possible in very demanding lesions." ***Gunnar Tepe***

balloon) to treat steno-occlusive lesions of the superficial femoral artery (SFA) and the proximal two segments of the popliteal artery. The coating on the SeQuent® Please OTW DCB comprises paclitaxel at 3 µg/mm² integrated into a matrix with resveratrol 0.9 µg per 1 mm² balloon surface. This is naturally occurring resveratrol that is anti-oxidative, anti-inflammatory, and vaso-active. Nearly 24% of lesions were TASC C and D lesions, and had a mean lesion length of 13.2 cm.

Results showed statistically significant superiority of the SeQuent® Please OTW DCB compared to percutaneous transluminal angioplasty (PTA) alone, even in long femoropopliteal lesions after six and 12 months. The final angiographic and clinical 24-month results of the CONSEQUENT trial were presented at LINC by Principal Investigator (PI) Thomas Albrecht (Vivantes Klinikum Neukölln, Berlin, Germany). Of the 153 patients, 78 received DCB and 75 POBA, and the primary endpoint was late lumen loss at six months (Core Lab quality assurance) and secondary endpoints included binary restenosis rate > 50% at six months, clinically driven target lesion revascularisation (TLR) at six, 12 and 24 months.

Professor Albrecht reported

Thomas Zeller

that predilation was performed in 55.6% of patients and bailout stenting was performed in 16.3% (14.1% in DCB versus 18.7% in uncoated balloon). Late lumen loss was 0.35 mm in the DCB group versus 0.72 mm in the uncoated balloon group (p=0.006). TLR at 24 months was 19.1% in the DCB group versus 40.6% in the uncoated balloon group (p=0.007); patency was 72.3% versus 48.4% respectively (p=0.006), so significantly higher, reported Professor Albrecht. "SeQuent® Please OTW delivers sustained clinical outcomes in patients with long lesions up to 24 months," he reported.

The long lesion cohort of the prospective IN.PACT Global registry (mean length 26.4±8.61 cm), treated with a DCB, resulted in a provisional stent rate of 40.4%, and cumulative primary patency after 12 months was 91.1%. However long stents can cause trauma to the vessel wall and for this reason spot stenting might be preferable after DCB or standard PTA.

Spot stenting with VascuFlex® Multi-LOC

Addressing spot-stenting at the symposium, Professor Zeller remarked: "Spot stenting is different in that we use a very short stent of 13 mm length. Unlike traditional nitinol stents, the VascuFlex® Multi-LOC comes as a series of six short stents on one applicator, each of which can be delivered in different places in the vessel," said Professor Zeller. "We know that a full metal jacket – full coverage of a lesion – is associated with relatively high restenosis, risk of stent fracture that might harm vessel wall integrity, and can create restenosis in the area of stent fracture," he said, adding: "The idea is to limit the extent of lesion coverage with foreign body and to place shorter stents in areas of focal recoil eliminating the need for implanting longer stents."

VascuFlex® Multi-LOC spot stenting can be used in patients who have been treated with plain old balloon angioplasty (POBA) or a DCB, and require bailout stenting to improve the outcome in the femoropopliteal artery. Spot stenting limits the amount of restrictive metal implanted and as such is more suitable for high-movement arterial segments. The device reduces the risk of thrombosis and restenosis and at the same time the natural movement of the artery remains. Spot stenting eliminates

Continued on page 52

"We know that a full metal jacket – full coverage of a lesion – is associated with relatively high restenosis, risk of stent fracture that might harm vessel wall integrity and can create restenosis in the area of stent fracture." ***Thomas Zeller***

Spot-stenting promises to undress the full metal jacket

Continued from page 51

dissections or flaps and segments with elastic recoil due to calcification or scar tissue after previous interventions that can all limit flow.

Comprised of six individual nitinol stents loaded onto one 6-F multiple stent delivery system (MSDS) separated by spacers of 5 mm length, each stent has a closed cell design of 13 mm in length, with diameters ranging 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 which also has a radiopaque tantalum marker fixed into the spacer that prevents the stent from jumping. This should remain fixed on the applicator until the outer sheath is withdrawn and the single spot stent deployed.

Referring to a 2015 publication from a group in Seoul, South Korea, that compared the outcome of selective stenting versus full lesion coverage, Professor Zeller highlighted that the study concluded the primary patency was significantly higher with spot stenting than with long stenting following a sub-intimal approach for long femoropopliteal chronic total occlusions. The risk of restenosis was especially higher when long stenting was extended to the distal popliteal artery.

Gunnar Tepe

"Their retrospective analysis found that lesions treated with spot stenting showed a better 12-month patency compared to full, long metal stenting," reported Professor Zeller. The adjusted-primary patency was 77% versus 47%, ($p < 0.001$) in the spot stent group versus the long stent group, and adjusted-freedom from TLR was 52% versus 84% ($p < 0.001$) at two years – so significantly lower in the spot stenting than in the long stenting group. Compared with spot stenting after adjustment using inverse probability of treatment weighting, long stenting, especially involving the P2 or P3 segment of the popliteal artery, was independently associated with 7.5-fold increase in restenosis risk ($p < 0.001$).

Having had considerable experience with the VascuFlex® Multi-LOC system, Professor Zeller shared his thoughts on use of the device. "The application is easy, the device offers a good compression resistance – so in the case of calcified lesions and recoil there is resistance," he said, adding: "Personally, I feel the acute experience is promising but we don't yet have longer term experience to determine the degree of flexibility and if this leads to improved patency and reduced re-intervention rate."

He pointed out that every aspect of stent design and placement has some association with restenosis including mesh configuration; chronic outward force (stent oversizing); stent material; strut thickness; stent length and stent overlap. "Spot-stenting might preserve superior re-treatment options compared to those available for diffuse in-stent restenosis. Treatment of diffuse in-stent restenosis is very challenging. There might be some focal diffuse in-stent restenosis and this might be easier with spot stenting."

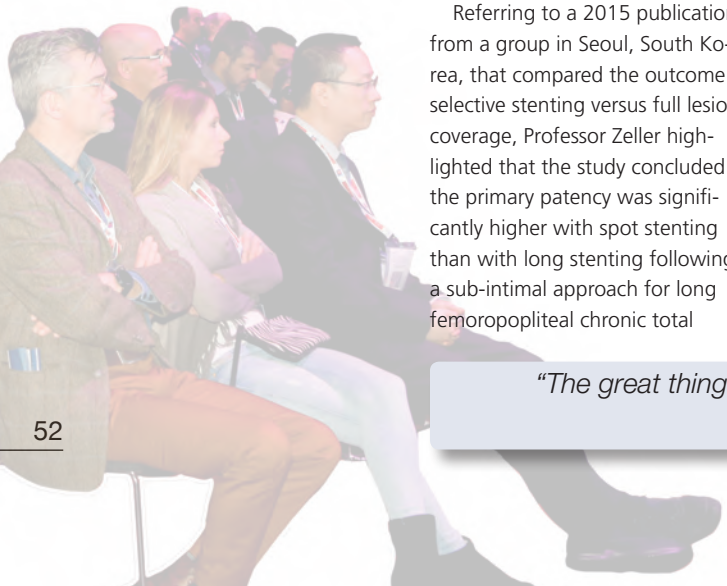
DCB & spot stents in fempop lesions

Professor Tepe took to the stage to discuss use of the SeQuent® Please OTW DCB with which he has experience via trial and clinical work.

He explained why he felt there was an unmet medical need for DCB followed by spot stenting in some cases. "With DCBs we've learned that as the lesion becomes more challenging, we need more stents and that in very long lesions we might need stents in 40-50% of patients."

"The idea of DCB therapy is

"The great thing about this is that we can place the spot stent wherever it is required whether an area of dissection or recoil, wherever it is focally required." ***Gunnar Tepe***



to leave nothing behind, but this is not possible in very demanding lesions. We could just use a traditional long stent and cover the whole lesion. However, after this procedure there would be a lot of foreign material in the vessel left behind, so in these situations we suggest spot-stenting," Professor Tepe remarked.

"For this purpose B. Braun has developed the VascuFlex® Multi-LOC stent which we can deliver very focal stents," remarked Professor Tepe, who took the audience through some of his procedures with DCB followed by spot stenting. "The great thing about this is that we can place the spot stent wherever it is required whether an area of dissection or recoil, wherever it is focally required. The only restriction is a recommendation to leave half a centimetre between two stents to avoid overlap, and to fix the vessel. Six or fewer stents can be used and any left over can be disposed of."

Professor Tepe noted that B. Braun hopes to develop longer stents in the future that might be around three centimetres, and also a device with fewer than six short stents because very often short stents are wasted when fewer than the full six are required in one procedure.

He also referred to the CONSEQUENT study and the LOCOMOTIVE registry study in his talk. This prospective multicentre LOCOMOTIVE registry is collecting all-comers data on procedures as well as preliminary safety and efficacy data of VascuFlex® Multi-LOC. To be included on the registry, femoropopliteal lesions are prepared with uncoated or paclitaxel-coated DCBs, and if flow-limiting dissections, elastic recoil, or calcification occur and require stenting, then spot stenting using the VascuFlex® Multi-LOC is deployed. Six-month target lesion revascularisation rate is the primary endpoint.

The six-month results, presented at last year's LINC, showed that 176 target lesions had been treated, of which 51.1% (90) were TASC class C/D lesions, and overall total lesion length was approximately 14.5 cm; 97% were severely calcified.

At six months, TLR rates were 5.3%, and primary patency was 90.7% overall, and spot stenting strategy was considered safe and effective in femoropopliteal lesions. Analysis of procedural data showed that technical success rate was 100% (no flow-limiting dissections or residual stenosis > 30%), and nitinol stent length was reduced by 50%.

Twelve-month results of the LOCOMOTIVE study presented by Professor Klaus Amendt (Mannheim, Germany), earlier in the day during a late-breaking trial session showed that the primary patency (primary unassisted patency – diameter stenosis <50%) was 86.7%; all TLR rates were 9.3%.

"We are also evaluating this device in the SPORTS trial where we compare different approaches in long lesions with a DCB versus drug-eluting stent (DES) versus normal stent," remarked Professor Tepe. "We are following a spot stenting strategy with the DCB. Those that require spot stenting receive the VascuFlex Multi-LOC."

He concluded: "DCBs, in particular the SeQuent Please OTW DCB perform very well, especially in long lesions. But if a spot spenting strategy is required, then the VascuFlex Multi-LOC stent will be placed."

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The SeQuent Please OTW DCB performs very well, especially in long lesions." ***Gunnar Tepe***

Helical fixation anchors lend weight to EVAR outcomes

Mid-term results from the ANCHOR study were exhibited, detailing the latest update on the use of the Heli-FX™ EndoAnchor™ system (Medtronic, USA) for independent transmural fixation of compatible endovascular aneurysm repair (EVAR) endografts to the aortic wall.[1]

Presented by Colin Bicknell (Imperial College London, UK), ANCHOR's results mark an intriguing update to an inherent sealing and fixation technology that aims to bring the stability of the surgical anastomosis to EVAR and TEVAR.[1] Dr Bicknell spoke to *LINC Review* to explain more about the device and the ANCHOR study.

Please introduce the Heli-FX system and its treatment potential.

The Heli-FX EndoAnchor system and the Heli-FX Thoracic EndoAnchor system allow the placement of a series of helical fixation anchors during or after EVAR, which is proving to be a safe and effective treatment for more complex anatomies. This system is intended to provide fixation and sealing between endovascular aortic grafts and the native artery.

Endoanchors are indicated for use in patients whose endovascular grafts have exhibited migration or endoleak (or are at risk of such complications), in whom augmented radial fixation and/or sealing is required to regain or maintain adequate aneurysm exclusion. This means that endoanchors can be implanted at the time of the initial endograft placement, or during a secondary (i.e. repair) procedure.

