Acute deep vein thrombosis
A pressing live case

Steven Black and Michael Lichtenberg headed a panel of discussion on the topic of acute deep vein thrombosis during yesterday's early morning session, which included two live cases and a selection of presentations on the topic.

The first live case came from the Berne University Hospital Heart and Vascular centre, with the team headed by Nils Kucher and Torsten Fuss, who tackled an iliofemoral venous intervention in a patient with mechanical compression of the left iliac vein resulting in its total occlusion.

The patient was a 52-year-old male who previously received conservative treatment (anticoagulation) for iliac vein thrombosis on the left side in 2013. The patient then suffered left iliac vein thrombosis again in 2015, and, as a result of osteosynthesis of the L4/5 vertebrae, developed significant manual compression of the left iliac vein.

Presently, venous claudication was evident along with swelling of at least 2cm in thigh circumference, despite compression therapy. The patient was able to walk 500 m without pain. No skin changes or varicose veins were evident.

Duplex ultrasound evidenced moderate post-thrombotic changes in the iliac vein with total occlusion of the external iliac. The common femoral vein also displays post-thrombotic changes, although it remained patent along with the superficial femoral vein. The deep femoral and popliteal veins were also patent.

“I think we have a very interesting patient here,” began Professor Kucher. “The patient is in full anaesthesia, as we do most venous interventions in the prone position.”

The procedure began via venous access with ultrasound guidance in the left popliteal vein (using a 10 French standard sheath), and wire crossing

Continued on page 2
Acute deep vein thrombosis  Main Arena 2  Tuesday  8:00–9:20

Continued from page 1

using the Terumo 0.035” stiff angled wire.

“The [patient’s] metal plate has really displaced the common iliac vein. It was not easy to wire this lesion. We managed to get the wire up for a selective venogram. I would like to mention that selective venography is very important; it is something that you wouldn’t do for arterial occlusions.”

Once the lesion was crossed (with notable difficulty) into the iliac vein, the team used a NaviCross catheter (Terumo Interventional Systems), which Professor Kucher described: “This is hydrophilic and easily navigated up to the iliac vein even inside occlusions. We managed to wire the external iliac vein. But we got stuck right where the osteosynthetic material is. This will not be an easy case.”

In another selective venogram taken inside the occlusion, the team used prolonged imaging to show flow within the inferior vena cava (IVC) and contralateral iliac vein.

Finally managing to cross the occlusion into the IVC, an attempt was made using a 12mm Atlas balloon (Bard Peripheral Vascular) to pre-dilate. “We cracked these lesions open with what is really a big balloon inside the common femoral vein,” commented Professor Kucher.

“But it was not possible to use the Atlas balloon to cross the total occlusion at the site where the osteosynthetic material is. It just would not follow the wire. Now we have used a 6mm balloon and are barely able to get this balloon through the occlusion. We also used a long destination sheath, because we needed a telescoping technique to get more support and advance the balloon through the occlusion. Then, we dilated the occlusion with the 6mm balloon.”

Professor Kucher commented that, due to the metal plate distorting the common iliac vein, it would be difficult to advance large balloons, and finally the stent, past it. In a change of tack, the team reintroduced the destination sheath in an attempt to advance a larger 10mm Atlas balloon into the occlusion.

Asked what he made of this special scenario, moderator Dr Black commented: “I don’t think that many of us have seen a big metal plate like that displacing a vein in the cases we have done. I am not sure how that is going to impact on your ballooning and stenting. But without good predilation, and the forces you have got there, I don’t think you will get anywhere. So you have to keep going.”

Continued on page 3
Acute deep vein thrombosis  Main Arena 2  Tuesday  8:00–9:20

Continued from page 2

With the balloon safely through the occlusion, the team surmised that stent advancement would demand a long, 10-12mm sheath. Amid a brief interlude for panel discussion, a 12mm Atlas balloon was advanced.

“The question is now,” asked Professor Kucher, “What kind of stent would you use in this scenario?”

Moderator Dr Lichtenberg responded: “This is really a tough case, definitely. I would be in fear that even a high radial force stent would have a problem with that osteosynthesis material. Of course, you should go for a high radial force stent.”

Summarising what he saw as the possibilities in the presence of such significant vessel compression, Professor Kucher said: “The first option is the Vici stent (Veniti), which is a closed-cell design stent with flexible interconnections – self-expanding of course. That could be used in this scenario.

“Another stent could be the Sinus Obliquus stent (OptiMed), because especially in the proximal part we have a closed-cell design. The only problem with the Sinus Obliquus is that the closed-cell part is quite short – approximately 3cm – and here we probably would need a longer part with a lot of support and radial force. This would be the case for the Vici. I would definitely not use the Wallstent (Boston Scientific) in this situation because you have seen the curve that our stent has to make [around the obstruction] and the Wallstent is definitely too stiff for this situation.”

Panel member Raghu Kolluri then asked: “Are you concerned about any erosion of the stent with this metal plate? This was clearly an anterior approach for that, but we had one episode of very large osteophyte and the concern for us at that time was erosion of the stent. Would it be displaced anteriorly, ventrally?”

To which Professor Kucher responded: “I have done five similar cases in my career so far. They are all doing fine with high radial force stents that we now have available. You can see how the 12mm Atlas balloon now displaces anteriorly. I think the displacement will be just enough, and there should be no disruption or compression of the stent. But I am not sure, because this is really a big plate. We will see.”

Opting for the Vici stent, the Atlas balloon was removed, and a further IVUS was taken to gain further insight into the venous anatomy around the IVC and its relation to the compression present around the osteosynthetic material. In this way, the team were also able to set a marker at the exact point at which the proximal part of the stent was destined.

“The IVUS is also important to define the distal landing zone,” noted Professor Kucher. “This is because the venography is not really telling us where to land the stent. Here, this could be just below the inguinal ligament.”

On the question of whether to use a shorter or longer stent, Professor Kucher said: “We know we have to stent up to the common femoral vein because the external iliac was also bad. I suggest using a Vici stent – the longest available stent of which is 120mm.

“Then we will probably need another stent [lower down]. I do not use the Vici stent in the common femoral vein because it is too stiff. I would probably use a more flexible stent in external iliac and common femoral to treat the post-thrombotic changes that we have seen, even after predilation, are severe.”

An additional venogram was performed in order to define the contralateral inflow. “For May-Thurner stenting in our hospital we have defined standard operating procedures – one being a bilateral venogram prior to stent placement. This is because if you just do a unilateral venogram,
Continued from page 3

you will never see the contralateral IVC wall and also you will never see the carina. These are very helpful in defining the proximal landing zone of the stent.”

After an interlude for flash presentations, the team returned to show the results of Vici stent placement. IVUS indicated that the stent was slightly compressed, while the XL Flex stent that was placed further down to the common femoral vein had opened adequately.

“The flow is not perfect yet; it is quite slow,” commented Professor Kucher. “We have identified the problem; it is not a big problem, but we need to do something about that heavy compression around that osteosynthetic material.”

The team concluded the procedure with the in-stent placement of another Vici stent of the same diameter (14mm) and slightly shorter length (90mm). This was followed by large balloon post-dilation to open up the stent.

For more exciting venous cases and presentations, head to the session ‘Venous interventions: Current status and open questions’ in Main Arena 1 at 09:30–11:00 this morning.
The International Symposium on Endovascular Therapeutics (SITE) will be holding a collaborative session at LINC this afternoon. The SITE@LINC session takes the format of a discussion centred around problematic and perhaps neglected areas within EVAR and TEVAR. Session moderator and SITE chairman Vicente Riambau (University of Barcelona, Spain) spoke to LINC Today ahead of the session to explain the importance of such open debate in articulating the questions of future clinical study.

The SITE meeting is a biennial international event that has been held in Barcelona since its beginnings in 2000.1 Identifying the complementary features of LINC and SITE, Dr Riambau noted that their differences go beyond their delegation – SITE being attended by no more than 700 people, while LINC draws around 4,000: “The LINC meeting is huge in terms of number of attendees,” he said, “But the format of SITE is much more local, thinking more about Spanish-speaking people.

“At SITE, we try to bring in the most relevant speakers in the different subsets of each topic. We put this together in two and a half days – but without live cases at this moment. We did have live cases at the beginning, but we decided that there are kinds of ethical issues surrounding the live cases. So we, along with the board of directors, decided to replace within our structure live cases with pre-recorded live cases.

“The most attractive part of LINC is probably the live cases,” he continued. “Live cases require a very organised schedule and lots of effort in order to combine them with the main programme. This is something exceptional. Probably there are some other meetings in the world similar to it, but I think LINC is probably the best or one of the best in this particular format.”

Originally a meeting of Spanish-speaking endovascular professionals with an international faculty, SITE has evolved to become an international discussion of current technologies and future directions in vascular diagnosis and advanced endovascular therapies. Language and inclusiveness have remained a prominent thread in its development.

“SITE is offering – to the Spanish-speaking and Spanish-understanding people particularly – a simultaneous translation from Spanish to English and English to Spanish. This allows them to have contact with our outstanding faculty in their own language. We are giving this kind of opportunity to people who have difficulty speaking or understanding.”

“I will be the moderator, and I will try to direct some questions to the audience in order to get the best thoughts in those particular subjects that are still very hot or unmet for us.”

Vicente Riambau
SITE@LINC: Unmet needs on EVAR/TEVAR and beyond
Discussion Forum Wednesday 15:00–16:00

Continued from page 5

English. That is our focus – Spain and Latin America mostly, although it is in fact an international meeting. There is a lot of space for discussion.”

In addition to SITE’s main symposium, the SITE Update is held every other year and has a smaller, single day format, providing status updates on two central endovascular themes. Drawing together advanced endovascular practitioners, experts from the field of bioengineering, health managers and industry managers, the meeting effects open discussion of the unmet needs and future of endovascular procedures, unsolved clinical cases and clinical limitations – all of which are then uploaded online (www.endovascular.tv). “This is like a multilateral brainstorming day,” noted Dr Riambau. “There are also some industry present, talking about their pipelines, and this is much more technical.”

The SITE@LINC session follows the format of the SITE Update. No presentations will be given; rather, a discussion will be led and directed by Dr Riambau and the panel via a series of scripted questions.

Coming to a better understanding of how exactly to address unmet needs will, it is hoped, be the outcome of the session. “We are discussing all this not to get the solution, but probably to orientate the solution by collaborating with industry and our colleagues from the medical side – to solve these problems. We also try to involve the audience – it is not possible to have just one perspective, so we try to involve the audience. I will be the moderator, and I will try to direct some questions to the audience, in order to get the best thoughts in those particular subjects that are still very ‘hot’ or unmet for us.”