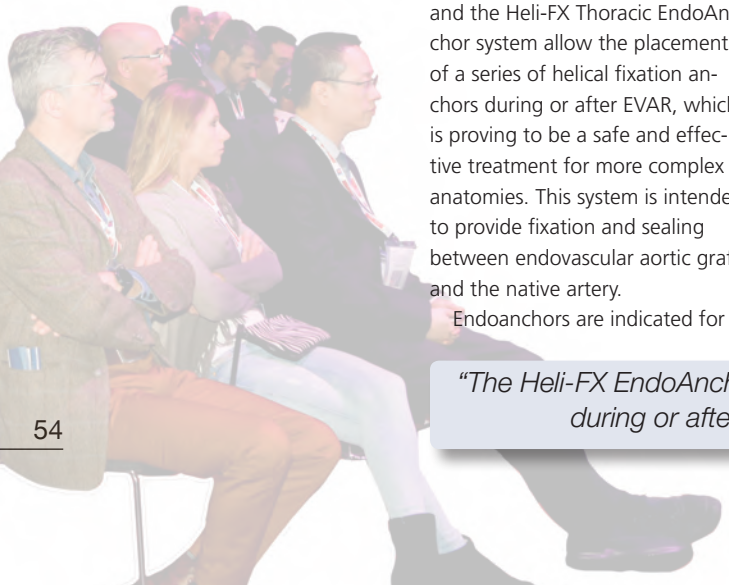
The potential for this system in AAA treatment is threefold. Firstly, to treat patients with a greater degree of confidence when the neck is hostile, by providing fixation to prevent migration and endoleak. Secondly, to treat patients more effectively, as type 1 endoleak can be dealt with by fixation of the proximal endograft sealing zone. Lastly, and most relevant to this talk, recent evidence has demonstrated that the treatment of short necks seems effective with an Endurant graft [Medtronic] and endoanchor placement. The Endurant II/IIs stent graft has recently received FDA approval and CE marking to treat abdominal aortic aneurysm patients with neck lengths from 4 to 10 mm (as long as the infra-renal angulation is less than 60 degrees).

The expanded indication means there is potential to treat a wider range of patients with short, hostile aortic neck anatomies, without the need for complex aortic repair strategies.

The ANCHOR study is a prospective, observational, international, multicentre, dual-arm registry. Talk us through its key design specifics.

The ANCHOR registry commenced in April 2012, led by Will Jordan in the US and Jean-Paul DeVries in Europe. The ANCHOR registry is made up of two groups. The primary group contains subjects undergoing initial (primary) endovascular repair of an AAA, and where the investigator believes the proximal aortic neck is challenging. In other words, there is a risk of failure because of issues arising from proximal fixation and/or sealing. This group includes EVAR patients who had a type 1 endoleak on the table which was tackled with endoanchor placement.

The revision groups includes subjects who have previously undergone an EVAR procedure, and in whom the investigator believes the use of the Heli-FX EndoAnchor System is warranted to treat graft migration or type 1a endoleak, with or without the concurrent use of an extension piece. This group also includes subjects with an exist-



"The Heli-FX EndoAnchor system and the Heli-FX Thoracic EndoAnchor system allow the placement of a series of helical fixation anchors during or after EVAR, which is proving to be a safe and effective treatment for more complex anatomies." ***Colin Bicknell***

in latest study update

ing EVAR believed to be at risk for migration and/or type 1a endoleak

ANCHOR is currently enrolling patients at clinical sites across the U.S. and Europe. There are 43 U.S. sites, and 40 sites in Europe. The target is to enroll up to 2,000 patients between the primary and revision groups.

More recently in the ANCHOR registry there has been a redesign to enable the inclusion of thoracic and more complex patients (including branched/fenestrated and arch hybrid procedures).

Patients enrolled in ANCHOR with AAA tend to have more complex aortic anatomies, including conical, short, angulated or wide necks. The data from the ANCHOR study examines the results of this group, and also looks at therapeutic applications for intra-operative type 1a endoleak, late type 1a endoleak, and graft migration.

What mid-term results from ANCHOR will you be sharing?

The results overall show that Heli-FX EndoAnchors enhance outcomes and durability in patients with complex AAA anatomies – particularly those who have hostile aortic necks.

Patients in the ANCHOR registry have difficult AAA neck configurations. In the registry there is a 1.3% type Ia endoleak rate, and no migration at two-year follow-up after prophylactic implantation (median neck length: 11.5 mm), and there is also a significant incidence of sac regression in patients with EndoAnchor fixation at the same time.

One group of patients of particular interest in the ANCHOR registry is those with short-necked AAA. Seventy patients have been treated with neck lengths of 4-10 mm on core lab analysis. With an average neck length of 6.86 mm, this cohort was treated with a procedural success rate of 97.1%, a type 1 endoleak rate of 1.9% and no migration at one year.

It seems this technology not only allows for the safe and effective treatment of more complex AAA anatomies with confidence, but it has the potential to change the way physicians approach the treatment of short-neck AAA patients who otherwise might not have been candidates for EVAR. This means there is a change in the potential options available to the physician in these cases.

What are some of the key lessons learned thus far?

Put simply, the data from the ANCHOR registry shows that grafts implanted into aneurysms with difficult neck configurations (that may degenerate further, leading to migration and endoleak), in which endoanchors are placed, do very well through two years. Thus we can treat patients with a greater degree of confidence when the neck is hostile.

The results from the short-neck cohort demonstrate that there is an option to treat this group effectively, at least over one to two years, without the need for complex strategies involving the renal and visceral branches.

What's next for the device, ANCHOR and/or other studies?

The ANCHOR registry is a long-term study. What we do want to know is how these grafts, once endoanchors are implanted, behave late on. These are a group of patients enrolled that have hostile necks, and the results out to five years will tell us whether this system really does effectively prevent migration and loss of sealing long term. Updates will continue to be shared on the progress of the ANCHOR study and its performance in patients with complex aortic anatomies for a few more years.

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"One group of patients of particular interest in the ANCHOR registry is those with short-necked AAA." ***Colin Bicknell***

New technology on the horizon below-the-knee

Patterns of vessel calcification in below-the-knee (BTK) and below-the-ankle (BTA) arteries, and their implications for vessel preparation and atherectomy, were discussed by Jihad Mustapha (Advanced Cardiac & Vascular Amputation Prevention Centers, Grand Rapids, MI, USA).

Dr Mustapha opened by stressing the importance of accepting that tibial arteries are different from all other arteries – especially the superficial femoral artery (SFA) and coronary arteries. He added: "We need to think about the SFA, popliteal and tibial and pedal arteries as we plan our therapy."

New technologies, he said, have evolved to address new challenges brought about by improved understanding of plaque composition in the BTK region.

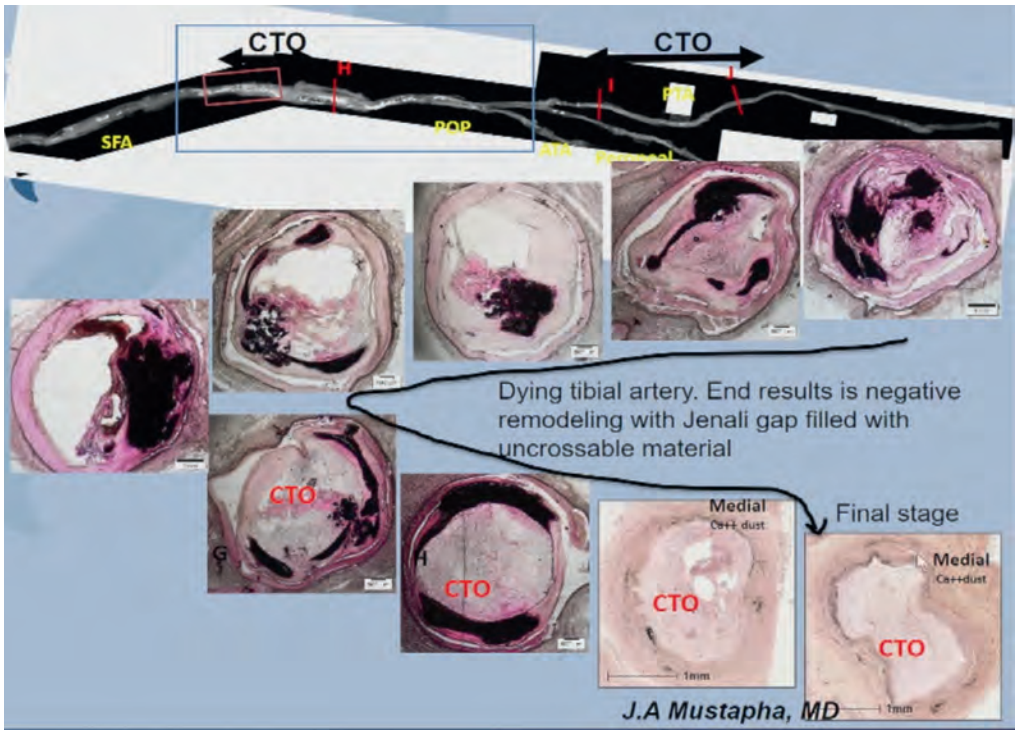
One of these technological developments is in atherectomy. Dr Mustapha cited a novel orbital atherectomy device currently being investigated for debulking below the knee, the FreedomFlow (Cardio Flow, Inc., USA). This system incorporates spiralling discs of ranging diameter designed to accommodate varying vessel sizes up to 8 mm.

Discussing his recently published work on the topic of infrapopliteal calcification patterns in critical limb

Jihad Mustapha

ischaemia[1], Dr Mustapha noted that within the tibial segment plaque composition varies with implications for its treatment. Cholesterol crystals, he explained, are present in proximal to mid-tibial lesions and that this is associated with the presence of intimal calcium and leads to the development of calcified atheroma and occlusive lesions. More distally, fibrotic tissue is characteristically associated with medial calcium and leads to stiffening and decrease in arterial wall elasticity and compliance, which leads to stent fracture or collapse.[1]

"The evolution of the chronic total occlusion [CTO] in the tibials is extremely unique," explained Dr Mustapha, noting that radiographic evidence of gaps in CTO is a sign of negative remodelling, and often indicates uncrossable material. "When you see calcium, no calcium, and calcium again – this is a dying vessel. There is no structure to it any more, and we call that the Jenali gap. When we see something like this, a lot of the time we do give up." (Figure 1)



Source: www.leipzig-interventional-course.com

Figure 1. The evolution of tibial disease leading to formation of CTO. (Top right) Radiographic image indicates the Jenali gap, which is characteristic of negative remodelling. (Bottom right) At the culmination of CTO development, the intimal area is completely occupied by elastin fibres, surrounded by a purely calcific portion.

Contrasting the composition of CTOs from the SFA to the popliteal and tibial arteries, Dr Mustapha continued: "If you were to cross an SFA CTO, you would cross it a lot quicker [than a tibial CTO] and you would get great results. Which atherectomy could you use? You could use many atherectomy devices here, and you would get great results. As you go down towards the popliteal you have to start being a bit more careful, because the combination of the disease stage and the components that make the disease stage are changing. As you get nearer the area of the P3 seg-

"Finally we have something that we can use below thea ankle, in terms of plaque and recoil." ***Jihad Mustapha***

ment and the tibials, the medial calcium and the neointimal hyperplasia become extremely extensive."

Referring to the tibials, he went on: "The absence of calcium here is worse than the presence of calcium. It tells you that the vessel is dying, [with] negative remodelling of it."

Questioning what can be done in such cases, Dr Mustapha looked to developments in stenting below the knee, such as the MicroStent (Micro Medical Solutions, USA), which last year received CE mark approval. "What is unique about this stent is that it allows all branches to stay intact. That is extremely important, especially when you are talking about distal tibials or transpedal stenting… This is an area that we usually don't like to treat because it recoils immediately. The stent accommodates itself to the vessel size it is in, [which] eliminates the recoil.

"Finally we have something that we can use below the ankle, in terms of plaque and recoil," he concluded. "Atherectomy and other devices are on the horizon."

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CCT@LINC

Giancarlo Biamino (Impruneta, Italy) joined Kazushi Urasawa (Tokeidai Memorial Hospital Sapporo, Japan) to moderate this year's CCT@LINC session, which centred on peripheral chronic total occlusion (CTO) crossing techniques in segments including below-the-knee (BTK), below-the-ankle (BTA), and the superficial femoral artery (SFA).

As one of the course directors of the Complex Cardiovascular Therapeutics (CCT) Peripheral meeting, Dr Urasawa spoke to *LINC Review* about CCT's continuing exchange with LINC: "Last year, the collaboration between LINC and CCT jumped up to the next stage.

"We had two LINC@CCT sessions at CCT Peripheral 2017. Professor Giancarlo Biamino, Dr Andrej Schmidt and Dr Yvonne Bausback gave us very informative lectures and pre-recorded video cases. Their fully updated presentations and outstanding video cases enthralled all participants of CCT Peripheral 2017. It is a great honour for us to be able to play a part in the LINC 2018 programme."

This year, Drs Urasawa, Ando, Nakama and Iida all introduced "Japanese-style" endovascular therapy based on pre-recorded video cases. The session covered the endovascular techniques used for femoropopliteal, BTK and BTA lesions in Japan.

Dr Urasawa himself presented on SFA CTO crossing techniques during this session. "I have focused on how to set up bi-directional wiring in the treatment of long femoropopliteal occlusive disease for the last 12 years," he said. "And, in past LINC meetings, I have introduced transcollateral wiring and various puncture techniques such as distal SFA anterior puncture, distal SFA medial puncture, anterolateral popliteal puncture, high tibial puncture and distal peroneal puncture (I learned the last two puncture techniques from Dr Schmidt)."

A recently published study by Dr Urasawa and colleagues on the feasibility and safety of an anterolateral popliteal puncture technique as a retrograde access to CTOs in the femoropopliteal segment[1] formed the meat of his presentation. The single-centre series comprised 20 consecutive patients, with P3 access via a sheathless technique followed by wire rendezvous in the CTO, and antegrade wire advancement. "By using this puncture technique, you

Hiroshi Ando

can access the P2 or P3 segments of the popliteal artery without changing the patient's position. It is a very effective, safe and robust technique to establish bidirectional wiring setting in cases with very long femoropopliteal occlusive disease."[1]

Dr Urasawa has previously spoken about the superior wire skills in the Japanese endovascular community being born out of device lag. Is this still the case, or has some progress been made in speeding up the review process? "Unfortunately, we are still struggling with device lag," he said. "We have already finished two clinical trials of atherectomy devices. And, time consuming reviewing processes are ongoing.

"The good news is that two drug-coated balloons [DCBs] finally obtained approval quite recently. The ministry of health and welfare (NHLW), however, ordered those companies to complete a large post-marketing survey in a limited number of institutions before the full launch of DCBs. As such, the majority of the Japanese peripheral interventionists have to wait one or two more years.

"Japanese medical insurance for the whole nation is well known. All Japanese people have equal accessibility to any kind of medical treatments and medicines with reasonable cost when we need them. But at the same time, this system creates huge financial deficit for the government. In order to suppress the rapidly growing deficit, the government and NHLW lower the price of medical devices and medicines every two years. At the same time, NHLW requests newly approved medical devices to be capable of replacing previous devices. For example, we cannot use both DCB and self-expandable nitinol stents together in a treatment of femoral lesion. One of

Continued on page 58

"I do hope that many LINC 2018 attendees also participate in the upcoming CCT Peripheral 2018." ***Kazushi Urasawa***

Continued from page 57

them is not reimbursed if we use both. It means that add-on type devices (such as atherectomy devices) are hard to get approval for."

The upcoming CCT meeting takes place between 25 and 27 October 2018, at the Kobe International Exhibition Hall and Portopia hotel (Kobe, Japan). The meeting is composed of CCT Coronary, CCT Peripheral, CCT Surgical, CCT Structure Heart Disease and CCT Co-medical. "Every year, more than 5,000 attendees join the biggest cardiovascular intervention live course in Asia," said Dr Urasawa.

"I have charged CCT Peripheral as the course director for last five years. Dr Hiroshi Ando (Kasukabe Chuo General Hospital, Japan) will charge the meeting with me. I do hope that many LINC 2018 attendees also participate in the upcoming CCT Peripheral 2018, and enjoy the Japanese-style endovascular therapy and the beautiful nature of Japan."

Aggressive, yet effective methods below-the-knee

In his presentation during the session, Hiroshi Ando (Heart Center, Limb salvage Center at the Kasukabe Chuo General Hospital in Saitama, Japan) addressed the audience on how to cross BTK CTOs.

"The main problems when performing endovascular therapy are long CTOs, calcification, BTK or BTA lesions," he explained. To overcome these kinds of problems, he added, it's important to establish bidirectional approaches, for instance the transcollateral approach (TCA), the transpedal approach (TPA), distal puncture (DP), extreme DP, or unique techniques.

Dr Ando presented a number of case examples, noting: "Sometimes I perform the wound puncture in the area that is already amputated, and I insert the needle from the wound area to open up blocked vessels."

He demonstrated one particular case where the plantar artery was punctured using a local anaesthetic and a microcatheter under fluoroscopic guidance. In another case, a metatarsal artery puncture, he used the same needle, and tried a back-and-forth movement of the wire in order to pass it through.

Dr Ando demonstrated what he calls the needle-cracking technique. This unique technique, he said, is used when there is total occlusion that cannot be opened up because of severe calcification. He demonstrated breaking through the calcified region using a needle to achieve a puncture, saying: "I controlled the direction and the depth of the needle and punctured the calcified region. The tip of the needle went towards the proximal microcatheter and I made a crack into the calcified plaque. It was a very hard plaque so I had to rotate the needle and push forcibly. Finally, I could pass the wire."

Next up was a procedure nicknamed the 'Jet Mole Attack'. Dr Ando described how he can manipulate the wire: "In this case, I rotate the wire clockwise, the tip of the wire works like a screw … and moves towards the pedal loop."

Introducing another innovative technique, Dr Ando said: "We can pass the wire to severe and complex regions, however we sometimes encounter situations when no device can pass through the region after passing the wire."

One can try using a range of devices to pass through the lesion, said Dr Ando, but recently he is more likely to try The BAlloon Deployment using FORcible Manner (BADFORM) technique[2]. "First of all, we externalise the wire, and if we can externalise it, we can get a strong backup force. In many cases it's easy to push a balloon into the region, but sometimes we fail," he explained. "In that case I attach a torque device to an over the wire balloon hub to create a unified system. And then I pull the guidewire retrogradely so consequently the balloon forcibly draws into a blocked region."

Giancarlo Biamino (right) and Kazushi Urasawa

Essentially, BADFORM allows calcified plaque to be removed cylindrically like in endarterectomy, noted Dr Ando: "The BADFORM technique can be the most promising option for device delivery failure. An artery is not likely to be ruptured by the BADFORM technique."

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"The main problems when performing endovascular therapy are long CTOs, calcification, BTK or BTA lesions." ***Hiroshi Ando***

2018

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The Complex Aortic & Vascular Symposium

JUNE 12-13, 2018

New York, New York

Mount Sinai Heart

Symposium Directors

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Symposium Overview

LINC Mount Sinai is a multidisciplinary live case based education conference for physicians and healthcare professionals dedicated to treating patients with vascular disease. Attendees will learn the most up to date diagnostic techniques and cutting edge treatment strategies utilizing innovative technologies, live case demonstrations from national and international sites, as well as creative learning platforms. The world renowned faculty emphasizes unbiased and critically evaluated educational content that highlights multidisciplinary perspectives and collaboration.

We will achieve this by bringing together colleagues of different specialties from across the country and abroad, who perform Endovascular Interventions. This two-day course will focus on presenting concise and current information that will update you with the latest techniques and technologies.

Highlights

- Focus on critical limb ischemia, aortic and aneurysmal disease, drug coated technology, carotid and cerebral vascular disease, venous disease, dialysis access, pulmonary embolism, chronic total occlusions
- Didactic lectures from physician leaders selected for appeal to the conference's multidisciplinary audience
- Live case broadcasts in HD from multiple national and international centers, with discussion between panelists, case operators and audience members
- Industry-sponsored sessions on hot topics related to treatment of PAD and CLI

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OMNIA tissue oxygen microsensors for CLI

Extreme below-the-knee (BTK) interventions were the order of business when Marianne Brodmann (Medical University Graz, Austria) presented first-in-man data on a novel tool for the assessment and clinical management of critical limb ischaemia (CLI). The OMNIA tool (PROFUSA Inc, USA) has been designed to guide peripheral interventions or endovascular procedures for CLI patients in a superior way compared to existing techniques, she explained to *LINC Review*.

Oxygen saturation of the foot is understood to be crucial for improvement of CLI in the optimisation of the biological processes necessary for wound healing to occur. Evidence suggests that improved oxygenation of foot wounds may speed recovery, although study is lacking in humans on optimal conditions for the promotion of cell proliferation, angiogenesis, granulation and collagen synthesis.[1] Recent study continues to explore avenues from aggressive revascularisation strategies to hyperbaric oxygen therapy, to bring more oxygen to the ischemic wound environment.

The issue remains, explained Dr Brodmann, that tools to capture tissue oxygen saturation are not very objective. "We have $TcpO_2$ measurements, but this is only measuring everything that is on the outside.

"At this time, we do not have any appropriate tool providing us objective haemodynamic or other parameters in CLI – neither for diagnosis nor follow-up.

"The unique thing about the OMNIA tool is that sensors are injected into the foot into the area under the skin. So the skin is not a barrier. In CLI patients the skin is sometimes very thick and therefore oxygen saturation measurements from outside are not good because we do not capture the right oxygen saturation."

Current prevalent techniques for measuring tissue oxygenation in use in the clinical setting – all of them non-invasive – include pulse-oximetry, near-infrared spectroscopy (NIRS) and $TcpO_2$. However, recent literature notes their limitations: pulse-oximetry relies on the presence of a pulse, and NIRS provides an indirect estimate of oxygenation only. $TcpO_2$, while being the best validated, has been described as time-consuming and complex with possible interference from local environmental factors such as inflammation and oedema.[2]

Marianne Brodmann

In OMNIA, sensors contain a light-emitting component which fluoresces in the presence of oxygen molecules. The biocompatible sensors are 500 µm in diameter and 5 mm in length, and as such can be injected precisely into areas of interest.

Currently the only objective tool used to diagnose and follow-up CLI is the WIfI classification[3], "with all the limitations that this has", explained Dr Brodmann. "There is a lot of scientific work going on in the meantime trying to solve this issue because we know that we don't have anything in our hands providing exact data on these patients. OMNIA is the most developed tools at this time."

The OMNIA tool, she continued, reflects the latest understanding of how important the microcirculation is, and can be used at the various stages of the management of the patient with CLI. But does Dr Brodmann think that it can help us to more clearly define the cut-off point for the definition of CLI? "At this time, the WIfI classification is at least quantifying patients' CLI. With the WIfI you can get a certain feeling – who is the patient at risk or not at risk for losing their toes, limbs, etc.

"But this is not something objective. With the OMNIA, we get the sense of what sort of oxygen saturation is necessary and what kind of oxygen saturation is important for wound healing. This is also something you can use as a follow-up tool in a very objective way. The sensors stay in there for the next months. This is one thing just for quantifying and qualifying this kind of patient and getting a certain cut-off for what kind of level of blood flow is necessary, because oxygen saturation is in relationship to blood flow."

Describing its other advantages, she went on: "When you are in the middle of a procedure, we open all kinds of vessels that we think are relevant for adequate blood flow to the wound area. But we don't know whether these are the right vessels we need to open to get enough oxygen to where it is needed. So OMNIA is also for procedure guidance.

"This is why it is so important to develop such tools, because what we are doing right now is treating a vessel going by what we see on the x-ray. And that is not correct, especially not in these kinds of patients."

Looking beyond the first-in-man data that she presented. Dr Brodmann and colleagues are anticipating the second-in-man study. The hope is to improve the usability of the tool further: "There is the development of the sensors, development of the ease of deployment, etc.," noted Dr Brodmann. "This will be the issue, and the aim of the follow-up study."

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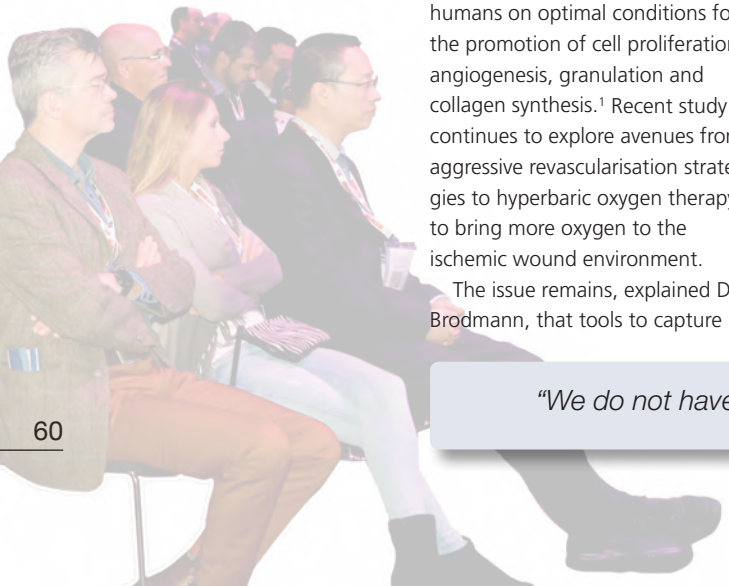
"We do not have any appropriate tool providing us objective haemodynamic or other parameters in CLI." ***Marianne Brodmann***



IN.PACT Global CLI sub-study 'outstanding'

Michel Reijnen (Rijnstate Hospital, Arnhem, the Netherlands) presented first-time data from a subgroup analysis of the IN.PACT Global study. The data relates to outcomes of drug-coated balloon (DCB) use in femoropopliteal lesions in patients with critical limb ischaemia (CLI) of Rutherford class of 4 and 5.