Explaining some of its key issues, Dr Riambau stressed the prematurity of endovascular approaches for aortic pathologies, highlighting that data is not convincing enough for it to consistently be the first choice. “It is still is too early to decide,” he said. “We probably need more evidence for one side. We need more improvements in technology in order to reach this particular position for the first option of aortic pathology.

“Up to now, we are witnessing some kind of explosion in endovascular procedures for the aorta and thoracic procedures. But there are still many complications and probably unreported difficulties and problems. We need to fix this, in order to convince the unbelievers as well as convincing ourselves about the durability of those procedures.

“That is part of the reason of this particular session, talking about paraplegia and stroke prevention, about the first choice of TEVAR for thoraco-abdominal aneurysms, about what is happening with type B dissections, and also about the arch and ascending aorta. Type II endoleaks are also a nightmare! These are probably some of the most relevant hot topics – the more important critical issues facing EVAR and TEVAR right now.”

The SITE@LINC session ‘Unmet needs on EVAR/TEVAR and beyond,’ takes place in the Discussion Forum this afternoon between 15:00 and 16:00.

References


Continued on page 6
The great debate on in-stent restenosis

A debate that poses the question of whether ‘drug-elution’ or a ‘mechanical barrier’ is superior for the treatment of in-stent restenosis (ISR) will take place this afternoon, with two esteemed speakers stepping up to share their perspectives in what is sure to be a lively to-and-fro.

The speakers will be Peter Soukas (The Miriam Hospital, Providence, Rhode Island, USA) – who will largely fall down on the side of stenting – and Hans Krankenberg (Cardiovascular Center Bad Bevensen, Germany), who will offer up some talking points for drug-eluting balloons.

Mechanical barrier

Peter Soukas

Explaining the background to his ‘Pro mechanical barrier’ position, Dr Soukas told LINC Today: “Dr Krankenberg is going to be taking the position that drug-eluting balloons are the best treatment for ISR, and while we certainly love DEB for how they have dramatically altered the way that we practice medicine, I think that this boundless enthusiasm for DEB should perhaps be tempered a bit.”

Dr Soukas then commented on the FAIR trial, “This was a randomised trial of angioplasty versus DEB for ISR, which unequivocally showed that there was a statistically significant

Continued on page 8
benefit in terms of primary patency associated with the DEB arm.¹

“However, there are a couple of important caveats to that study. Namely, the suitability of DEB for very short lesions (on average they are only about 8cm), that’s not really what we see in the real world in terms of ISR, where they can be any-

“A clear treatment recommendation can be already made for drug-eluting balloon angioplasty in superficial femoral artery in-stent restenosis up to 15cm in length.”

Hans Krankenberg

where between 15-30cm. So we really don’t have very much data in the way of randomised control trials in terms of long lesions.”

One study that did address ISR in long SFA lesions is the RELINE trial, a prospective, randomised, multi-centre study investigating the safety and efficacy of a covered stent graft (VIABAHN Endoprosthesis, W.L. Gore & Associates, USA), with plain old balloon angioplasty (POBA)².

Describing the study, Dr Soukas said, “The RELINE study was in European RCT of stent grafts versus PTA, specifically for patients with ISR, and the two year results were presented last year at LINC. This trial looked at much longer lesion lengths, in fact 19cm, and showed a very dramatic difference in favour of the stent graft group. Furthermore, for lesion lengths of more than 20cm the primary patency with plain old balloon angioplasty was pretty dismal – only about 23%. One thing that we can say for certain is that plain old balloon angioplasty for ISR just doesn’t work except for very short lesion lengths.

“So I’ll be making that argument that until we have that ‘head to head’ data in a randomised fashion between stent graft and DEB for long lesions, and while the stent graft may not be the ‘new kid on the block’, it is still a very effective and durable treatment.

“Another issue with studies presented in favour of DEB is the very short follow-up period

Continued on page 9
whereby primary patency tends to drop between 12-24 months. So the other point that I’ll be making is that we have to take a longer view. While DEB initially really works quite well for the patients there is a significant attrition between 12-24 months and so we really need to have 24-month data before we can make any meaningful conclusions. The gist of the argument is that we have got very good prospective level one data in favour of stent grafting, particularly for long lesions.”

Dr Soukas then pointed out that with longer and more proliferative lesions where the vessel is completely occluded, if using DEB there may be problems with neointimal hyperplasia and recoil: “The enduring benefit of the stent graft is improved acute luminal gain; stent grafts provide a suitable barrier to prevent migration and proliferation of smooth muscle that ultimately re-narrow the artery, as often happens with DEB.”

He added: “For many DEB studies, patients who had significant stent fractures were often excluded, and this is another area where the stent graft is superior.”

Commenting on whether different types of stent may be more suitable for ISR in very long lesions, Dr Soukas concluded: “In my mind the woven stents like the Supera [Abbott Vascular, USA], and helical stents, still will suffer from the same mode of failure, namely neointimal hyperplasia, so again, there doesn’t seem to be any superiority of one stent over the other in terms of the likelihood of developing ISR.

“The enduring benefit of the stent-graft is improved acute luminal gain.”

Peter Soukas

“And when it does happen you still have the same issues. The stent literature has a lot of single centre studies with pretty modest short lesions lengths. What we are really lacking in the field is real world studies looking at very long lesions and we do have that data for stent grafting.”

Concluding, Dr Soukas was keen to emphasise: “Here there won’t be any ‘DEB bashing’, because they are wonderful, and do work really well for short and medium length ISR. But for the long lesions – particularly if there are in-stent fractures – I think that the stent is probably a better a scenario.”

Drug-eluting balloons
Hans Krankenberg

Dr Krankenberg’s standpoint about DEB angioplasty for the treatment of superficial femoral artery in-stent restenosis is of keen interest because stenting of femoropopliteal lesions has become so mainstream in recent years. However, despite its popularity as a technique, the five-year primary patency after stenting is reported to be between 34% and 50%.

Speaking to LINC Today, he first described some small comparative studies: “A small registry was the first to show results on DEB for in-stent restenosis. This registry showed a recurrent re-stenosis rate of 7.9% at 12 months and of 29.7% at 24 months.

“A second small pilot study – the DEBATE-ISR – was carried out in diabetic patients, and this showed a recurrent restenosis rate of 19.5% (8 of 41 patients) after DEB, which was significantly lower than historical diabetic controls (71.8% [28 of 39 patients]), treated with plain old balloon angioplasty.

As did Dr Soukas, Dr Krakenberg also touched upon the FAIR trial, this time summing it up in a few short positive words: “For the first time, efficacy was proven,” he said. “Additionally, clinical improvement without the need for revascularisation was more frequent after DEB. No difference in safety was apparent.”

Dr Krankenberg bolstered his ‘Pro-DEB’ evidence with the preliminary results from the COPA CABANA trial, which was presented at LINC 2015: “They reported that the DEB was associated with significantly lower late lumen loss and a higher freedom

Continued on page 10
Continued from page 9

from TLR rate than the standard balloon at six months. In summary, at this stage, a clear treatment recommendation can be already made for drug-eluting balloon angioplasty in superficial femoral artery in-stent restenosis up to 15cm in length.”

Regarding the performance of the DEB versus DES, Dr Krankenberg explained that although they are both superior to POBA, this has not been directly studied. “Both DES and DEB proved to be superior to POBA for de novo superficial femoral artery disease. Thus, the randomised, controlled ZILVER PTX trial showed a higher two-year primary patency than POBA (75% versus 27%, p<0.01).

In addition, provisional drug-eluting stenting was superior to provisional bare-metal stenting (two-year primary patency 83% versus 64%, p<0.01). Even over a five-year period, the THUNDER trial demonstrated that the reduced TLR rate was maintained with DEB (21% versus 56% after POBA, p=0.0005).

“Because prospective, direct comparisons comparing DEB and DES, or between DEB and bare-metal stents have not been performed, inferences can be made only using indirect comparisons; for example, a comparison of DEB and bare-metal stents from 11 randomised, controlled studies showed a comparable efficacy.”

He added: “Therefore, at the present time, the concept of ‘leaving nothing behind’ may support the decision in favour of DEB. However, there is no evidence available.”

A recent study showed that DEB and DES to have similar performance in very long femoropopliteal lesions. Commenting on the quality of these studies, Dr Krankenberg said: “The current data situation on DES for the treatment of long femoropopliteal lesions is poor and in part contradictory. A subgroup analysis of the single-arm ZILVER PTX study showed a promising one-year primary patency of 78% for long lesions (mean length of 23cm). In contrast, results from the STELLA-PTX registry on long lesions (mean length 25cm) were discouraging: The one-year primary patency was only 53% and 12.5% stent fractures were seen.

“Thus, the efficacy of DES for long lesions still needs to be proven by a randomised, controlled study. The same applies to drug-eluting balloon.”

He concluded by adding: “In the case of long lesions, it would be also interesting to compare drug-eluting devices with the interwoven-wire Supera stent.”

References:
Experts will gather in the Technical Forum this morning for a session that explores interventional treatment approaches for oncological patients and those with portal hypertension. Opening the discussion with a look at state of the art treatment options for primary liver malignancies and metastatic disease will be Peter Huppert, who is Head of the Department of Diagnostic and Interventional Radiology at the General Hospital Darmstadt, Germany.

Professor Huppert began by outlining the most important interventional options for treatment of primary liver tumours (hepatocellular and cholangiocellular carcinoma: HCC, CCC) and liver metastases originating from various primary malignancies. Put simply, the core techniques include: percutaneous transhepatic thermoablation; percutaneous transhepatic portal vein embolisation; percutaneous transhepatic biliary drainage; conventional transarterial chemoembolisation (cTACE); drug-eluting transarterial chemoembolisation (deTACE); and radioembolisation.

Delving deeper into the techniques, he told LINC Today: “For primary liver tumours and liver metastases, resection – if possible – is still the gold standard.” However, percutaneous techniques for local thermoablation either by radiofrequency ablation (RFA), microwaves or laser light offer similar results in lesions up to 3cm in size (in metastases) and near to 5cm in size for hepatocellular carcinomas [HCCs]. However, a limitation of these techniques, besides lesion number and size, are lesions located in a distance of less than 1cm to critical hilar structures, and those adjacent.

“To facilitate liver resection in patients with extended liver metastases, the technique of portal vein embolisation of the right liver lobe induces hyperplasia of the future remnant liver volume of the left liver lobe, allowing extensive right hemi-hepatectomy in patients with small left liver segments. This technique has been used over the last 10 years. Biliary drainage and stenting are well established safe and effective treatments for recanalization of biliary obstructions and recon-
Moving on to radioembolisation (RE), Professor Huppert first described its workings: “It is a kind of brachytherapy caused by microspheres emitting β-radiation into tumour lesions,” he said. “These microspheres are catheter-directed, delivered similar to the technique of cTACE. “Because only minor embolisation effects are related to RE, this treatment is also possible in patients with main portal vein thrombosis, which is usually a contraindication for cTACE. Compared to cTACE, clinical outcome after RE is similar in patients with HCC and those with metastases. In advance, non-target arteries have to be excluded by bland embolisation, and significant intratumoral arteriovenous shunts have to be ruled out: i.e. treatments are very expensive!”

In his closing remarks, Professor Huppert turned to drug eluting techniques, emphasising that they are an important step forward for TACE. For example, drug-eluting technology allows sustained drug delivery and enhanced exposure in liver malignancies, and electrostatic binding of positively charged drugs in negatively charged backbones of microspheres allows loading and precise delivery into tumours.

“Today this technique is available for antracyclines (doxorubicin, epirubicin) to treat HCC’s and for irinotecan to treat colorectal cancer metastases,” said Professor Huppert. “However, new types of microspheres are already in the pipeline able to load not only other cytotoxic drugs, but also analgesics and biologicals. This makes drug-eluting technology one of the most developing fields for interventional treatments in liver malignancies.”
Carotid revascularisation has been the subject of much research over recent years. With that in mind, the latest advances related to this work will be discussed this afternoon in the session ‘VIVA @ LINC: Next steps in carotid revascularization’

Moderating the session will be Peter Schneider, a vascular surgeon from Honolulu, Hawaii, USA, who is on the Board of Directors of Vascular Interventional Advances (VIVA) Physicians, a not-for-profit organisation dedicated to advancing the field of vascular medicine and intervention through education and research.

VIVA, comprised of physicians dedicated to vascular care and education, who meet each Autumn in Las Vegas, are a longstanding friend of LINC, and the VIVA@LINC sessions are always popular. Speaking of the relationship between LINC and VIVA, Dr Schneider told LINC Today: “There are many similarities with LINC; interest in live case demonstrations, multiple venues for learning, and enthusiasm about the future of the vascular field.”

He added: “There’s also a mutually-held high level of energy about contributing to the future of our chosen field.”

Speaking more specifically about the carotid revascularisation session, Dr Schneider went on to stress that research had come a long way in carotid revascularisation, but that there was still work to be done. “Because of all the studies carried out over the past 15 years and the ones that are enrolling carotid stenosis patients now, the field has advanced significantly. There are unanswered questions, but the main issues are shaping up.”

He highlighted that it was known that both carotid endarterectomy and carotid stents played a role in managing these patients, and that technology for stenting was being improved. “In this session we will highlight advances in trial design, cerebral protection during the procedure, and specific stent designs,” he said.

He added that the VIVA @ LINC session was fortunate in having one of the leaders in the field, Kenneth Rosenfield, Section Head for Vascular Medicine and Intervention at Massachusetts General Hos-
Continued from page 13

pital, Boston, USA, offering his projections on the future and how some of the major issues will be solved.

In addition, Gary Ansel, an interventional cardiologist/cardiac and peripheral vascular intervention specialist from Columbus, USA, will discuss proximal protection and whether it is the way forward. Referring to this topic, Dr Schneider discussed the Mo.Ma proximal cerebral protection device (Medtronic, USA), noting it was well known and there were significant data available with this device. He also acknowledged the Silk Road device (Silk Road Medical, USA). “This is a proximal occlusion balloon where the contents of the carotid bifurcation are aspirated prior to re-opening the artery,” he explained. “The Silk Road device is a transcervical, proximal occlusion, reversed flow device. The particulate generated at the target site are collected in a filter and the effluent blood goes back into the venous system.”

According to Dr Schneider, both devices have been shown to generate fewer diffusion-weighted magnetic resonance imaging lesions after stenting, however he added that there were downsides. “There are a small number of patients that will have intolerance to proximal occlusion. With the Silk Road device, the aortic arch and its embolic potential is also avoided.”

Dr Schneider will take to the stage himself to discuss whether mesh-covered stents will reduce the risk of stroke. He explained that there were three stents in development, all with some clinical information. “They are covered with a nitinol, [PTFE], or polyethylene terephthalate [PET] mesh of varying aperture sizes, in the hopes of reducing plaque prolapse and embolisation of plaque material through the struts of the stent,” he explained, adding that early results were promising.

The VIVA @ LINC session ‘Next steps in carotid revascularisation’, will take place this afternoon at 15:00–16:30 in Main Arena 1.

References
As part of a symposium focusing on the phenomenal technological progress of drug-elution, Jaydeep Kokate (Boston Scientific, MN, USA) will discuss the Eluvia stent (Boston Scientific, USA), a drug-eluting stent (DES) which has achieved the highest 12-month primary patency rates in comparable trials of such devices in the region of the superficial femoral arteries (SFA).

As an engineer leading the technical development of the Eluvia stent, Dr Kokate explained the process of DES design to LINC Today, detailing the scientific rationale behind its development. In particular, he said, the exemplary results that have been achieved with DES in the coronary region provided a reliable, yet in many ways contrasting, template for his work.

“One of the fundamental stages in developing a device for the SFA was trying to understand the differences between the coronary and SFA vascular beds,” he said.

“We took a deep dive into understanding the differences that may have led to better outcomes in coronary stents compared to what had been observed in SFA stenting. We also looked at stent design, including the choice of drug and polymer. DES had been somewhat effective in the SFA, but not nearly to the same extent as in the coronaries.”

And there are two key elements responsible for this disparity, he explained. The two arterial regions differ in terms of their structure and func-

“...”

“...”

Jaydeep Kokate

“We are excited about it. We are looking at this being a mainstay of therapy in the SFA for a long time.”
tion, which reflects their local environment under healthy conditions; when this goes awry, disease development and progression are similarly idiosyncratic.

The second element involves the way in which the coronary stent design addresses restenosis, said Dr Kokate: “Restenosis tends to happen sooner in the coronaries than it does in the SFA. So the team focussed on identifying a polymer that would allow us to sustain drug release for a longer period of time to match the disease process in the SFA.”

In terms of addressing the relatively physically stressful environment of the SFA, he continued: “Eluvia is a durable stent. We designed a stent that is strong, flexible and fracture resistant, because we recognised that the mechanical environment in the SFA is much harsher than the coronaries.

“At the same time (and because we are talking about drug elution), we recognised that the stent and the delivery system had to enable a uniform deployment of the stent that then ensures a uniform delivery of the drug.

“The final piece of the design is the coating, which had to be durable, biocompatible in terms of eliciting a benign biological response from the vessel, as well as eluting the drug for a long period of time that matches the restenotic process in the SFA.”

Eluvia’s 12-month data (the Majestic trial!) will be presented during the same session by Thomas Zeller, immediately following Dr Kokate’s presentation. The prospective, multicentre Majestic trial enrolled 57 patients from Europe, Australia and New Zealand. A primary patency rate of 96.1% was reported after 12 months, with 94% of patients returning at 12 months with no or minimal claudication (Rutherford 0 or 1). The target lesion revascularisation rate was 3.8% (2/53) at 12 months, with no observed stent fractures or amputations, and an improvement in ankle brachial index from 0.73±0.22 at baseline to 1.02±0.20.

The cohort was recruited as a reflection of real-world complex lesions, with an average lesion length of 70.8±28.1mm and degree of stenosis of 70% or greater; 46.2% of lesions were CTOs and 64.9% severely calcified.

The patient cohort in the Majestic trial suggests that Eluvia could find a place in treating a broad spectrum of lesions in the SFA. “We are excited about it,” enthused Dr Kokate. “We are looking at this being a mainstay of therapy in the SFA for a long time.”

Asked what he envisions for the DES, especially amid the success of drug-coated balloon (DCB) technologies, Dr Kokate suggested: “With the advent of DCB, the concept has of course been to leave nothing behind.

“But one would think that it would be even more significant in the coronary setting to leave nothing behind. I think ‘leave nothing behind’ as a concept has come forward lately, especially considering that outcomes in the SFA have never been as good as in the coronaries.

“Now that we finally see that stenting outcomes can be similar between the two vessels, leave nothing behind seems less relevant. This is because the concern with leaving nothing behind arises if there is a significant risk of reintervention. If you are getting outcomes that are 90% plus, chances are that one may be less concerned about coming back to reintervene. I think there are a number of aspects of this technology that make this concept less relevant.”

One of the strongest features of DES is their ability to elute anti-proliferative agents over a period of many months. This contrasts starkly to DCB,
Continued from page 16
where this process is inher-
ently less controlled. With
the disease process so much
lengthier in the SFA, explained
Dr Kokate, delivering a single
drug bolus simply may not be
as effective as a polymer-mod-
ulated drug delivery system.
“Again, we looked at our
insights from our coronary
experience. Because the lesions
tend to be more fibro-calcific
in the SFA, we dosed higher
than what we would have in
the coronaries. We know what
levels are safe and effective
in the coronaries. And recog-
nising that the dosage needs
to be higher and to last for a
longer period of time was a
conceptual path that the team
took. Then we tested it in pre-
clinical studies, and confirmed
the dose to be safe. This was
the dose that was used in the
Majestic trial.”
The Eluvia stent will undergo
further testing as part of the
Imperial trial, which is currently
recruiting internationally.2 The
study aims to compare the
safety and efficacy of the Eluvia
stent with the Zilver PTX DES
(Cook Medical, USA), in SFA and
proximal popliteal artery lesions
up to 140mm in length.
“We have extensive preclinical
work where we have compared
with competitive DES,” said
Dr Kokate. “But in the Imperial
trial, we will compare head-to-
head with the Zilver PTX.”

References
1. Stenting of the Superficial Femoral and/
or Proximal Popliteal Artery Project (MA-
NCT01820637 (retrieved January 2016).
2. ELUVIA Drug-Eluting Stent versus Zilver
gov/ct2/show/NCT02574481 (retrieved
January 2016).
**SeQuent Please DCB: first data from the CONSEQUENT trial**

"At six months, we found a significantly lower LLL of 0.49mm compared to 1mm in the control group."

---

**InC TODAY** reached out to Thomas Albrecht (Vivantes Klinikum Neukölln, Berlin, Germany) following yesterday’s session on the changing paradigms and future concepts in peripheral interventions, in which he will presented the first angiographic and clinical data from the CONSEQUENT trial (Clinical Trial on Peripheral Arteries Treated With SeQuent Please P Paclitaxel Coated Balloon Catheter).¹

Despite advances in contemporary technology, restenosis remains a major limitation following revascularisation procedures of the AFS and popliteal artery. The SeQuent Please DCB (B. Braun, Germany) may offer some advantages over previous DCBs.