"When we talk about the subset of patients with CLI, we talk about the most advanced stage of peripheral artery disease [PAD]," Dr Reijnen told delegates. "When not treated, this leads to amputation in more than 20% of cases. Although an endovascular-first strategy is not generally recommended in the guidelines, it is increasingly being performed in CLI.

"There are global registries examining real-world evidence on DCBs. However, we need more data on patients with CLI. Most studies combine patients with claudication with CLI, and mostly only Rutherford 4."

The IN.PACT Global study was a real-world, prospective, multicentre, single arm, independently-adjudicated femoropopliteal study with the objective of expanding clinical evidence of the IN.PACT Admiral DCB in the treatment of a real-world patient population. Of 1,535 subjects who were enrolled, 1,416 formed the clinical cohort, the remaining 119 subjects comprising the 150-mm DCB cohort. This was an all-comers registry, which included bilateral disease and multiple lesions of the SFA and popliteal arteries. Lesions included were of TASC A-D, Rutherford class 2-4, *de novo*, in-stent restenosis, long lesions, and chronic total occlusions (CTO).

Returning to the CLI sub-study cohort, Dr Reijnen said: "It is important to realise that within this sub-study, patients were included with Rutherford 2-4. So the Rutherford 5 [patients] I'm going to show you were actually protocol violations."

The sub-study's primary efficacy endpoint was freedom from clinically-driven target lesion revascularisation (CD-TLR) at 12 months. The primary safety endpoint was freedom from device- and procedure-related death through 30 days, and freedom from target limb major amputation and CD-TLR at 12 months.

This subset of 156 patients, classed as Rutherford 4 and 5, were of mean age 71.8±10.4 years; 55.8% of patients were male, and 54.5% were diabetic.

Michel Reijnen

Hyperlipidaemia described 63.3% of subjects, hypertension 85.3%, coronary heart disease 44.0%, and current smokers made up 22.4%. Renal insufficiency occurred in 20.1% of patients. Mean ankle brachial index (ABI) at baseline was 0.60±0.26. "When we compared this group of patients with the overall group, there were more patients with renal insufficiency, more patients with diabetes, and more patients with coronary heart disease. This was a sicker patient group than the overall group."

De novo lesions made up 74.2% of this cohort. 8.8% were restenotic (non-stented), with a further 17.0% in-stent restenosis. Mean lesion length was 13.94±10.55 cm. Total occlusions comprised 41.2% of lesions, calcifications 76.8%, and severe calcification 11.3%. "When we compared this group to the overall group, there were more severe lesions, with regard to lesion length, number of occlusions, and calcium."

Predilatation was carried out in 75.0% of patients, and post-dilatation in 34.4%. The number of flow limiting dissections were low at around 1-2%, with provisional stenting being carried out in 23.4% of cases. Procedural success was achieved in 100% of cases, device success in 99.7%, and clinical success in 98.7% of cases.

Turning to Kaplan-Meier estimates in this cohort through one year, Dr Reijnen said: "Freedom from amputation is very high – 99.1% in Rutherford 4, and 97% in Rutherford 5. Looking at CD-TLR at one year, this was 14.1%. Looking at when this was performed, it was about three months after the procedure, which is sooner than what we have seen in the overall cohort.

"Looking at safety, all-cause death was 7% at one year, and there was one procedure-related death. That was a patient with an extended history treated for Rutherford 5, who went into cardiac arrest at 28 days after the procedure.

"There were two [major target limb] amputations. One patient, treated for Rutherford 4, underwent an amputation of the target limb two months after procedure due to wet gangrene. Another one, treated for Rutherford 5, had worsening of wounds that led to amputation three months after the procedure."

Clinically-driven target vessel revascularisation occurred in 14.8% of patients, with thrombosis in 4.9% of cases.

"ABI at all timepoints was increased compared to the baseline," said Dr Reijnen. "The same is true for Rutherford category. At six months, 88% had an improved Rutherford score, and at 12 months 89% had improved. Looking at quality of life, there is an improvement in all domains."

Summarising the study, Dr Reijnen concluded: "We have a remarkable effectiveness with regards to TLR, and an outstanding limb salvage rate. Obviously there are some limitations – [e.g.] only a limited number of Rutherford 5 [patients], and no Rutherford 6."

"We need more data on patients with CLI.
Most studies combine patients with claudication with CLI, and mostly only Rutherford 4." ***Michel Reijnen***

VIVA@LINC: Is vessel prep a fad, or fundamental?

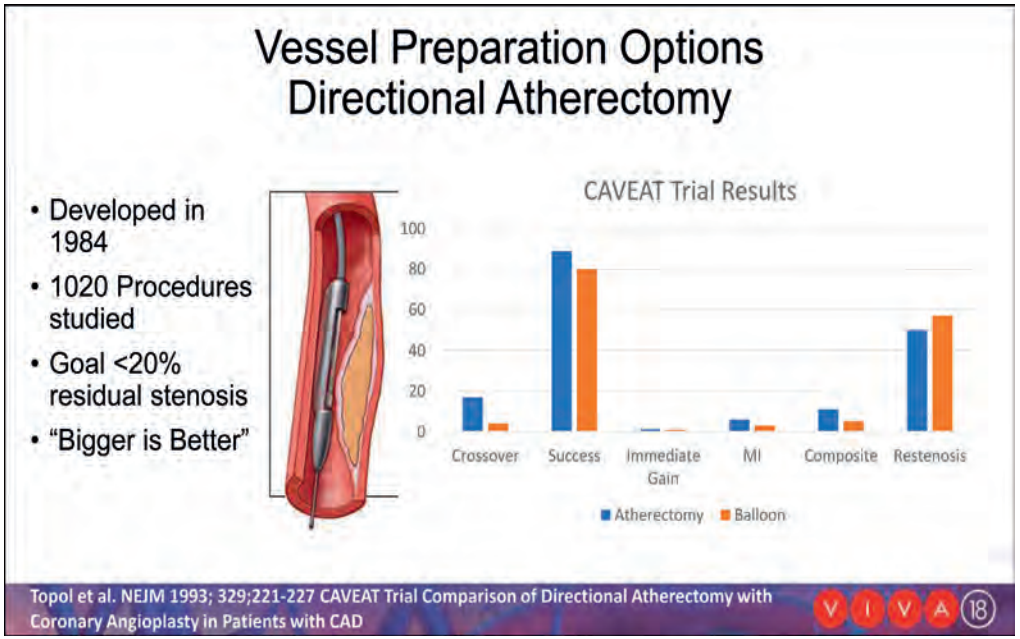
The VIVA@LINC programme offered a "deep dive" into vessel preparation, posing the question of whether it is truly an imperative part of modern practice. Answering the question was Tony Das, a VIVA co-founder and interventional cardiologist at the Walnut Hill Medical Center, Dallas, Texas, USA, who offered some perspectives from a coronary perspective as well.

In an interview with *LINC Review*, Dr Das began by noting that the paradigm of vessel preparation has evolved in recent years, leaning on emphases such as 'changing vessel response' and suchlike. "This could be pre-dilatation before stenting for optimal expansion, to preparation of vessels with atherectomy in order to increase uptake of drug-eluting technologies," he said.

Touching on atherectomy in particular, he stressed that all of the common modalities, e.g. rotational, orbital, directional and laser have had historical value in vessel preparation, but that calcified lesions have been known to herald poor intraprocedural and post-procedural outcomes when compared to non-calcified lesions.

"[One focus is] data supporting adequate vessel expansion and evaluation of post stent luminal cross-sectional areas by IVUS [intravascular ultrasound], which have been directly shown to improve outcomes. At least in the US, atherectomy is adequately covered for vessel interventions in both the peripheral and coronary space. The time addition for setup and treatment is minimal, and some studies have shown that in severely calcified vessels, this time spent upfront preparing the vessel is time well spent, decreasing procedural failures and increasing immediate lesion success."

Tony Das



Source: www.leipzig-interventional-course.com

Expanding on the role of imaging and assessment of vessel calcium, Dr Das continued: "In the coronary and peripheral space, visual identification and quantification of calcium has been proven to be limited. IVUS increases moderate and severe calcium detection in the coronary and peripheral space, and in addition, OCT has been shown to increase calcium burden awareness in the coronary circulation."

Looking to the data, what would Dr Das say to the argument that while the theory of vessel prep (bigger lumen, deeper penetration of drug, reducing plaque burden etc.) is palpable, the hard data from trials does not necessarily stack up?

"Trials like REALITY[1] will hopefully help answer the questions that DEFINITIVE AR has raised. The theoretical improvement of drug penetration and delivery by atherectomy still remains to be proven, but certainly has a scientific appeal."

Moving forward, Dr Das noted some of the more potentially fruitful avenues of focus that might secure the future of vessel preparation. "[Devices] to enhance drug uptake that also show better patency at 12 months would certainly support the development of new tools," he said. "Some animal and bench

"The idea that drug elution improves with vessel preparation appears to show a positive signal, but will require more clinical support with trials like REALITY." ***Tony Das***

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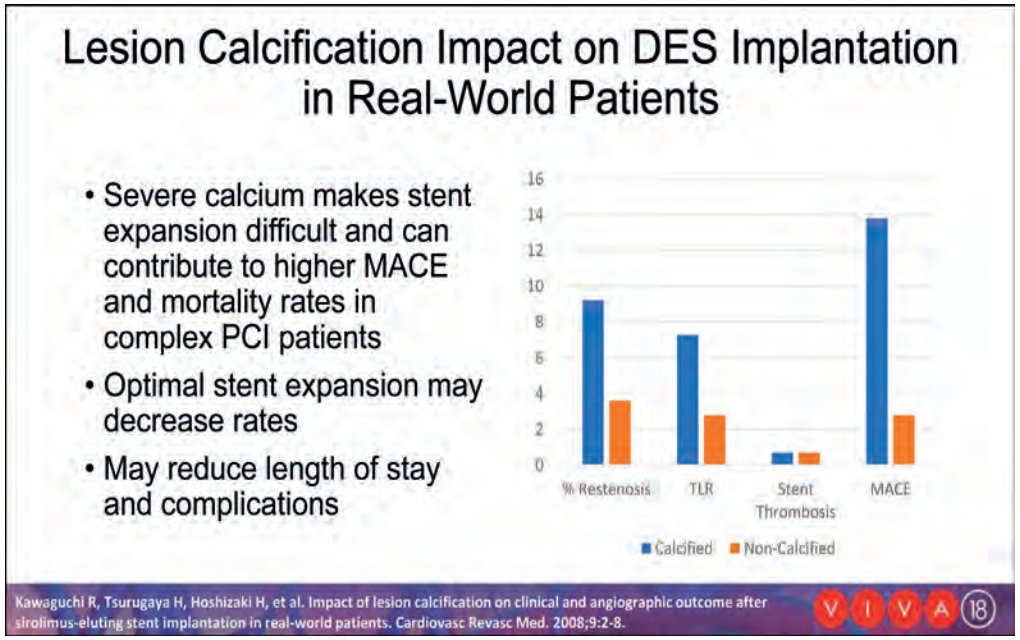

data suggests devices like scoring balloons, i.e. Serranator [Cagent Vascular, USA], and Chocolate PTA or AngioScore [Spectranetics, USA] may have a role in difficult lesion subsets."

In terms of trials, Dr Das reasoned that studies on vessel preparation are important both to expand the scientific logic, as well as provide a bedrock of proven outcomes and patency on which to base our confidence in vessel preparation modalities. This is especially important, he added, when taking into account rising healthcare costs, which demand better justification of supposedly adjunctive treatments.

Dr Das offered his take-home message: "Although coronary interventional vessel preparation methods have evolved over the last 20 years, the basic philosophy of pre-treating severe calcium to allow adequate stent expansion remains a provable concept. The idea that drug elution improves with vessel preparation appears to show a positive signal, but will require more clinical support with trials like REALITY."

"The theoretical improvement of drug penetration and delivery by atherectomy still remains to be proven, but certainly has a scientific appeal." ***Tony Das***

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The Straub Endovascular System is a Swiss Army Knife

Mechanical debulking is a safe and efficient treatment option for combatting vascular occlusions, delegates heard at LINC during a symposium dedicated to the role of purely mechanical debulking in thrombus-containing arterial and venous lesions.

Two devices from Straub Medical AG, Switzerland were showcased. The first, Aspirex®S, aspirates fresh thrombus and emboli, fragments aspirated material and transports it out of the body. The second, Rotarex®S can be used for performing fast and efficient atherectomy for acute to chronic occlusions in native vessels, stents, bypass grafts and for dialysis access.