Professor Albrecht began setting the scene by describing the device and highlighting some important characteristics: “The SeQuent Please OTW Paclitaxel Coated Balloon has a paclitaxel-matrix coating that upon balloon-vessel contact, delivers a contact a ‘one shot’ of paclitaxel to the arterial wall. The delivery of the hydrophobic paclitaxel into the arterial wall tissue is mediated by excipients, which play a very important role in this process.”

“A key feature in the SeQuent Please DCB is the new excipient – resveratrol, a natural anti-oxidative compound. Pre-clinical work has revealed that this new matrix coating on the SeQuent Please balloon surface can very effectively deliver Paclitaxel into tissue and is stable even in difficult-to-cross lesions².”

Explaining this Phase III clinical trial and its findings, Professor Albrecht told us, “This is the first presentation of preliminary six-months results of the CON-
SEQUENT study. In this German multicentre trial, we included 153 patients with steno-occlusive lesions of the SFA or popliteal artery. “Patients were randomised on a 1:1 basis either to treatment with plain old balloon angioplasty (POBA) or with the new SeQuent Please drug coated balloon. The primary endpoint was late lumen loss (LLL) at six months as assessed by quantitative evaluation of follow-up angiograms.”

Detailing the preparatory stage, he commented: “Debulking by atherectomy was not allowed in the protocol. Predilatation was used 56% of lesions – it was mandatory in cases of total occlusions but otherwise left up to the discretion of the interventionist.”

The results, which are being presented for the first time, are very encouraging, Professor Albrecht explained: “At six months, we found a significantly lower LLL of 0.49mm compared to 0.98mm in the control group. This resulted in a significant reduction of the binary restenosis rate from 47% in the POBA group to 21% in DCB group.

“Interestingly, we found positive remodelling in over a third of patients treated with DCB. Clinically driven target lesion revascularisation rate was 12% with DCB compared to 26% with POBA. Importantly, we saw marked clinical improvement after DCB treatment with an increase of walking distance by 137 m at six months compared to just 71 m in the POBA group. The CONSEQUENT Trial investigated the primary efficacy endpoint of six-month LLL, an approach similar to that of other DCB trials. Professor Albrecht said, “With regards to the reduction of late lumen loss and target lesion revascularisation, the results were very similar to previous studies.”

However, two main differences with the CONSEQUENT trial versus previous DCB studies were the lesion length and complexity: “We treated patients with more complex lesions than has been performed before with such devices; the average lesion length was 13.2cm and thus substantially longer than in any other previous DCB study that I am aware of.

“Furthermore, we included a relatively high rate of TASC C or D lesions of 23.5%. Our study is therefore probably more representative of the clinical, real-life situation, where we treat more and more patients with long and complex lesions.”

A clinical trial cohort rarely reflects the true clinical and angiographic patients in real-world practice, however, the common complexities of SFA and popliteal artery are length and calcification have been addressed in this study, meaning that these findings could have great impact.

Noting again that this trial randomised its cohort to either the SeQuent Please DCB or an uncoated balloon, Professor Albrecht concluded: “Comparison with other DCBs would certainly be of great interest, but was not part of the current protocol. This could be a matter for the future.”

References
2. Data on file at B.Braun Melsungen AG, Vascular Systems
Endovascular treatment options for iliac aneurysms will be dissected this afternoon, with a range of devices, trials and concepts laid out for the audience. One such device is the GORE EXCLUDER Iliac Branch Endoprosthesis (IBE) from W. L. Gore & Associates, Inc. (USA) – an iteration of the EXCLUDER platform that marks the first complete system fully designed for the iliac branch. CE marked in 2013, the device has since garnered significant interest. “We started to talk about this new device, and how we needed to know more about the performance,” Michel Reijnen (Rijnstate Hospital, Arnhem, the Netherlands) – who is principle investigator of the Iliac Branch Excluder ReGistry (IceBERG) – told LINC Today.

IceBERG is a post-market registry with two separate retrospective and prospective components. The first retrospective part of the trial, spanning from November 2013 to December 2014, was tasked with evaluating the technical success of EXCLUDER IBE implantation across 13 sites in the Netherlands. All-told, 51 common iliac artery (CIA) aneurysms in 46 patients were included.

With results from the retrospective part of the trial now submitted for publication, Dr Reijnen will be taking to the stage at LINC to relay the data. “The retrospective data went surprisingly well,” he said, noting high procedural success, and low incidences of endoleak and re-intervention in particular.

Along with a detailed account of the retrospective data, during his presentation, Dr Reijnen will also take the time to introduce the prospective stage of the IceBERG registry – a multicentre, observational, post-market real-world registry which will include a minimum of 100 patients from 10 European sites. Adult, elective patients with indication for aorto-iliac endovascular stent...
primary endpoints will focus on primary patency of the hypogastric side branch at one year, and successful exclusion of the aneurysm without type I endoleak (also at one year). follow-up will extend out to five years in total, with analysis on an intention-to-treat basis. “we are now at 11 patients, but enrolment should go quickly,” commented dr reijnen, noting that it is hoped that enrolment will be completed within the year. while those in the field wait with baited breath for the outcomes of the prospective phase of iceberg, other studies are already in the planning stage, as dr reijnen described: “we are planning some geometrical studies, and some dynamic studies as well, but in the end we need some kind of a comparative trial. and then it is the question of whether you are going to combine two iliac artery-preserving devices with each other, or are you going to take [a position] where you sacrifice one internal iliac artery? that trial has also never been performed. patient selection is essential, but at this point we don’t really know which patients benefit most from iliac-preserving techniques.”
“No protection, no CAS!”

Yesterday’s Deep Dive into carotid artery stenting featured Giancarlo Biamino (Impruneta, Italy) speaking about the importance of proximal embolic protection in CAS. During an interview with LINC Today ahead of the session, he explained that, while proximal protection represents a new gold standard for CAS, the ultimate gold standard remains operator experience.

“So-called ‘low risk’ CAS do not exist,” said Professor Biamino, stressing that, because embolic risk is not a quantifiable parameter, protective measures must be taken case-by-case.

“Each case has to be analysed individually, and the procedure has to be tailored to the specific case with regard to access selection, type of cerebral protection and stent selection. But it is practically impossible during the pre-procedural analysis of each single case to predict the potential amount and the size of debris released during the stent delivery and the final post-dilatation.

“Echolucent plaques may have a major risk of embolisation, and new MRI technologies with the possibility of a three dimensional reconstruction may improve the pre-procedural analysis of the plaque. In any case, the strict rule is: no protection, no CAS!”

While embolic protection devices have become routine in CAS, currently both distal and proximal cerebral protection systems are employed – proximal occluders and distal filters. Currently, noted Professor Biamino, the only FDA-approved proximal protection system in use is the Mo.Ma (Medtronic, USA).

“At the moment we have one proximal protection system and about eight different filters,” he said. “It is very difficult to make a comparison; nobody will support such a study. Many interventionalists, and particularly vascular surgeons, prefer to use filters, because they are relatively easier to position. But the effectiveness is practically impossible to control, because during the intervention you cannot establish the adaptation of the filter to the wall of the distal part of the carotid artery. You can only hope that you are catching all the material.

“Personally, on the basis of an experience of nearly 15 years, I would strongly recommend for the majority of the cases proximal protection. In fact, the Mo.Ma system is safe, easy to use and effective with < 2% MACCE at 30 days.1,2

“Furthermore, the literature is indicating, on the basis of diffusion-weighted MRI (DWMRI) studies (e.g. DEVERSE3) that the number of new lesions after CAS is in the same range, after supraaortic diagnostic angiographies. The analysis of MRI, particularly if you look at the PROFI study4 shows that in comparison to filters the number and size of post-procedural cerebral ‘le-
Continued from page 22

sions’ is significantly lower; they have found new lesions using filters in 85% of the cases. So using the filter, you may catch major debris, but you are surely not catching all the debris.”

Understanding the significance of such DWMRI lesions is not straightforward, however. While it is safe to say that cerebral emboli are responsible for the creation of ischemic lesions, and that they increase cerebrovascular risk, these lesions do not always lead to clinically observable neurological events and may bear no prognostic impact. Recent work has shown that the natures of ischemic brain lesions occurring in CAS and CEA are distinct.

“Particularly if you only have single lesions in DWMRI, these lesions are totally asymptomatic,” said Professor Biamino. “Nobody knows, because we do not have follow-up analysis, what happens with these lesions. Neurologists are saying that they are disappearing. We don’t know if these are artefacts, air bubbles, or disease. We only know that we can’t find these lesions in the brain anymore.”

Even so, the use of DWMRI lesions as a proxy measure of clinical risk posed by emboli has proven useful in clinical study. Minor stroke co-occurs with multiple cerebral lesions, noted Professor Biamino, although they do not always correspond to expected symptoms from that particular brain area.

Although further study would be useful to make sense of which brain lesions pose a risk, the incorporation of DWMRI into clinical practice would be extremely costly, he continued: “From the logistical point of view this is very difficult, because you have to have an MRI a few days before the intervention and at least one 24 hours after the intervention. In many hospitals this is very difficult to organise. This is the first point. Second of all, reimbursement is not routine. And many patients refuse to have this type of analysis because they are not strictly recognised as a part of the procedure.”

The question of stent design is another of the field’s open questions. Sharing his viewpoint on established and up-and-coming designs, and the effects these may have on post-procedural stroke rates, Professor Biamino said: “Regarding open versus closed cell design, this is more a philosophical than a scientific question.

“In fact we observed during the last five to seven years a continuous debate about the question without a clear answer. We do not have any real scientific substratum. Prominent interventionalists in the field of CAS have, however, some recommendations: (a) open cell for following complex, tortuous lesion contour; (b) closed cell for ‘preventing’ plaque prolapse in straight lesions; and (c) hybrid geometry for combining scaffolding and conformability.

“Regarding mesh-covered stents in CAS, we will hear about new data during this LINC meeting. I suppose that it is still too soon to establish relevant advantages for mesh covered stents. With regard to the post-procedural stroke incidence in relation to the stent design I do not know any relevant data. We can only confirm that a large number of MACCE (nearly 2/3) are occurring in the first 24 hours post-procedure.”

With reason and some evidence supporting the superiority of proximal protection (and with only one approved proximal protection system in Europe and USA), patient selection is, therefore, one of the controllable variables that influence outcome in CAS – and selection itself relies upon operator experience.

In a recent editorial, Stabile and Esposito argued that “operator’s experience is the most ef-
ficient embolic protection device for CAS". For those starting a CAS program, Professor Biamino recommended avoiding anatomically complex lesions and to exclude arch II and III anatomies, adding that for the first 100 cases, angled lesions, calcified sub-occlusive lesions, ulcerated soft and dis-homogeneous lesions should also be avoided.