Bruno Migliara

ISR-treatment – The Leipzig experience with purely mechanical debulking

The University Hospital in Leipzig is one of the leading centres for treating arterial in-stent re-occlusions. In his opening talk of the symposium, University Hospital's Sven Bräunlich explained that for this indication, a complete removal of the occlusive material is essential. He stated that as a stent forms a metallic barrier, drug-coated balloons (DCBs) should be considered an adjunct therapy, not a stand-alone treatment. Dr Bräunlich recommends the Rotarex®S as a first option. He underlined his statements with data from his single centre registry, enrolling an impressive 1,809 patients, of which 338 had in-stent restenosis (ISR).

"Using purely mechanical debulking with Rotarex®S reduces a procedure to a single session treatment, without further need of local lysis, which is always associated with additional ICU stay and bleeding complications," he told *LINC Review*.

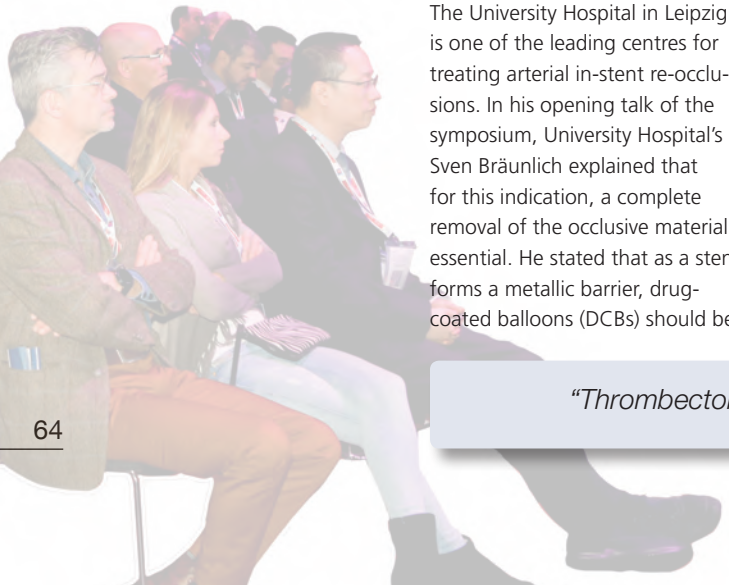
After Dr Bräunlich's talk, a live case was performed in the University Hospital Leipzig: A 62-year-old male patient with an in-stent occlusion in the right SFA presenting with Rutherford class III symptoms lasting for more than six months was treated with Rotarex®S as primary treatment. Gerry O'Sullivan, an interventional radiologist at University College Hospital, Galway, Ireland, who moderated the symposium, was very enthusiastic when seeing the result: "You must have used Photoshop™, the result is just too good," he said.

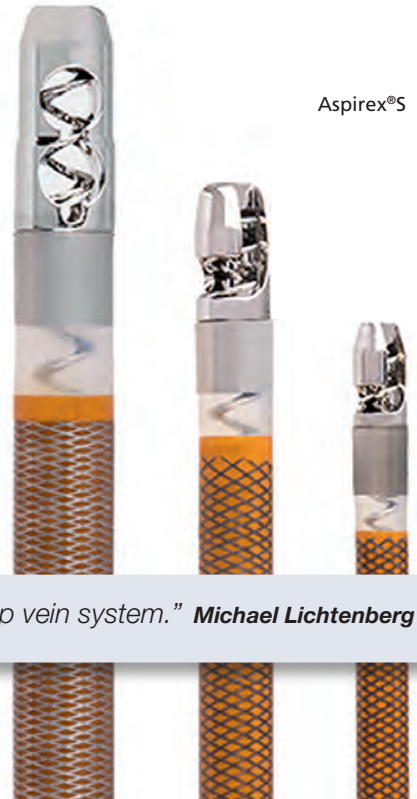
Mechanical debulking in bypass occlusions is very fast and highly effective

The second speaker, Bruno Migliara (Peschiera del Guarda, Italy) also declared his deep satisfaction with the Rotarex®S device; as the high aspirational forces allow the debulking of occluded bypass grafts. In his registry, he treated 37 patients with critical limb ischaemia (CLI; Rutherford Class IV-VI), 18 of which were above knee and 19 below the knee. He achieved a 100% procedural success rate without any major complications. Out of these 37 patients, only four had minor complications. The follow-up showed a primary patency rate of 70.3% and a secondary patency of 81.1%.

Patients with acute proximal DVT – Effective thrombus removal with purely mechanical thrombectomy can lead to better outcomes

Michael Lichtenberg from Arnsberg, Germany spoke about his experience in treating iliofemoral deep vein thrombosis (DVT) patients with purely mechanical thrombectomy (PMT). He relayed to *LINC Review* that post-thrombotic syndrome (PTS) is a frequent but underestimated chronic complication after a DVT; more than 25% of DVT patients are at risk, with 5-10% developing a severe form of PTS. Early thrombus removal and restoration of flow is critical for the prevention of PTS, added Dr Lichtenberg, and the shorter the treatment time, the higher the rate of stenting will likely be.





Aspirex®S

"Thrombectomy is the most effective strategy for removal of thrombus from the deep vein system." ***Michael Lichtenberg***

for vascular intervention

During the session, Dr Lichtenberg spoke specifically about the Arnsberg Aspirex® Registry using the Aspirex®S device. "The indications for this type of mechanical treatment are pretty clear – to prevent PTS," he said. "These patients are at high risk of persistent swelling, venous claudication, problems in the groin, as well as a high risk of having another DVT."

His study included 56 patients, with a mean age of 52. All patients had hypertension. Seven percent had a current active malignancy, 5% had had a malignancy condition in the past, and 7% had experienced immobilisation. Forty patients (71%) had an acute occlusion, and 13 (23%) a subacute occlusion. All patients had an underlying lesion, 25 (45%) of which were May Thurner lesions, 14 (25%) undetermined and five (9%) due to cancer. Another five lesions (9%) were due to post-thrombotic alterations.

In 42 (75%) of the patients in the study, the occlusion was located in the left complete pelvic veins – including common femoral, left superficial femoral veins (with possible inclusion of profunda and distal inferior vena cava).

Michael Lichtenberg

Sven Bräunlich

Rotarex®S

Seven (13%) occlusions were in the left common iliac vein only, three (5%) in the left common iliac vein or left external iliac vein (without common femoral vein involvement), and four (7%) were in the right pelvic veins. The mean length of occlusions was 156.6 mm. 5,000 IU heparin was used to treat 50 (89%) patients. Three (5%) were treated with 10,000 IU heparin, and another three (5%) were treated with 7,000 IU, 7,500 IU and 9,000 IU, respectively. Four patients (7%) were treated with thrombolysis. Technical success was achieved in 56 (100%) cases and all of the patients had stents implanted (mean 1.9 stents).

In terms of safety, 45 patients (80%) had no adverse event and of the remainder who did, none of these cases were device related. The adverse events included haematoma, puncture site infection and bleeding complications. Eight (14%) patients experienced serious adverse events (which were procedure-related, not device-related). These included rehospitalisation, reocclusion of the target vein, prolonged hospitalisation due to AV fistula operation or operation due to access site complications. There were no reports of device malfunction or complaints regarding Aspirex®S. Patency (including secondary patency) after 12 months of follow-up was 92%.

Regarding PTS outcomes, 34 patients (64%) had low severity PTS, while 19 (36%) had moderate to severe PTS. "PMT in proximal deep vein occlusions is not only fast and effective, but also avoids local lysis with its spectrum of negative side effects such as bleeding risk and the need for additional ICU stay," said Dr Lichtenberg. "Aspirex®S reduces the treatment to normally only one session in the cath lab. Thrombectomy is the most effective strategy for removal of thrombus from the deep vein system."

The effectiveness and safety of the Aspirex®S catheter in the treatment of acute venous occlusions is also currently being evaluated in the multicentre international clinical study, the P-Max trial. "We must have more prospective well-controlled trials with mechanical or pharmacological therapy," said Dr Lichtenberg, adding that there are excellent venous thromboembolism (VTE) guidelines for anticoagulation therapy but no consensus guidelines for endovascular treatment of DVT.

He ended his presentation with a call to replace catheter directed thrombolysis (CDT) by PMT.

"Using purely mechanical debulking with Rotarex®S reduces a procedure to a single session treatment, without further need of local lysis, which is always associated with additional ICU stay and bleeding complications." ***Sven Bräunlich***

Percutaneous tumour ablation making inroads

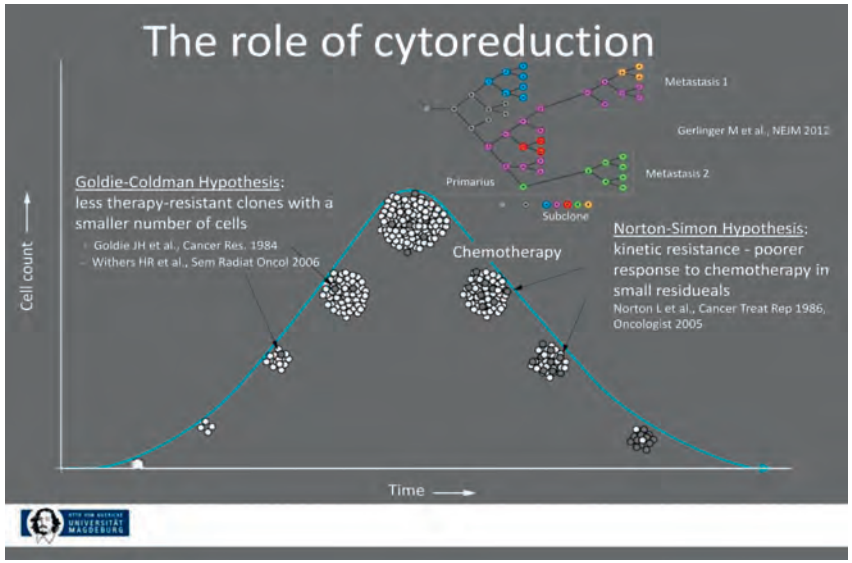


Figure 1. The role of cytoreduction: in the early stages (left) fewer therapy-resistant clones are present. Following chemotherapy (right), remaining cells are more resistant to therapy.

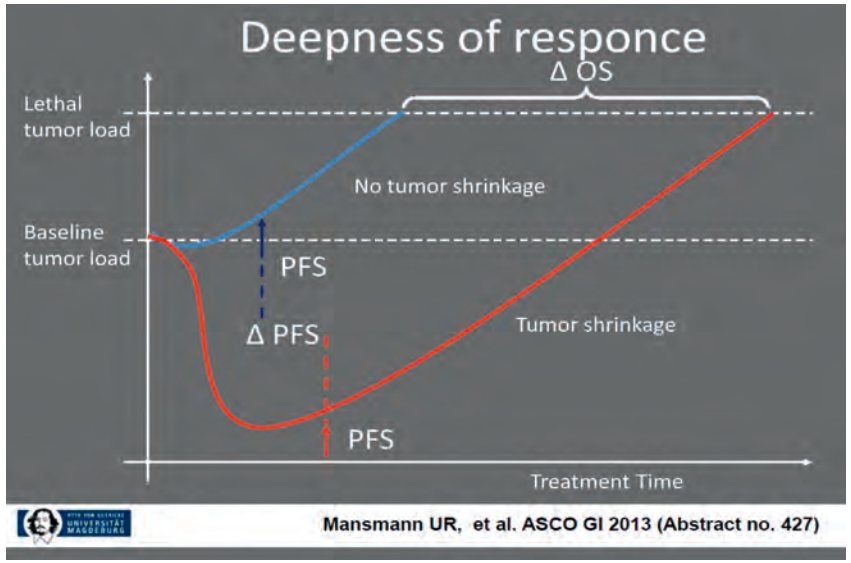


Figure 2. The concept of deepness of response indicates that change in progression-free survival (ΔPFS) remains constant; therefore, achieving a greater initial reduction in tumour cell number may improve overall survival.[7]

Source: www.leipzig-interventional-course.com

Maciej Pech (Clinic for Radiology and Nuclear Medicine, University Clinic Magdeburg, Germany) provided a brief overview of indications and technical innovations in percutaneous tumour ablation, during a session focused on embolisation therapies and interventional oncology.

Referring to Abraham Maslow's 'hierarchy of needs' – Maslow famously having said, "If your tool kit consists only of a hammer, you tend to see a nail in every problem" – Dr Pech began: "At the end, we need a whole toolkit of techniques to be successful in interventional oncology."