Offering further thoughts on proximal protection, in reference to recent work on occlusion intolerance in CAS, he continued: “In using a proximal protection system, you have to know how to deal with a case of flow blockage intolerance. In nearly all cases it is possible to conclude the intervention. After restoring the antegrade flow at the end of the intervention a complete recovery will be achieved within two to five minutes without any medication. In some cases it will be necessary to increase the blood pressure. Bradycardia after stent post-dilatation can induce an intolerance; this is why I recommend the application of 1mg atropine before starting any manipulation around the lesion.”

Clearly, wise decision-making requires education and experience. Having a better understanding of what level of ability an interventionalist must reach in order to carry out CAS without complications would help, said Professor Biamino, as would establishing rules to that effect. This poses something of a bugbear, especially given that a consensus document containing clear recommendations exists, having been published in 2006 by Cremonesi et al.

This was the first consensus document of the ICCS (Italian Consensus Carotid Stenting)-SPREAD joint committee, an Italian multidisciplinary taskforce, which concentrated not only on methodology, indications and procedures, but credentials and competency – suggesting training, acceptable complication rates and certification. The committee recommended that physicians undertake (as a minimum) at least 150 diagnostic procedures of supra-aortic engagement within two years, of which at least 100 as primary operator. In addition, at least 75 CAS procedures, of which at least 50 as primary operator (within two years), should be undertaken. Then, the minimum requirement to maintain the technical skill (competence) is 50 CAS procedures performed and documented by each primary operator per year.

Such recommendations have not generally been taken up as strict guidance, said Professor Biamino. “In my opinion, the future of CAS will not only depend on the technological improvement, but predominantly on education,” he said. “On the one hand, the training time for an interventional cardiologist or a vascular surgeon takes around five years; on the other hand, everybody can start a CAS program without a certification. Is that right?”

“The prerequisite for radiologists to start supra-aortic interventions is 50 diagnostic cases (not interventional cases). Everybody else can just start, and the same is for vascular surgeons – they do not normally have to have any peripheral or cardiac tutelage. At least the cardiologists have training to manoeuvre a guidewire in the coronary artery; cardiologists know how to pass the aortic arch, but the vascular surgeon starts without any education and you cannot control that.

“This is the same in all other countries in Europe. In the US you do not have a strict recommendation. Nobody is taking care of these recommendations. If you look at the guidelines for CAS, you don’t see anything about the qualification of the interventionalist.”

Notably, a 2008 study of the Cristallo Ideale stent saw 124 patients undergoing implantation using either proximal...
He went on to cite the AR-MOUR study, wherein complications were only recorded in asymptomatic patients, urging that further attention towards asymptomatic patients is needed: “We should, again, discuss what is symptomatic and what is asymptomatic. Some patients have such superficial, minimal and intermittent that they do not recognise that this is a symptom.

“Nevertheless, the general amount of complications in CAS is relatively low, so to demonstrate the validity of all these impressions is really very difficult. What is absolutely correct, though, in my personal opinion is that if you have more than a 1% complication rate you have to stop your program. You cannot accept more than a 1% complication rate, including all type of arches, independent of age, and independent of whether the patient is symptomatic or asymptomatic.”

It is clear, concluded Professor Biamino, that it is time to move on from the CAS-CEA debate in many respects. “The data of these last years clearly demonstrates that both techniques are acutely and on the long term equivalent,” he said. “So we should stop the debate, avoiding any type of ‘turf battle’ between interventionalists and vascular surgeons. We have to decide which technology to use in connection with the expertise and the experience of the single centre, and we have to tailor the intervention to the patient.

References
Portal hypertension is a serious complication associated with cirrhosis of the liver, but treatment using transjugular intrahepatic portosystemic shunt (TIPS) is a viable salvage therapy\(^1\). The TIPS procedure uses imaging guidance to connect the portal vein to the hepatic vein in the liver with a stent, allowing the blood to drain from the bowel to the heart while avoiding the liver. TIPS may successfully reduce internal bleeding in the stomach and oesophagus in patients with cirrhosis. By replacing bare metal stents with polytetrafluoroethylene (PTFE) covered stents, shunt patency has improved dramatically and this is reflected in patient outcomes\(^2\). The GORE VIATORR TIPS Endoprosthesis has reduced-permeability expanded PTFE (ePTFE) graft lining that minimises transmural permeation of bile and mucin and also minimises tissue ingrowth into the graft, facilitating surgical dissection during liver transplantation procedures.

With more than 15 years experience using the GORE VIATORR TIPS Endoprosthesis, Geert Maleux (University Hospitals Leuven, Belgium) has an impressive follow-up cohort to demonstrate the device’s effectiveness in improving vessel patency.

“We have the GORE VIATORR TIPS Endoprosthesis, which hugely improves the primary patency rates and also translates into better survival rate.”

Geert Maleux

“In my talk on the VIATORR endoprosthesis I will first give an overview of the procedure itself: I will discuss all the different steps for the TIPS procedure, which includes graphic visualisation of the surgical procedure, a full description of every stage and how to insert the covered stent,” he told LINC Today.

“After we have completed the TIPS procedure, we do a post dilatation with a conventional angioplasty balloon. We end the procedure by performing a control angioplasty pressure measurement to check whether everything is OK. And then we have finished.

“We started using this device in the year 2000, so that’s more

Continued on page 27
Continued from page 26

than 15 years experience; in Europe we were one of the first to start with this device, since then we published several articles\(^3,4\) on the short-term follow-up, and also about using the device in paediatric populations. More recently we prepared a paper on the long-term effects of the device\(^5\). We have quite a lot of experience.”

Professor Maleux then described his newly analysed data of a remarkably large cohort of cirrhotic patients: “Our most recent paper, which has been accepted for publication, involves the long-term results. In this 10-year follow-up analysis, 300 patients – many of whom are severely ill – were studied. We measured the Kaplan-Meier survival estimate and primary patency in this patient group.”

He added: “The survival rate was 70% at one year, 50% at four years and 30% at 10 years; and the primary patency rates were very high: at one year 90%, two years 89% and five years 85% – and at 10 years it was still very stable, without a decrease in primary patency.”

Explaining the longevity of his studies, Professor Maleux said: “The main reason that we have such a long follow-up is because we were one of the first to start using this device ... although at the time there was not much choice in this indication.”

Indeed, this initial lack of treatment options led to very high numbers (more than 350), being employed in the study over the last 15 years.

Looking to the future, Professor Maleux contemplated whether there was still room for improvement: “Before the year 2000, we could only use a bare metal stent, whereas now we have the GORE VIATORR TIPS Endoprosthesis, which hugely improves the primary patency rates and also translates into better survival rate in these patients. This device is the reason that the results we have obtained in the last 15 years are so impressive.”

“I don’t think that we can actually improve on the device, per se, however, there are still some problems with the actual procedure. One of the main problems is hepatic encephalopathy, which is caused by the shunting of the portal vein. I believe that the GORE company has a new device in the pipeline that can be tailored to the diameter of the stent graft, and by doing this, we hope that we can decrease the number of patients with hepatic encephalopathy.”

In conclusion, he said: “On very rare occasions we also have seen patients with acute liver failure due to insertion of a TIPS stent graft. We have an article in press on this topic where we looked at TIPS patients with acute liver failure, and then reduced the diameter with a reduction technique to save lives.”

References

Drug-eluting stenting (DES) of femoropopliteal TASC C&D lesions results in improved primary patency and freedom from target lesion revascularisation (TLR) rates compared to bypass, delegates will hear this afternoon when preliminary results from an eagerly-awaited study are showcased.

The study, ZILVERPASS, is a prospective, randomised, multi-centre study pitching the Cook (USA) Zilver PTX drug-eluting stent against bypass surgery in these types of lesions. The primary endpoint is set as primary patency at 12 months, defined as an absence of binary restenosis or occlusion within the treated lesion, and without target lesion revascularisation (Zilver PTX group), or absence of binary restenosis or occlusion at proximal and distal anastomoses over the entire length of the bypass graft, without clinically-driven reintervention to restore flow (surgery group). Secondary measures including device malfunction, serious adverse or device-related events.

“...we might say the future for the Zilver PTX stent looks bright.”

Marc Bosiers

Continued on page 29
A total of 220 enrolments are planned, with patients randomised 1:1 to either Zilver PTX or bypass. Patients are included if they meet the criteria of: Lifestyle-limiting claudication, rest pain or minor tissue loss (Rutherford 2-5); stenotic or occlusive de novo lesions in the femoropopliteal arteries, suitable for both endovascular and bypass surgery; total target lesion length of at least 150 mm. “If we were to extrapolate these preliminary results, we might say the future for the Zilver PTX stent looks bright.”

Marc Bosiers Exclusion criteria include any previous surgery/endovascular intervention in the treatment vessel, an unsuccessful perioperative ipsilateral percutaneous vascular procedure to treat inflow disease just prior to enrolment, any planned surgery/intervention within 30 days of the study procedure, and major distal amputation in either limb.

Presenting results from the first 114 ZILVERPASS patients at LINC 2016 will be Marc Bosiers, who is principle investigator at the AZ Sint-Blasius study centre (Dendermonde, Belgium). “For the analysis, we have included all enrolled patients so far,” he told LINC Today. “Approximately 70 patients have reached their 12-month follow-up visit.”

While a detailed run-down of the results will be reserved for his presentation this afternoon, Dr Bosiers did share some key observations that should whet the appetite of those interested in knowing more. “[The Zilver PTX group had] a 78.1% primary patency at 12-months, versus 68.7% for the bypass group,” he said. “Freedom from target lesion revascularisation for the Zilver PTX group was 89.3%, versus 75.8% for the bypass group.”

Furthermore, the procedural time was significantly shorter (P < 0.001) in the Zilver PTX group (58.67 ± 39.72 minutes) versus bypass (103.25 ± 42.74 minutes).^2^ Adding his closing remarks, Dr Bosiers said: “It is too early to make a general conclusion, when only 70 out of 220 patients have reached the end of the primary endpoint window, but if we were to extrapolate these preliminary results, we might say the future for the Zilver PTX stent looks bright. However, differences were too small to be significant with this small number of patients, so let’s see where this might end!”

References


2. Bosiers M. Initial results of the ZILVERPASS study. LINC 2016 presentation slides (Obtained with permission)
The ‘SAFARI’ technique, otherwise known as ‘subintimal arterial flossing with antegrade-retrograde intervention’, has seen great intrigue for recanalisation of chronic total occlusions (CTOs) when subintimal angioplasty fails.\(^1\)

At its core, retrograde access – usually obtained via the popliteal, distal anterior/posterior tibial or dorsalis pedis artery – has the potential to offer a viable path to a vessel in situations where conventional access is not possible. Despite its relatively recent emergence, the high technical success of the retrograde approach has landed it as somewhat of a ‘hot topic’, although there is still a need for better understanding.\(^2\)

“From my experience, there are many patients who are greatly affected by their peripheral arterial disease but, for one reason or another, are not candidates for traditional surgical or endovascular techniques,” said Mike Watts, an interventional radiologist from Philadelphia, USA. Dr Watts will be sharing his perspectives on the use of retrograde access for peripheral interventions in a talk held this morning in the Global Expert Exchange Forum.

He continued: “Having the ability to complete an entire revascularisation procedure, sometimes a very complex one, solely through tibial artery access allows for the treatment of patients who otherwise would have no option.”

Given that data on the retrograde approach largely stems from small case series or reports, Dr Watts cautioned that it is difficult to tease out as to why the retrograde approach works as well as it does: “Besides obvious cases of ‘flush occlusions’ of the SFA where there is no access to the SFA from above, there’s not a lot of good data as to why coming retrograde works so much better for many of these occlusions. I’ve asked this question to some of the leaders in the field, and the response I’ve received is ‘I don’t know why it works so much better, it just does!’”

“Since the original publications on the SAFARI technique, case series’ have become more and more common, showing good results with pedal access. Whether or not physicians who do a lot of peripheral vascular disease work use SAFARI, or not, I think they [still] know it to be an effective option.”

He added: “There has also been an increasing body of work focusing on tibial angioplasty via pedal access, which seems to be more accepted recently. Vendors have created pedal access sets with very low

Continued on page 31
profile tibial balloons to use through very small sheaths. I think the idea of placing a 6 Fr sheath in a patent tibial artery to cross an SFA or popliteal occlusion is new to most people, and I’m trying to show, at least in a case series at this point, that it’s safe and effective."

Wire choice is an important consideration in the retrograde approach. That being said, in the cases that Dr Watts will be showing, the nuance of the technique is such that there is no snaring from the groin. His advice is for operators to continue with the wires that they would normally use for crossing chronic total occlusions from above. “In my case, that’s often an 0.035-inch stiff hydrophilic wire,” he said. “Once I’m across and back in the lumen of the vessel, I will generally upsize for a 6 Fr sheath for balloon or stent placement. I like to look at this method as an analogous method to treating from the groin, just coming from the opposite direction, with one access point only.”

Dr Watts went on to stress that patient selection and vessel planning are another important facet of the approach. Patients tend to have no surgical options, thus would be extremely difficult or impossible to successfully manage with groin access. “It’s important to choose an artery that is patent in its whole course, and isn’t extremely diseased,” he said. “Obviously, a larger artery is better, but it will expand to accept a 6 Fr inner/7 Fr outer sheath. Also, similar to a radial artery catheterisation, I do like to see that there is perfusion to the foot via another vessel.”

Commenting on the adoption of the retrograde approach, Dr Watts noted that, while there is a steep learning curve, skilled interventional radiologists will find their previous experience very helpful. “We’ve all put in scores of PICC lines; some of us have put them in infants,” he said. “We’ve targeted small bile ducts under ultrasound and biopsied things in locations that are very treacherous. Having the ultrasound-guided needle skills to access the artery is very important and only comes with practice.”

In terms of adjunctive steps to ensure success, Dr Watts added that generous heparinisation and vasodilation are a must, and despite not yet having seen a thrombotic complication of a tibial artery, it is still his biggest concern, and therefore mustn’t be taken lightly. With that in mind, he hammered home the message that the retrograde approach is really only reserved when alternatives are ruled out: “This is a procedure I’m using only for patients who really have no other options,” he said. “For example patients with kissing iliac stents that don’t allow up-and-over access, or people with bypasses or other altered anatomy (perhaps morbid obesity or previously scarred groins) who cannot have antegrade access.”

Of course, the live cases exhibited at LINC are one way in which techniques such as the retrograde approach can gather more widespread adoption – perhaps at the very least by settling trepidations. “I think someone experienced with the technique, showing an audience how straightforward a procedure can be, goes a long way towards spreading the word,” said Dr Watts. “It’s a lot less scary to do something that you’ve seen someone else do, rather than trying to figure it out yourself the first time from a written report or two.”

Dr Watts will be discussing ‘Retrograde access as the primary approach for peripheral interventions’ during the session ‘Deep dive session: Lower limb interventions’, held this morning at 08:00–10:45 in the Global Expert Exchange Forum.

References
A rteriovenous malformations (AVM) come to the fore in a session dedicated to the topic this afternoon at LINC 2016, bringing together experts from around the world in this highly specialised field. The session focuses on the emerging revolution in techniques that now brings cure to countless – in a realm where options were as limited as they were daunted by disappointment.

Session moderator Wayne Yakes (Swedish Medical Centre, CO, USA) and presenter Robert Vogelzang (Northwestern University Feinberg School of Medicine, USA) spoke to LINC Today during their winding journey from Paris to Leipzig – a journey broken up with a visit to Iris Baumgartner’s group at the University of Berne, where they demonstrated their knowledge in practice before doing the same at the LINC meeting.

“After LINC, I will be going to the University of Hamburg where we are going to treat more patients,” said Professor Yakes. “And I do this constantly.”

The complexity of vascular malformations as well as their rarity makes their treatment, said Professor Yakes, “the most challenging and difficult problem; the hardest thing that any physician can be tasked with.”

This is an orphan disease that nobody wants to deal with, he stressed. In such a challenging area, the rise of equally challenging treatment techniques demands an extensive raft of training initiatives the world over, which will allow technical expertise to trickle down to the fellowship level.

“A lot of fellowship programmes don’t even offer it because they don’t have the experience,” said Professor Yakes. “This is a problem. Now, it is now coming to the fore more and more and those that are involved with it are being called to make the treatments, and how to choose them, more known.

“Every nation has 1% of their population with this; it is not exclusive of anywhere. So, it is not the crazy aunt in the basement that you don’t want to intro-

Continued on page 33
Explaining how he became interested in AVMs, Professor Vogelzang added: “I became enthralled, as I think did Dr Yakes, by these very difficult problems with seemingly little or no solution. Over the ensuing decades since we started, spurred on by those like Dr Yakes and others of us all working together, we realised that we had some answers for these patients who here before had no answers.

“All of us are fascinated by the unusual. Interventional radiology is about problem solving. To that end, we are constantly faced with these challenges. Interventional radiology is a fascinating way of treating disease using what I call the most elegant and simple method ever devised in the history of medicine: needle-catheter-guidewire. And applying those methods to a variety of conditions is what we do. We came under the spell of AVMs and the difficulty in solving this problem.”

AVMs are wide-ranging in clinical presentation and course. Although a small proportion emerge post-traumatically, for the most part they are congenital – a vestige of the primitive blood vessels that grow during the early weeks of embryotic life. Under normal developmental conditions, these vessels are resorbed as a more mature vascular system develops – a process that goes on until birth.

“If the body makes a mistake in this process at this early stage, with incomplete resorption of some of these primitive vascular elements, then you have what is called a vascular malformation,” explained Professor Yakes. “There is no mechanism of resorption during the next months of life until you are born. You are born with it, and you are then stuck with it. There are heritable conditions, but those are very rare. The vast majority are these types of ‘glitches’ that occurs, and so we could all potentially have one.”

Manifestation of such ‘glitches’ can vary from the cosmetic to the life-threatening. And while a large proportion of vascular malformations are initially asymptomatic, they are also dynamic structures, as Professor Vogelzang explained: “I think many initially have minimal symptoms but eventually they will become symptomatic. There are some small ones that may simply be present, but the majority will ultimately become symptomatic at some point.

There are heritable conditions, but those are very rare. The vast majority are these types of ‘glitches’ that occurs, and so we could all potentially have one.”

“We realised that we had some answers for these patients who here before had no answers.”

Robert Vogelzang

Even small venous malformations can become painful.”

Treatment options comprise those operative and non-operative. Part of the expertise that Professor Yakes will impart during this afternoon’s session is an understanding of the clinical decision-making process – something that is tied up with the Yakes AVM classification system, which he recently proposed.2

At its beginnings, AVM treatment was done surgically. This had a very poor track record, with some patients getting worse while few improved. “All the papers show that it was an utter failure,” said Professor Yakes. “Recurrences were almost 100%. Complications were universal.”

With very few alternatives, surgery was a mainstay for some time, until the advent of catheter-based techniques. “We thought that maybe we could revascularise them,” commented Professor Yakes. “That if we clotted them off a bit, then the surgeon could resect them. But this failed miserably too.”

The essential lesson from these failures was that, in most cases, simply chopping out the AVM was insufficient in stemming proliferative mechanisms that would restore the structure. “Whether it was surgery, or endovascular embolisation, it was always temporary and palliative at best,” said Professor Yakes.
“That is clear from the world literature.

“Then I invented the use of alcohol and published the first paper in 1986 in the American Journal of Roentgenology. Now, the world of cures by endovascular means – non-surgical means – is a possibility. This is really a paradigm shift, because we can actually cure these lesions. That is how things have evolved.

“The reason why we do this is because no matter what we did, we were always beaten at the cellular level. Diseases are at the cellular level; if you have a cancer of the liver, you don’t just go cutting it or irradiating it – you have to find out what the cell type is. Is it a primary lesion of the liver, or is it metastatic from some other area? You have to first do this to determine what kind of therapy to use. The same thing applies to vascular malformations. We have to defeat them at the cellular level, not at the macro level, and that is what alcohol does.”

Ethanol sclerotherapy, as it is called, destroys the endothelial cells that line the vascular structures of the AVM (arteries, veins, capillaries and lymphatics). If endothelial cells are not destroyed, they react to insult by secreting angiogenesis and chemotactic cellular factors, causing vessel proliferation and macrophage recruitment. Sclerotherapy, therefore, results in a permanent destruction of the AVM.

“Alcohol must be used with extreme caution,” noted Professor Vogelzang. “It is an extraordinarily toxic material that has to be delivered at precisely the right spot in precisely the right dose. That is why it is so imperative that people come to these meetings to understand how to use it. Used improperly it can cause devastating complications. At the same time it has the opportunity to really cure.”

Professor Yakes will be comparing the Yakes AVM classification system with its two predecessors: the Houdart and Do classification systems. Comparing them, he said: “Emmanuel Houdart is director of interventional neuroradiology at Lariboisière Hospital in Paris. They have an outstanding programme, and they published in 1993 in the Journal of Neuroradiology on a classification system for AVMs on their morphology. Young Soo and his team are in Seoul, Korea. I started their vascular malformation centre for them in the 1990s – Professor In Wook Choo started it and Dr Do has run with it magnificently, and published his classification system, which is very similar to the neural classification.5,6 But there are some other angioarchitectures that these two classification systems do not encompass. That is why I came up with mine. But it is not just because the architecture is different; the most important thing is that the architecture determines how to treat each specific one – to cure. That is what I have come up with.”