Microtherapy lies between surgery and systemic chemotherapies, he continued. It includes local cytoreduction, which includes thermal devices (radiofrequency ablation [RFA], microwave and cryoablation) and non-thermal devices (interstitial brachytherapy, IR-electroporation and high precision RT), and locoregional cytoreduction, which includes embolic devices (radioembolisation SIRT and chemoembolisation TACE/beads) and local chemotherapy.

"Whatever we do, it is energy input to the tumour," said Dr Pech. "The discussion about the best device in whichever patient is defined by anatomy, tumour diameter, maybe location, and maybe the biology of the tumour."

Turning to percutaneous tumour ablation, he noted that microwave and cryoablation can be guided by ultrasound and CT. MRI is an additional possibility for therapies such as RFA. Dr Pech noted particularly reports of higher local recurrence rates with various percutaneous techniques, which, he said, "may be a question of the biology of the tumour and not a question of the indication of energy input at all."

Dr Pech then referred to the European Association For The Study Of The Liver and the European Organisation For Research And Treatment Of Cancer (EASL-EORTC) guidelines of 2012, which recommend the use of RFA (alongside resection and liver transplantation) in very early stage (0) or early stage (A) hepatocellular carcinoma (HCC), depending on indication.[1] Furthermore, the 2012 European Society for Medical Oncology (ESMO) guidelines on HCC in cirrhosis recommend curative resection, RFA or transplantation for very early stage or early stage HCC.[2] "The local therapies are

"The best device in whichever patient is defined by anatomy, tumour diameter, maybe location, and maybe the biology." ***Maciej Pech***

Maciej Pech

well accepted in the treatment of HCC," summarised Dr Pech.

He then discussed data comparing percutaneous local ablative therapy against surgical resection, citing work by Chen *et al*. (2006), which found percutaneous therapy to be as effective as surgical resection in the treatment of solitary and small HCC in a prospective randomised trial of 180 patients.[3] Conversely, however, Huang *et al*. (2010) found that surgical resection may provide better survival and lower recurrence rates than RFA in a randomised trial of 230 patients with small HCC[4].

"The question is, where is the difference?" Queried Dr Pech.

"Maybe we have to differentiate what is the size and the indication for the patient." Indeed, a cost-effectiveness meta-analysis by Cucchetti *et al*. (2013) indicated that for very early HCC and in the presence of two or three nodules ≤3 cm, RFA is more cost-effective than resection. For single larger early stage HCCs, however, surgical resection was found to be the best strategy, with better survival rates at an acceptable increase in cost.[5]

There is the possibility, noted Dr Pech, that image guidance in RFA could influence ablation completeness. "It is difficult to see this with ultrasound," he said. "CT could be supported by contrast media. But MRI control is the best. You see better placement during fluoroscopy in MRI, and you have successful control directly after the treatment."

Referring to a Markov model analysis by Cho *et al*. (2010), he added: "From a statistical point of view, it is not possible to decide which is better. And with good image guidance, results from surgery and RFA could be the same."[6]

He continued: "It is completely different when we talk about metastasis. In metastasis, we are balancing cytoreduction and metabolic death. Metabolic death is if the body is overloaded with a four-inch tumour, and the end of this is the metabolic death of the immunologic system of the patient. On the other hand, we have the role of cytoreduction. The Goldie-Coldman hypothesis [dictates] less therapy-resistant clones with a smaller number of cells in the early stage. After chemotherapy, the kinetic resistance is higher in the residual tumours [the Norton-Simon hypothesis]." (Figure 1)

With this in mind, the aim of treatment in metastasis is the prolongation of overall survival. "The question is, how do we make overall survival longer?" Asked Dr Pech. "There is the theory of deepness of response[7] – the [greater] you can do the cytoreduction at the primary point, the development of resistant cells is the same but the overall survival can be longer if you reduce the tumour number first as low as possible." (Figure 2)

Only one randomised controlled trial presently exists investigating the possible benefits of RFA in addition to systemic treatment versus systemic treatment alone, noted Dr Pech. Herein, Ruers *et al*. demonstrated that RFA plus systemic treatment resulted in significant longer progression-free survival, although the authors stressed that the ultimate effect of RFA on overall survival remains uncertain.[8]

In his concluding remarks, Dr Pech noted that local and locoregional ablative treatments are now well accepted for oligometastatic patients, appearing in the most recent ESMO guidelines (2016) and combining not only thermal and non-thermal local treatments, but radio- and chemoembolisation as well.[9]

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"With good image guidance, results from surgery and RFA could be the same." ***Maciej Pech***

Venous stenting: Expert opinions on patient selection,

Venous stenting was placed under the spotlight during a symposium held in the Global Expert Exchange Forum, with invited experts sharing their personal experiences, data and tips and tricks for success.

Stepping up to the podium to begin the session was Michael Lichtenberg, who gave a brief overview of his venous stenting experience at the Klinikum Arnsberg, Germany. As he noted, when a patient presents with unilateral and/or bilateral swelling of a lower extremity, a step-by-step process can guide in the treatment decision. This begins with ultrasound analysis for reflux, deep vein thrombosis (DVT) or chronic outflow obstruction, followed by conservative treatment with a compression stocking. If pain and swelling persists, intravascular ultrasound plus venography is utilised before deciding how to treat the obstructive lesion.

Olivier Hartung

Stephen Black

Adding his opening thoughts on venous stenting, Dr Lichtenberg underlined that there is no such thing as a perfect venous stent. Rather, depending on lesion location, certain stent attributes such as high radial force, flexibility, kink resistance and low fracture rate all need to be balanced according to the requirements of the anatomy. "You should base your decision for a venous stent on the underlying pathology, and on the knowledge of how the stent will perform in this indication," he commented.

That being said, Dr Lichtenberg did dive deeper into the attributes of a hypothetical "ideal" venous stent, reasoning that it should be self-expandable, crush resistant across its length, and with sufficient chronic outward force. Furthermore, it should have a predictable, consistent deployment – with minimal foreshortening – along with sufficient wall coverage. Finally, the stent should be flexible enough to resist kinking, and have the necessary durability to allow repeated shortening, twisting and bending at the groin.

He also emphasised the importance of stent shape in maximising flow. A perfect circular shape after deployment will ensure better lumen quality and better clinical outcomes, he noted. This was proven in a study by Cho *et al.*[1], who showed that significant stent compression was inversely correlated with stent patency ($p<0.001$) in 20-month follow-up of 48 patients with iliac compression and acute DVT.

Dr Lichtenberg presented results

"Patients feel substantially better: 85% of the population showed symptomatic improvement after venous stenting at 12 months." ***Michael Lichtenberg***

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technique and outcomes

Michael Lichtenberg

from the Arnsberg Venous Registry, which has been assessing the safety and effectiveness of venous stenting in patients with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment. The ongoing, prospective, non-randomised, single arm and single centre registry has included over 300 patients since 2013, with follow-up out to 36 months. Primary effectiveness is defined as primary patency/clinical outcome at 12 months.

Specifically, he shared the subgroup analysis of 90 patients using the VICI VENOUS STENT™ System. The Vici Venous Stent is a self-expanding nitinol stent that has been specifically designed to meet the challenges of venous anatomy[2]. It has a unique closed-cell geometry and high redial strength, providing excellent lumen quality without compromising flexibility or deployment accuracy[2].

Of the 90 patients, 49 had post-thrombotic syndrome (PTS), while 41 had non-thrombotic iliac vein lesions. The majority of patients had a CEAP (Comprehensive Classification System for Chronic Venous Disorders) score prior to stenting of 3(62%) or 4(22%), and almost all patients had pain, varicose veins and oedema.

After 12 months, primary patency was 92% in the cohort. Further sub-division into post- or non-thrombotic patients revealed patencies of 85.7% and 100%, respectively. Furthermore, revised Venous Clinical Severity Score (VCSS) and CEAP improvements were seen in subsequent follow-up out to 12 months.

"This is absolutely in-line with the already published VIRTUS feasibility study," said Dr Lichtenberg. The VIRTUS feasibility study evaluated the Vici Venous Stent in patients with chronic iliofemoral outflow obstruction. One-year outcomes for 30 patients were published recently[3], which Dr Lichtenberg summarised: "Primary patency in this feasibility cohort was 93%, with secondary patency of 100%. This also led to a very good clinical outcome in patients: 63% of patients had at least a 50% VCSS score reduction; 81% of patients had pain reduction at 12 months; and 78% of patients considered quality of life as 'improved'."

Dr Lichtenberg offered his own personal conclusions: "Use dedicated venous stents! But choose wisely based on lesion morphology, and choose wisely based on stent technology. Our initial six- and 12-month data are absolutely in-line with the VIRTUS trial."

He added: "Patients feel substantially better: 85% of the population showed symptomatic improvement after venous stenting [VCSS ≥2] at 12 months, and safety data raise no concern."

Also speaking during the session was Olivier Hartung, from CHU Nord in Marseille, France, who began by contextualising the three types of obstructive venous lesions: acute thrombotic, non-thrombotic iliac vein lesions (NIVL) with a compressive cause (May Thurner) and chronic post-thrombotic. He emphasised that neither current medical nor surgical treatments options are optimal.

Dr Hartung's experience with venous stenting began in 1995, and to date his centre has treated more than 500 patients with stents for iliofemoral and/or inferior vena cava (IVC) lesions. Preoperative workup includes a Duplex scan: "It is a good way to explore the common femoral vein, and one of the ways to guide whether you perform a percutaneous or hybrid procedure," he said. Computed tomographic venography (CTV), magnetic resonance venography (MRV) and iliocavography can also be employed as needed, he noted.

Describing the typical treatment steps for a stent implantation in his centre, Dr Hartung explained that he would usually begin with a percutaneous echo-guided puncture, followed by iliocavography and intravascular ultrasound (IVUS) when available to determine the size of the lesion. Catheterisation is then performed, proceeding to dilation and stenting as necessary. "It is very important to predilate to the diameter of the stent that you are going to use, and you also need to post-dilate after stenting," he said.

Mirroring Dr Lichtenberg's recommendations for the ideal stent

Continued on page 70

"[Outcomes are] absolutely in-line with the already published VIRTUS feasibility study." ***Michael Lichtenberg***

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Venous stenting: Expert opinions…

Continued from page 69

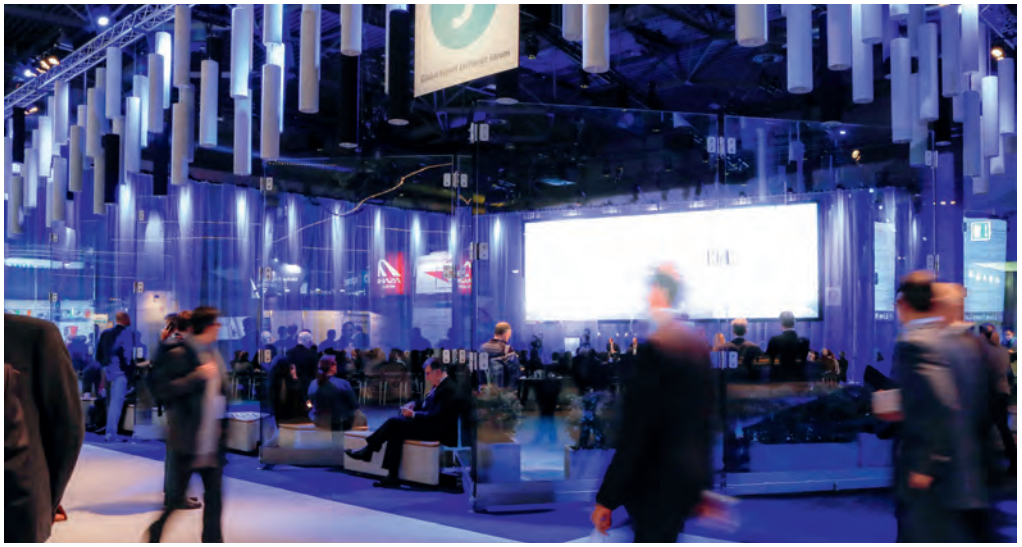
choice, Dr Hartung emphasised the importance of a self-expanding design, noting the importance for manufacturers to include a range of stent lengths and diameters, to achieve optimal lesion coverage and apposition. Dr Hartung emphasised the importance of stenting after balloon dilatation, explaining that the failure to stent leads to re-obstruction. He supported his views with recommendations from the Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS 2015[4]): "In our department we almost exclusively use the Wallstent (>97%)," he added.

Touching upon the Marseille experience in more detail, Dr Hartung introduced 10-year follow-up data from his May-Thurner Syndrome cohort, showing 88% primary patency, 98% primary assisted patency and 99% secondary patency rates in 184 patients. Recommendations for the postoperative course for May Thurner Syndrome patients included low molecular-weight heparin for three weeks, and clopidogrel for one year.