AVMs can occur in any soft tissue, organ, in the central nervous system and in bone. Professor Yakes will present a case study of the latter, and he explained some of the main issues that can arise in their treatment: “Bone AVMs can occur in any bone of the human body. What I have found (and I was the first to describe this) is that if one is involving an extremity (an arm, a leg) one has to look at the entirety of the extremity, because about 40% of the time there will be multiple AVMs.

“A patient may have a symptomatic one, but there may be others present. I want to stress the multiplicity that can occur in that particular entity that is really non-existent in the other entities. I will incorporate the Yakes AVM Classification system to describe the angioarchitecture of that which is in bone, and how to treat it.”

Following this case, Professor Vogelzang will speak about the different endovascular and percutaneous treatment options for AVMs. “I will be talking about a treatment method that has in my opinion revolutionised the treatment of a class of AVMs,” he reiterated. “Once we understood this (predominately

Continued on page 35
through the work of Dr Yakes) we came to the understanding that many could be treated very safely, and cured.

“This is something we did not really think was possible before. That is the basis of my talk, as well as a general discussion about how we identify these lesions. It has been a dramatic revelation. It is wonderful to be able to see a lesion and to say ‘we can cure this lesion, often in a single step by not exposing the patient to the risks sometimes that alcohol entails.” For those with adequate experience, he explained, alcohol is the principle treatment modality, although it depends on the clinical scenario, which includes the type of malformation in question, and the delivery options. “In the lesions that I am talking about, alcohol can be avoided altogether,” he said. “We can, for example, use fibred coils in the venous outflow and cure these lesions without the need for alcohol (or only minimal use of alcohol); or, alcohol delivered on the venous side where it has far less toxicity.”

The ‘Basics you need to know about vascular malformation’ session takes place this afternoon from 13:30–16:30 in the Global Expert Exchange Forum.

References
During the ‘Controversial issues, new insights and pioneering solutions for Critical Limb Ischemia’ session, held yesterday afternoon in Main Arena 1, a series of trial updates were laid bare for the audience, spanning concepts that included bioresorbable scaffolds, calcification, drug-eluting technologies and novel devices.

One such device is the Bullfrog Micro-Infusion Device (Mercator MedSystems, USA), the first catheter-guided system designed to infuse — directly and non-systemically — therapeutic agents safely through blood vessel walls into deep tissues.¹

“The Bullfrog device is a micro-infusion catheter that is able to deliver drugs accurately and effectively [into the vessel wall],” said Dr Adams as he summed up the merits of the device for LINC Today. “While the device has an excellent safety profile and the micro-needle has not created any complications in patients, its use is straightforward and fairly obvious.

“Since we mix a small amount of contrast with the drugs we deliver, I am able to ‘paint’ the lesion with the drug/contrast mixture and get immediate feedback from the visualisation.

Targeting inflammation appears to interrupt the cascade from vessel injury to restenosis, and since the Bullfrog device can deliver drugs efficiently, it is the first technology that can truly target inflammation, rather than eluting a more cytotoxic drug meant to target downstream proliferation. Thus, I believe that Bullfrog micro-infusion could be part of the treatment algorithm for revascularisations, since we know that all mechanical intervention leads to injury and inflammation to some degree.”

The Bullfrog device is being studied in two randomised critical limb ischaemia (CLI) trials: LIMBO-PTA² – which is being headed-up by Principle Investigator Dierk Scheinert in German centres – and LIMBO-ATX³ in the US, of which George Adams (REX Hospital, University of North Carolina Healthcare, USA) and Donald Jacobs (Saint Louis University Hospital, USA) are principle investigators.

Each trial will be examining the Bullfrog’s effect on restenosis rates after either percutaneous transluminal angioplasty (PTA) or atherectomy (ATX). Discussing the trial genesis, Dr Adams took note of the DANCE trial,⁴ which used the Bullfrog device in the SFA/popliteal arteries. “The interim results from DANCE are promising, and they set the premise for translating this technology into the BTK space,” he said.

“With drug-coated technologies, ultimately there can be a dosage limitation due to transit time and smaller surface areas, but with the Bullfrog delivery of liquid therapeutics, that limitation is resolved. With LIMBO-ATX, we designed a randomised

Continued on page 37
Continued from page 36

A study that would be able to show a difference between the drug therapy as an adjunct to standard atherectomy revascularisation versus atherectomy alone.

“For this study, we wanted a more informative endpoint for patency instead of late-lumen loss [LLL] or duplex ultrasound, since long BTK lesions are more complex than what those endpoints reveal.”

With lessons learned from DANCE, Dr Adams noted how they have now incorporated novel components into LIMBO, including a biomarker study – since the presence or absence of inflammatory biomarkers in the circulation is able to show at the earliest stage whether one is able to affect the disease – and Transverse view Vessel Area Loss (TVAL) – a measurement that integrates the percent diameter stenosis along the entire lesion length.

TVAL was developed by Professor Scheinert, Dr Ulrich Bechorner, Dr Kirk Seward from Mercator MedSystems, and Dr Adams himself. “This will help us understand how patients with long, diffuse disease below their knee may benefit from drug delivery,” he said.

“We also have more common markers (like LLL at six months, and Duplex Doppler Ultrasound Patency at one year) as secondary endpoints, so that we can compare our data to what has been published before. Beyond that, we have secondary endpoints that help to understand how the therapy works, such as the inflammatory biomarker measurements we make at baseline, 24-hours and four weeks after the therapy.”

As Dr Adams outlined, enrolment into LIMBO-PTA began this month, while LIMBO-ATX has been submitted to the Food and Drug Administration in the United States for their review. “We hope to have final data on 120 patients from LIMBO-ATX by mid-2017,” he said.

Commenting on the future for the Bullfrog technology, Dr Adams offered his perspectives: “I believe that the technology will become integrated into the standard treatment regimen during intervention based on the DANCE data, since anti-inflammation is a key goal in eliminating restenosis. Beyond that, I am looking forward to the use of the technology in CLI, where we still have difficulty with patency. I know that the company has been working with more advanced drugs that have other effects on the artery, including anti-proliferatives, and biologics that regenerate tissue or improve vascularity, and even a protease that can potentially reduce elastic recoil. I am particularly excited about this last drug, as it could change the way we approach CLI revascularisation.

“Mechanical revascularisation has been iterated, and come so far, so fast. I believe we are now about to see the same thing happen on the pharmaceutical and biological side. The immediate success of drug-coated balloons is just the beginning. There are so many drugs and techniques we can use to try to improve outcomes for our patients, and it’s rewarding to be pioneering a novel drug/device combination like this one.”

For more information on the DANCE trial, refer to the commentary by Professor Owens in Issue 1 of LINC Today (Available via the LINC App).

References
Home-made fenestrations: where is the niche?

During this afternoon’s session looking at cost-effective off-the-shelf solutions for challenging situations in EVAR, Armando Lobato joins others to discuss the clinical utility of inventive solutions such as parallel grafts, snorkels, and chimneys, which plug the therapeutic gap for emergency cases and high-risk patients.

Mario Lachat (University of Zurich, Switzerland) will present some long-term results of parallel grafts in the aortic arch, after which Giovanni Torsello (St Franziskus Hospital, Munster, Germany) discusses the clinical and technical advantages of parallel grafts in treatment of failed EVAR and Type I endoleaks.

Eric Ducasse (University Hospital, Bordeaux, France) concludes the session with a comparison of home-made versus regular fenestrated endografts. Speaking to LINC Today, he explained where their suitability lies: “Ideally, and usually, home-made fenestrations are made for the emergency setting.”

Eric Ducasse

Other anecdotal indications are that these cases are technically contraindicated for standard fenestrated, for reasons of challenging accesses and/or specific angulations. The most important factor of success is the absence of tortuosity in the cannulation area and also the quality (diameter, tortuosity) of the targeted arteries.”

Home-made fenestrations are not used in a great deal of cases, he stressed, and only in expert hands within the setting of a large volume centre. Literature on the topic is sparse, and with very few cases reported. “The only literature we find is reporting on short series of cases,” he said.

“There is very little regarding the home-made fenestration. It is very artisanal, so you cannot compare the different home-made fenestrations made by different physicians. This is an off-label group that demands very expert physician for some very dedicated cases. But we need to report that experience, because there may be some indications there.”

The first report of home-made fenestration was made in 1999 by Farugi et al. in a case of a type I endoleak following an aortomonoiliac aneurysm ex-
Continued from page 38

clusion.1 Arguably, longer-term data could shed light on specific complications such as migration and visceral branch loss.

Modified endografts present a viable alternative for those complex patients who cannot afford to wait for a custom-made endograft, in those patients with unsuitable anatomies, and in high-risk patients unsuitable for surgery or debranching procedures. However, the long-term durability of EVAR procedures is still in question. “The boundaries between open repair and endovascular treatment are still not clear,” stressed Dr Ducasse. “It really depending on the patient’s clinical status, the centre and surgeons’ experience there in the two techniques. It also depends on the volunteering of the patient.”

Going on to describe the process of selecting a fenestrated approach, and the construction of the graft, Dr Ducasse continued: “First, (and I have to say this legally) I practise this only in emergency cases. If this is an emergency case, there are only three solutions. There is the surgical solution, or the use of the chimney technique, or the home-made fenestration.

“I need to confess that in some cases I combine the last two techniques. I do one or two chimneys plus one or two fenestrations. This is also very helpful. After that, the use of homemade fenestration depends on the target artery. If it is a very large artery without any angulation, without any stenosis, I think this is a pure case for fenestration.

“We then perform the fenestration on the graft using a cautery pen, performing the same sizing as in a regular case. So it depends on the rotational angle, the length between the start of the graft and the ostium of the target artery – is this a visceral or a renal artery?”

Cost-effectiveness is the theme of the session, an issue relevant for some countries more than others. With a look to the relative cost of the home-made fenestration, Dr Ducasse commented: “It is certainly cheaper than the chimney technique, and certainly cheaper than the off-the-shelf CE marked fenestrated graft (that is also very rare). But it is really cheap; we use a regular standard graft and we just practice the fenestration upon that graft. This is usually reimbursed, as although we are using the graft off-label we are still using it in the normal way (just making some holes in it). This is a cheaper solution for all those emergency cases, versus the off-the-shelf option.