He went on to note that 162 attempts of recanalisation of chronic total occlusions in the iliac veins or IVC were performed. In terms of aetiology, 148 were chronic post-thrombotic. The common femoral vein was diseased in 119 cases (55 occlusions), and the IVC in 44 cases. "In this cohort, the primary, assisted primary and secondary patency rate were respectively 68%, 86% and 90% at 90 months," said Dr Hartung, showing patency rates comparable with previous research, but with a longer follow-up. Post-thrombotic or acute-thrombotic patients received a pneumatic compression device, and were given clopidogrel and oral anticoagulation for at least one year with a goal INR of 2.8-3.2.

Technical success was achieved in 85% of patients, and no patient's condition deteriorated as a result of intervention. "Failure to recanalise does not mean you cannot treat the patient," said Dr Hartung. "For example, in one patient we were unable to recanalise the common iliac vein and the IVC, but we stented the patient all the way along the left ascending lumbar vein up to the left renal vein."

Offering his conclusions, Dr Hartung stressed that "Current recommendations support stenting as the primary treatment option for patients presenting with symptomatic ilio-caval obstructive venous disease." He added that venous stenting is a highly effective and safe alternative to medical therapy supported with excellent long-term clinical and patency outcomes from centres like Marseille and Modena, Italy. Patient selection and surveillance are key factors to ensure continued success.



During a panel discussion at the end of the session, moderator Stephen Black (Guy's and St Thomas' NHS Foundation Trust, London, UK) asked what advice the experts would give to those embarking on venous stenting. "The learning curve for venous interventions is difficult," Dr Lichtenberg replied, adding: "I think the whole setup of a venous clinic for treating these patients needs to be defined before starting … you need to know which problems can occur, and you need to know about bailout options."

He continued: "I would say start with easy cases, start with compression syndromes, and then go step-by-step towards more complex patients. What I have personally learned is that it is very important to work closely with vascular surgeons … we are doing a lot of hybrid cases together."

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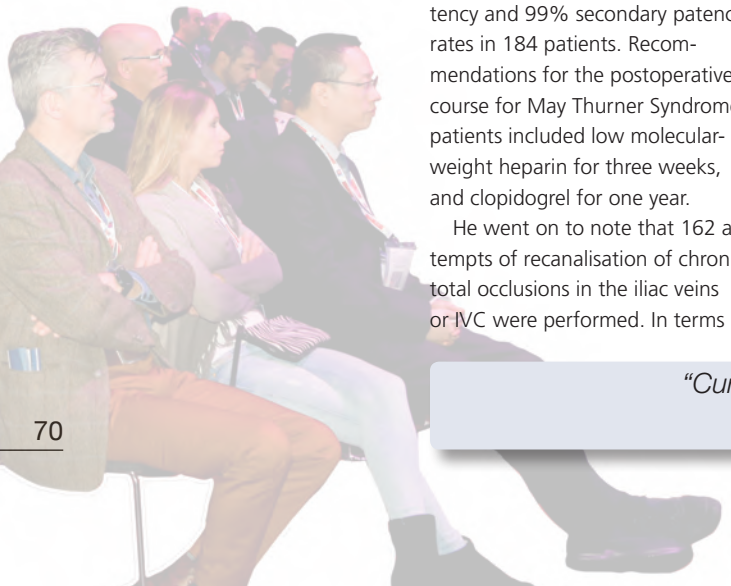
"Current recommendations support stenting as the primary treatment option for patients presenting with symptomatic ilio-caval obstructive venous disease." ***Olivier Hartung***



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EVAR: Closing the gender gap

The difference in outcomes between men and women following treatment of abdominal aortic aneurysms (AAAs) was laid bare by Erik Debing (University Hospital Brussels, Belgium), during the Critical issues and pioneering solutions in aortic endografting session, held on the final morning of LINC 2018.

As he explained, it was previously thought that the impact of AAAs was worse for males, owing to a 4:1 male to female predominance. It's now clear that women fair worse, however. "[Women] have a faster rate of aneurysm growth, a four-fold higher risk of rupture, a tendency to rupture at smaller diameter and most worryingly, experience a three-fold higher mortality following rupture compared with men," he said.

Such startling figures may suggest that women should have a lower size threshold for repair. Indeed, many studies have shown that women have worse outcomes following endovascular repair for intact AAAs, he explained.

Professor Debing presented an EVAR study using first-generation stent grafts between 1995 and 2009, which showed a significant difference in outcomes. Specifically, 30-day mortality was higher in the female group compared with the male group[1]. "The same study shows a higher incidence of conversions and aborted interventions – and a higher incidence of endoleaks – in women compared to men," he said.

With second-generation stent grafts, the picture is no better. A study of EVAR with second-generation stent grafts between 2011 and 2014 again showed a significantly higher mortality in the female group compared with the male group.[2] "And even TEVARs for intact thoracic aneurysms show higher rates of 30-day mortality and one-year mortality in women compared with men," he added.

There are several hypotheses for this gender disparity, explained Professor Debing. "One is that up to menopause, women are protected by hormones leading to a slower progression of atherosclerosis. However, from menopause, they catch up and finally have higher incidence of endovascular therapy," he said. Another hypothesis is the time of presentation. "Women are older and have more underdiagnosed and undertreated comorbidities," he said. "But the most important reason for the gender disparity is that women have more challenging anatomy."

He added: "Women have smaller and more tortuous vessels, leading to less suitable AAAs for EVAR, and leading to more complications and more additional procedures."

The question arises, therefore, as to whether introduction of third-generation, low-profile stent-graft devices can improve EVAR outcomes in female patients. "Lower-profile devices increase the number of patients that are suitable for EVAR and TEVAR," said Professor Debing. Remarkably, he added, many studies of EVAR with low-profile devices – including female patients with very small access vessels or tortuous access vessels – show no higher incidence of limb occlusions, endoleaks, conversions to open repair or higher incidence of mortality.

He presented results from the Belgian National Registry, including more than 6,000 EVAR, TEVAR and FEVAR procedures utilising second- and third-generation stent grafts with low profiles. "Most of the patients were men, and there were no significant differences in ages between women and men," he said. "The size of the aneurysms were smaller in the female group compared with the male group."

Here, 30-day mortality figures were more equal, noted Professor Debing. "There is no longer a significant difference in 30-day mortality between and men and women; that's in [all groups]," he said. Importantly, the TEVAR group also showed no significant difference in mortality.

Looking at the survival rates and the incidence of endoleaks, there were also no significant differences between men and women. The same was true of the TEVAR group. "So low-profile devices have the potential to change the way we plan EVAR and TEVAR," said Professor Debing. "The early results of the low-profile devices are encouraging, and demonstrate that favourable mid-term outcomes can be achieved using low-profile technology in female patients with unfavourable iliac anatomy."

Further studies are required to substantiate these early results and to assess long-term outcomes, Professor Debing concluded.

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"Women have smaller and more tortuous vessels, leading to less suitable AAAs for EVAR, and leading to more complications and more additional procedures." ***Erik Debing***

Finding a good APPROACH to complex endografting

The tricky decision-making process when treating complex aortic pathologies was the focus of a presentation by Konstantinos Donas (St. Franziskus Hospital, University of Münster, Germany).

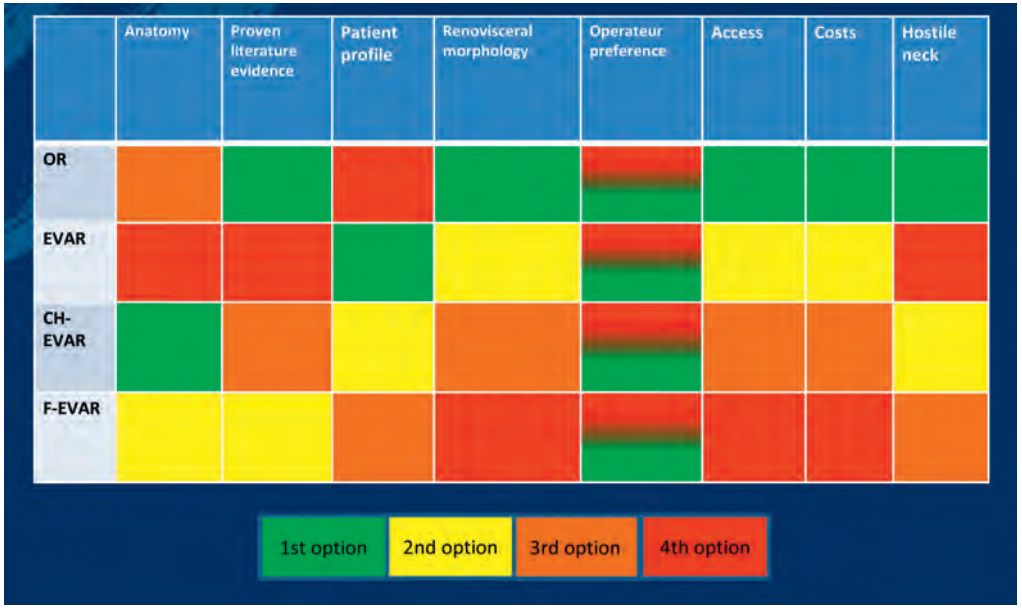
Dr Donas raised a situation familiar with many delegates – the ongoing debate about the best solution for complex aortic pathologies. "We have had this debate at several meetings," he said. The problem is what to do in real-life situations, he added, which can be very different to that which is presented at meetings such as LINC: "If the next day you go to the hospital and see a patient in the clinic, there is a different clinical reality," he explained. "In trying to evaluate and treat the patients based on the recommendations from the meetings, in the majority of cases, you are probably going to have big issues. [As such] is it possible to perform the techniques suggested at meetings?"

Bearing this in mind, Dr Donas presented a new concept to evaluate decision-making factors for complex aortic pathologies: APPROACH.[1] This is designed to help surgeons decide the appropriate course of action, depending on different complex pararenal aortic pathologies; those with a short or no neck, or with the involvement of more than one target vessel, for example. Dr Donas focused specifically on aneurysms, penetrating atherosclerotic ulcers (PAU), para-anastomotic aneurysms (PAAs) and type IA endoleaks.

Konstantinos Donas

The goal of this APPROACH concept is to identify the reasons influencing the selection of treatment options. "It gives the opportunity to design studies that incorporate factors reflecting final clinical reality, not the theoretical explanation," said Dr Donas.

The APPROACH technique was developed following an evaluation of a number of different factors by Dr Donas and his colleagues Giovanni F Torsello and Giovanni B Torsello. "Indeed, there are eight different factors, encompassed by the acronym," he explained. These are: Aortic pathology, Patient's clinical profile, Proven literature evidence, Renovisceral morphology, Operator's preference and skills, Access issues, Costs, and Hostile neck features.



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Creation of the Approach Concept Score System (ACSS)

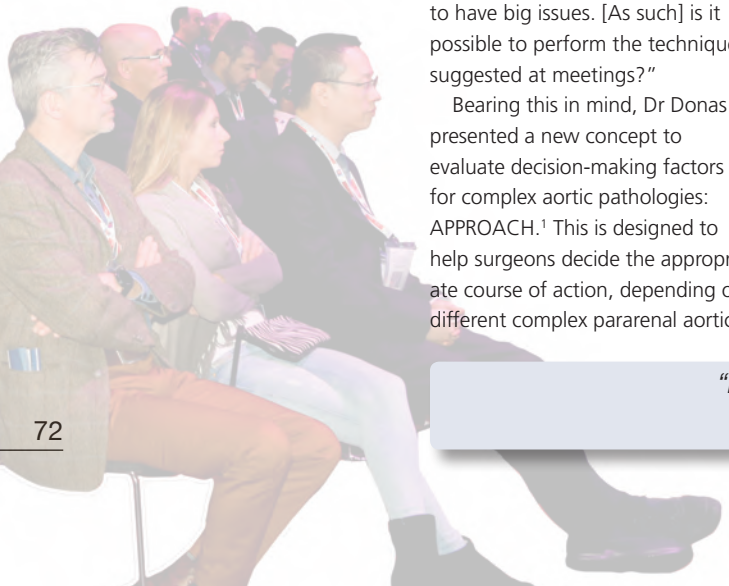
Looking at each factor in turn, Dr Donas first focussed on pathology. If, for example, a case has a degenerative aneurysm with a short neck, it may be possible to treat that anatomy with several different options as there may be good access from the iliac arteries.