Despite its low cost, the experience required to carry out home-made fenestrations presents something of a barrier in centres that do not have the high volume that breeds the required artistry. Making fenestrations takes time, which may be critical in emergent cases. Describing his centre, Dr Ducasse said: “We perform a lot of CE mark fenestrations; between 30 to 70 cases per year. But it remains that for the emergent cases we don’t have any such off-the-shelf solutions.”

Eric Ducasse

Dr Ducasse will take an in-depth look at home-made fenestrations during the CICE@LINC session, ‘Cost effective off-the-shelf solutions for challenging situations in EVAR,’ taking place in the Discussion Forum between 12:35 and 13:15 today.

References


Continued on page 39
Can mechanical debulking replace surgery and lysis?

Mechanical debulking was the order of the day in a Tuesday morning session that ‘cut-through’ the data for arterial and venous endovascular therapy. In his lecture, Miroslav Bulvas (King’s Vineyards Hospital, Charles University, Prague) shared the stage to present data using the Rotarex device (Straub Medical, Switzerland).

Professor Bulvas began by posing the question of why take an interest in the mechanical endovascular removal of thrombi and emboli? “The answer is that we would like to lower mortality and morbidity rates associated with surgical approach and thrombolysis in the therapy of acute and subacute ischemia of lower limbs,” he said.

He went on to introduce a study that has been tasked in finding out whether limb-threatening acute and subacute ischemia can be managed without thrombolysis and open vascular surgery. “From 2009 to 2015 we have managed 316 patients, 203 with acute lower limb ischemia, and the majority in stage IIB [73% versus 27% in IIA],” he said. “There were 113 with subacute lower limb ischemia, and patients suffered from critical limb ischemia, tissue defects and short claudication.”

He went on to describe the three techniques employed for mechanical removal in the study. “There was debulking with the Rotarex catheter, which was used in all 316 patients to debulk bypasses, aortoiliac and femoropopliteal segments. The mode of action of the device is mechanical fragmentation of occlusive material, aspiration and transport outside of the vessel.

“The second technique was a classical aspiration thromboembolectomy, which was used in 123 patients, representing 39% of patients. With this technique we removed residual filling defects, and infrapopliteal acute

Continued on page 41
occlusions. And the last mechanical technique was extraction with endomyocardial biopsy device that was used in 26 patients, representing 8%. It was used to withdraw recalcitrant thrombi and emboli, and short eccentric residual stenoses.”

The majority of patients had recanalised femoro-popliteal segments (73%), with bypass (24%), aorto-iliac segment (12%), deep femoral artery (10%) and in-stent occlusions (23%) representing the rest of the treatment spread. Mean occlusion length was 23 cm, and the occlusion was due to thrombosis/embolism in 81/19% of patients respectively.

In the majority of patients, Professor Bulvas and colleagues used a Rotarex 8F catheter (80%, versus 25% for 6F) and ipsilateral approach [90%, versus 12% contralateral). The mean number of Rotarex passes was 3.4, with a mean running time of 2.3 minutes.

Professor Bulvas showed some angiographic data of case examples before/after debulking, commenting in general on the success of the technique for particularly tricky occlusions, and noting the device offers an endovascular approach that “we could never imagine” in the recent past.

Getting into more specific data, he continued: “With Rotarex, we were able to recanalise occluded segments in all patients. In 51 patients [16%] there we no residual stenoses after Rotarex debulking ... Mean residual percentage stenosis was 39% with mean lengths of residual stenosis of 3.8 cm. There were some adjunctive PTAs in 78%, stenting in 44%. There was no open surgery for ischaemia.”

Talking of some of the challenges, Professor Bulvas said: “In the infrapopliteal region we had to perform PTA in 40% of patients, stenting in 18%. There was aspiration in 53% of patients and bioptome extraction in 13%. We could not avoid thrombolysis definitely. It was necessary in 29 [9%] patients. “Surgery at the 30-day [point] was performed for fasciotomy in 3 cases, retroperitoneal or groin bleeding in 7, amputation 15, and necrectomy 13.”

Outcomes at 30 days / 12 months are shown in Figure 1. Professor Bulvas highlighted that the Rutherford classification changed from approximately 4 to 1 after the therapy. In addition, Ankle-Arm Index was significantly increased after the therapy, and the number of patent calf vessels significantly increased after the procedure.

“There were some major complications in 11 patients (3.5%), and the minor complication frequency was 19%,” said Dr Bulvas.

Offering his conclusions, he said: “With the Rotarex device, we have re-established blood flow in 100% of aortoiliac and femoropoliteal arterial segments and bypasses. In 78% of those
Recanalised vessels, adjunctive endovascular techniques (PTA, stenting, atherectomy) were applied at the sites of residual stenoses. Additionally, 62% of patients required non-Rotarex infrapopliteal intervention.

“There was one death (0.3% of 316) associated with thrombolysis. Frequency of major complications was low and all minor complications were solved by endovascular or conservative means. Open surgery was not needed to manage limb ischaemia and thrombolysis was used to treat infrapopliteal occlusions in 28 patients (9% of 316).

“Rotational thromboembolectomy is an efficient, safe and rapidly-working technique for the therapy of acute and sub-acute ischaemia of lower limbs. It has good potential to reduce the number of thrombolytic and open surgery procedures, and their risks, and opens the way for immediate treatment of residual and parallel lesions. Additional extraction techniques were necessary for best results.”

Continued from page 41
Novel technologies and approaches in carotid artery stenting (CAS) were given their due focus on Tuesday at LINC, in a session that paid particular mind to micromesh stent technology in this treatment space.

Double layer mesh stents represent a hybrid technological advancement that endeavour to combine the optimal properties of open-cell stent designs (greater vessel adaptability) and closed-cell designs (plaque coverage) – characteristics that were historically more a case of ‘either/or’. They do this via a combination of an internal micromesh layer for the plaque coverage, and an external self-expanding nitinol layer that offers the kind of flexibility more akin to open cell designs.

Stepping into the spotlight during yesterday’s session was Alberto Cremonesi from the Maria Cecilia Hospital – GVM Care & Research, Cotignola, Italy, who introduced an Italian registry that has been tasked with examining the impact of a novel micromesh device in CAS. 

Perhaps we could begin with a recent history of CAS – in particular the data surrounding it, how it compares to endarterectomy, and what embolic considerations need to be factored in?

Carotid artery stenting, which has emerged as an alternative therapy to high-risk surgical patients, has become an increasingly important procedure in the optimal management of all patients with carotid disease.

What we have learnt from the latest randomised trials and
high-volume centre registries is that the real difference in neuro-events between carotid endarterectomy and carotid stenting occurs in the early post-procedural phase, mainly from the time of the procedure to the full re-endothelialisation of the stent frame (30 days).

After this vulnerable period, scientific evidence clearly demonstrates equivalent outcomes between surgical and endovascular treatment both in terms of stroke prevention and restenosis rate. The extensive use of embolic protection devices (EPDs) can dramatically reduce intra-procedural neuro-events, but obviously EPDs, acting only during the procedure, don’t impact on late neuro-events which are mostly related to intra-stent plaque protrusion and consequent distal embolisation.

It has been suggested that the ideal stent in the carotid region would manage to offer excellent apposition, flexibility and plaque coverage. Although no stent is perfect, are micromesh designs closing in on this ideal?

So far, the impact of stent design (i.e., open cell versus closed cell) on outcomes has not been fully elucidated. While open-cell stents allow for better conformability, closed-cell devices have superior scaffolding properties and plaque coverage. With that in mind, recently there has been development of novel carotid stents with double-layer mesh technology: Roadsaver (Terumo, Japan) and the CGuard Embolic Protection System (InspireMD, USA).

The Roadsaver stent is composed of an external self-expanding nitinol layer for offering the flexibility and conformability of an open cell design stent, while an additional internal nitinol micromesh layer should convey superior scaffold properties for optimal plaque coverage.

“To date, clinical results are striking, with no cerebrovascular events reported in any centre.”

Alberto Cremonesi

The CGuard stent is composed of a nitinol self-expanding frame, and MicroNet technology – an ultrathin polyethylene terephthalate (PET) material for optimal plaque coverage.

In both stent frames, the micromesh technology aims at preventing plaque protrusion though the stents struts, and ischaemic events sometimes observed following the procedure.

What can you tell us about the Italian registry that you have been overseeing?

We started collecting data about patients receiving a the Roadsaver stent about one year ago, when the device was introduced in our daily practice. Our main goal was to take a snapshot of Italian approach to carotid stenting, so we decided to include data from high-volume centres with different specialists treating carotid disease with their own perspectives: interventional cardiologists (Maria Cecilia Hospital, Cotignola), vascular surgeons (Siena University Hospital, Siena) and vascular radiologists (AOU San Giovanni Battista, Torino). We believe this strategy could give a more faithful picture of the effective impact of this new-generation device on carotid stenting.

What early data are you going to share at LINC? Are results promising? And when will the next data likely be ready for showcasing?

All patients completed their 30-day clinical follow-up, and to date, clinical results are striking, with no cerebrovascular events reported in any centre. We are going to present our population characteristics and procedural data, together with the 30-day clinical outcomes. Interestingly, some patients underwent an optical coherence tomography (OCT) evaluation of their final result: the results we are going to show suggest a very low risk of plaque prolapse with this stent and could be hypothesis-generating for larger and properly addressed trials to estimate...
the OCT role in carotid stenting as a tool to better stratify short-term clinical outcomes.

Hopefully, we will soon be able to complete six-month follow-up in order to assess both six-month neurological events (which we don’t expect to be much different than those at one-month follow-up) and stent patency (as assessed by Echo-Doppler routine evaluation).

Tying in with the advent of new stents, and the registries/trials examining them, do you think the future is now much brighter for CAS?

Our personal perspective is that double layer mesh stent technology represents a breakthrough in carotid stenting. Today we have consistent data suggesting that a new paradigm in ischaemic stroke prevention and in the endovascular approach of carotid bifurcation lesions can be safely offered to only very simple anatomies to those with very complex anatomical scenarios, considering both the carotid lesion and the vascular anatomy involved.

Similarly, is it the beginning of the end for added embolic protection devices? Or would you recommend they are still used at least for the time being?

Even if I strongly believe in the concept that stent scaffolding and conformability play a significant role not only for achieving good procedural results, but also for improving 30-day outcomes, I continue to think that the extensive use of embolic protection devices is still mandatory, both in symptomatic and asymptomatic patients.

With double-layer technology we are demonstrating that stents may exert sustained intrinsic anti-embolic properties, but many data support the evidence that the most dangerous phase of the endovascular procedure occurs during the stent implantation and post-dilatation. During this phase embolic protection systems represent a valid and still unmatched way to reduce neuroembolic events.

References