Conversely, a completely different approach may be required in other cases, according to Dr Donas, for example saccular aneurysms. These, along with PAUs of the aorta have a higher risk for rupture compared with fusiform aneurysms of comparable size, he explained. "So probably we need options that could treat the pathology in the immediate setting," he said. "This highlights how important the anatomy of the pathology is in decision making."

Regarding the second factor, the patient's clinical profile, Dr Donas continued: "We are well aware that demographics, comorbidities, age and also life expectancy significantly influence decision making." He added that in terms of proven literature, one could ask what kind of evidence really exists for therapeutic options, e.g. case series or randomised controlled trials?

Turning to renovisceral morphology, he said the orientation of the renal arteries can be a key

"It is very important to create a score system which will be an important tool for the physician, [guiding] the decision-making in cases of complex aortic pathologies." ***Konstantinos Donas***



decision-making factor when considering fenestrated stent-grafts or chimney EVAR. Downward-oriented vessels simplify cannulation from the upper extremity, while an upward-going renal artery is better approached by transfemoral access, he explained.

Operator preference and skill are also key for decision-making. Dr Donas referred to the chimney technique and looked at the performance of two different abdominal devices that may be chosen. "For example, a nitinol endoskeleton can be nicely wrapped up around the chimney graft," he explained, "and a stainless-steel endoskeleton is more rigid."

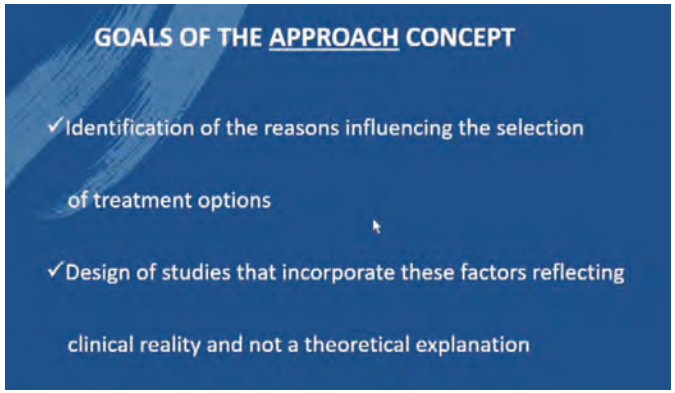
Access is key, he added. This criterion includes the morphology of the iliac vessels as well as the supra-aortic arteries, he explained. Where there is kinking or elongation, the presence of occlusion or high-grade stenosis, thrombotic material, or excessive calcification, the use of devices with different crossing profiles and trackability could be warranted.

Costs are also important, he added: "Not only [absolute] cost, but cost effectiveness. A re-intervention can also influence the decision."

Last but not least is the shape of the neck. Presenting a case with a very short neck and a very straight anatomy, Dr Donas relayed that the patient was treated with a triple fenestration. However, in another case, this time where there was severe angulation of the short neck, the patient was successfully treated with a flexible abdominal device with a single chimney instead. "You see how important the shape of the neck is in the decision-making," he explained.

Interestingly, said Dr Donas, at an endovascular masterclass last year, a number of experienced physicians were asked to vote on which of the APPROACH factors were most important. "The anatomy of the pathology, patient profile and the shape of the neck seem to be the most crucial factors which influence the decision in cases of short neck," he said. "The least important factors seemed to be cost, and also the literature. We don't have enough literature to influence decision-making."

But the APPROACH system is merely a springboard, said Dr Donas. If it's obvious that anatomy plays a crucial role in endovascular options, then it's important to rate that accordingly. "It is very important to create a score system which will be an important tool for the physician, [guiding] the decision-making in cases of complex aortic pathologies," he concluded.



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"[APPROACH] gives the opportunity to design studies that incorporate factors reflecting final clinical reality, not the theoretical explanation." **Konstantinos Donas**

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Optimal medical treatment for patients with TBADs

Medical management in patients with type B aortic dissection was discussed by Christoph Nienaber (Royal Brompton and Harefield NHS Foundation Trust, UK) during a session on a range of acute aortic syndromes. Professor Nienaber offered a summary of past and recent data on pharmacological therapies to reduce blood pressure, as well as addressing the importance of lifestyle modification in this patient group.

He was involved in discussion published in 2014 on the feasibility of setting up a trial investigating intensive medical management of aortic dissection[1], although this did not come to fruition. Alternative strategies to lower blood pressure, such as renal denervation, did not prove significant in patients with dissection[2].

Therefore, he explained, only pharmacological therapy persists as a course of medical management. He said: "The aim of medical management in the setting of dissection is of course to reduce the shear stress to the aortic wall."

This, however, does not always translate into long-term benefits, he said, with patients being susceptible to late aortic events such as false lumen aneurysm. Nevertheless, the recommendation of current guidelines centres overall on the idea of medical therapy – a Class 1 recommendation, but with a level of evidence of C[3].

Collating multiple guidelines, Professor Nienaber noted recommendations for medical therapies including maintenance of heart rate <60 bpm, systolic blood pressure <120 mmHg, with the use of beta blockers, calcium antagonists, and combinations with other drugs. "There is no specific recommendation, because there are no data," he said. "We do not have a single randomised trial to show us the effect of any kind of medication or cocktail to lower blood pressure, reduce shear stress, and reduce the burden to the dissected aortic wall."

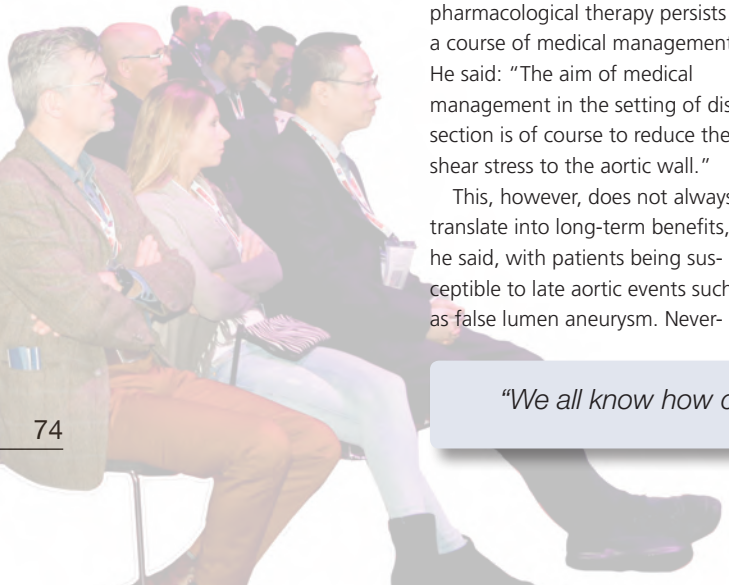
He then cited five major non-randomised studies on the effect of antihypertensive medications in aortic dissection[4-8]. Genoni *et al*.[4] evidenced chronic beta blocker therapy as improving outcome and reducing treatment costs in chronic type B dissection, helping to reduce the speed of aortic diameter dilation. Takeshita *et al*.[5] showed the effect of angiotensin-converting enzyme (ACE) inhibitors to reduce long-term aortic events in patients with acute type B aortic dissection. Then, Sakakura *et al*.[6] demonstrated that all-cause mortality was less frequent with the use of calcium channel blocker.

Christoph Nienaber

The largest study comes from the International Registry of Acute Aortic Dissections (IRAD), where Suzuki *et al*. found beta blockers to improve survival among surgically-treated type A aortic dissection patients. In the same study, in medically-managed type B dissection, calcium channel blockers influenced mortality favourably.[7] "This is hard to believe and to understand," commented Professor Nienaber.

The most recent study by Melby *et al*. of patients after repair of type A aortic dissection showed that systolic blood pressure >120 mmHg and absence of beta blocker therapy were each risk factors for late reoperation[8]. Professor Nienaber added: "If you look a bit more granular to this data you can see – and this is a reality in our clinical scenario – that only those patients that had a systolic blood pressure over the next 10 years of <120 mmHg benefited, with a relatively plateauing outcome curve. The others, between 120-140 mmHg

"We all know how difficult it is to keep patients under 120 mmHg systolic with any kind of combination therapy." ***Christoph Nienaber***



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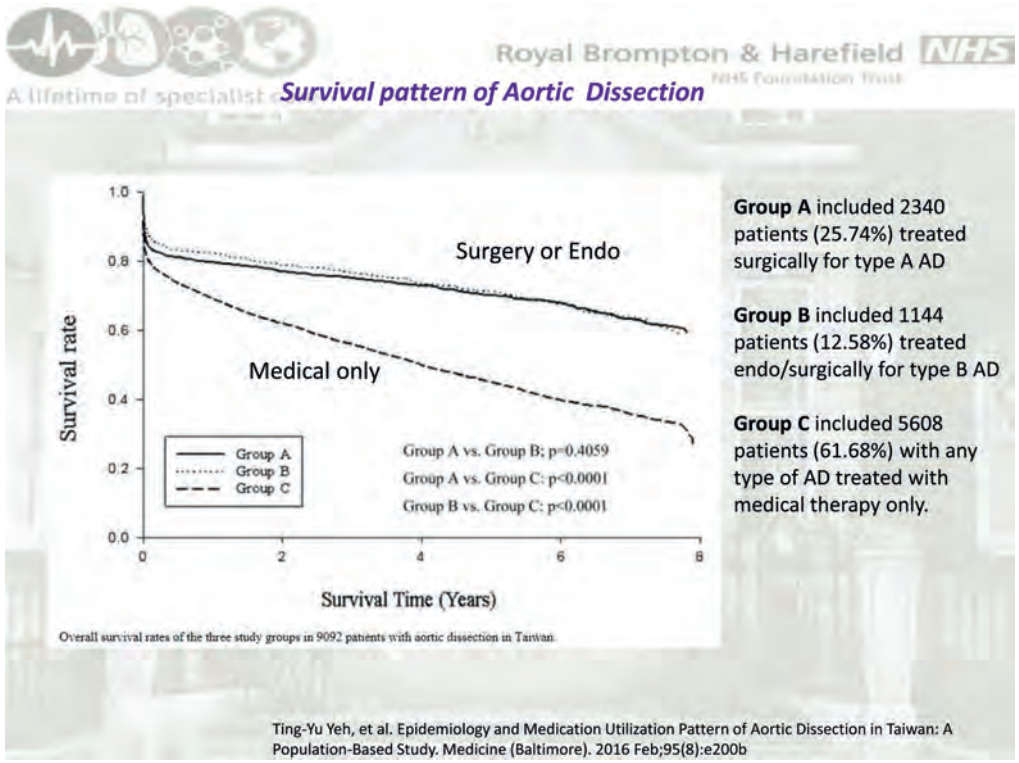

Figure 1. Recent work by Ting-Yu Yeh et al.[9] on the epidemiology and medication utilisation pattern of aortic dissection in Taiwan found significantly reduced overall long-term survival in patients only medically-treated compared to those treated by either surgical or endovascular repair, suggesting that medical therapy is effective only in an additive fashion.

and even above 140 mmHg, had a steep decline in survival rate."

Commenting on the experienced shared by many clinicians, he added: "We all know, dealing with patients, how difficult it is to keep patients under 120 mmHg systolic with any kind of combination therapy."

The most convincing data of the past two years, said Professor Nienaber, comes from recent work by Yeh *et al*. (2016)[9]. "This shows that medical management alone can only be an additive component to a patient either surgically or endovascularly treated. Patients without either surgery or endo did clearly worse than patients under medication only." (Figure 1)

Turning to other modifiable factors, such as lifestyle, he said: "After a dissection, which patients usually consider a very difficult moment in life, they have a difficult life even if they survive it."

Indeed, in a 2015 survey by Chaddha *et al*. on the themes of lifestyle modification, exercise practice and emotional state, a third of patients had new-onset depression, a third had new-onset anxiety, and a quarter no longer engaged in exercise. The majority of patients were no longer sexually active.[10].

"Those who exercised on a routine basis, surprisingly, eventually ended up with less markers of depression and lower blood pressure," noted Professor Nienaber in reference to the study. "So why prevent them from a normal life?"

Professor Nienaber summarised his advice given this lack of evidence supporting particular medical therapy choices, adopting the mnemonic 'EASY TIP': "Establish the underlying diagnosis; Achieve normal blood pressure by whatever means; Stop the patient from continuing smoking; Yearn to exercise moderately; Test first-degree relatives for thoracic aortic disease; Image the aorta over time; and Perform repair whenever appropriate."

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"Those who exercised on a routine basis, surprisingly, eventually ended up with less markers of depression and lower blood pressure." ***Christoph Nienaber***

Faculty @ LINC 2018

We would like to thank sincerely the outstanding faculty for their collaboration and commitment.

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