VERVE DAILY NEWS

Issue 1
Thursday 3 / Friday 4 December, 2015

in conjunction with LINC Australia

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Welcome to the 2015 VERVE Symposium

Welcome to the 3rd annual VERVE symposium, endovascular masterclass and global discussion forum. This year's program continues to mature into one of the best examples of a comprehensive, multidisciplinary, vascular discussion forum found in this part of the world. We have gathered together 15 international vascular leaders, as well as over 30 experts from the region to provide world-class education on the latest topics, technique advances and scientific data.

More than 80 quick-fire presentations will be given on topics which cover the breadth of vascular disease, diagnosis, interventional and open-surgical procedures. There will be case-based discussion forums and dedicated panel interactions during both the live transmissions and as part of structured aortic sessions. Seventeen live cases will be transmitted from the University Hospital, Leipzig and Sydney's Prince of Wales private hospital, to showcase cutting-edge interventional practice and technique. The latest scientific data will be presented to complement the body of knowledge which is currently applied to gold-standard vascular practice.

This year we have incorporated an ultrasound-focused component on the Thursday morning to address modern imaging dilemmas around the fast paced world of endovascular practice. Vascular specialists and sonographers will present side-by-side to share their individual experiences and we will demonstrate live scanning. In addition we have our first IRSA@VERVE session at lunch-time on Friday to encourage multi-disciplinary cross-pollination of ideas and techniques between specialties.

Once again this year we will collect all of the oral presentations and live case recordings to include in our online library. This will be accessible a month after the symposium for all registered delegates to access free of charge.

Finally, it pays not to miss the social opportunities at VERVE. Join us for a glass of Veuve Cliquot champagne on the Thursday night following the completion of the final session, and for the much anticipated Official Symposium Party on the foreshore of Sydney Harbour alongside the Sydney Opera House. These are great opportunities to network with colleagues and catch up with friends.

Ramon Varcoe
Course Co-Director, The VERVE Symposium and LINC Australia

300-strong update for innovative Nellix EVAS system

Thursday afternoon's programme will feature an update of results using the Nellix endovascular aneurysm sealing (EVAS) system (Endologix, USA) in the treatment of abdominal aortic aneurysms (AAAs). The Nellix EVAS system is the first device to treat AAAs by sealing the entire aneurysm sac, being designed with the aspiration to widen the accessibility of endovascular therapy, reducing all types of endoleaks, and improving stability and long-term patient outcomes.

From October 2013 to September 2014, clinical investigators at centres in Europe and New Zealand enrolled 300 patients in the EVAS FORWARD Global Registry – the first-ever prospective EVAS all-comers clinical study – in which Nellix's durability would be assessed via core lab assessment of CT scans along with independent physician adjudication of outcomes.

As one of the principle investigators of the study, Matt Thompson (St Georges Hospital, London, UK) will share an update of the latest results from 300 patients during a session dedicated to the unmet needs of AAA treatment. With that in mind, Professor Thompson spoke to *VERVE Daily News* to offer a glimpse of what he will be touching upon, beginning with a run-down of the EVAS-FORWARD registry particulars: "Unique to the study, 33% of treated patients had complex AAA anatomies including conical necks, short (<10mm) or angulated (>60∞) necks, and common iliac artery diameters >25mm," he said.

> "One-year follow-up results confirm the encouraging findings from earlier data presentations, adding to the knowledge base relating to the Nellix Aneurysm Sealing System." Matt Thompson

"Despite the complexity, we continue to observe good short- to mid-

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Session II: Unmet Clinical Needs in the Treatment of Abdominal Aortic Aneurysms Thursday **2:30–3:45pm**

300-strong update for innovative Nellix EVAS system

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term results in a patient population that had no screening or anatomical restrictions at enrolment, constituting the broadest range of aortic anatomies for any AAA study. Patients will be followed for five years, and results will be reported annually."

Earlier this year at meetings including the Leipzig Interventional Course, and The Charing Cross Symposium, Professor Thompson and other study leaders relayed good endoleak (30 days), reintervention and mortality results from early analyses of the data. At The VERVE Symposium, Professor Thompson will be offering longer-term data that builds on these early snapshots, and it seems the results are still acceptable: "The presentation of one-year follow-up results confirm the encouraging findings from earlier data presentations, and adds to the knowledge base relating to the Nellix Aneurysm Sealing System," he said.

As Professor Thompson outlined, key highlights from these recently reported data (mean follow-up of 14 months) include:

- 94.5% freedom from any endoleak from day 0 through 12 months
- 0.7% composite endoleak rate at one-year
- Low overall freedom of secondary intervention (92.3%)
- Low reintervention rate for limb occlusion (1%)
- Low aneurysm-related mortality (0.4%) and overall major adverse events (5.9%)
- 95% overall survival through year one

"In these data, the majority of Type 1a endoleaks occurred early, were attributed to early procedural learnings, and have since led to recently-described best practices such as endobag pre-fill for accurate volume and pressure estimation, accurate stent positioning in the infrarenal neck, and Nellix stent balloon inflation during polymer fill," continued Professor Thompson.

"We have also learned that transcatheter embolisation of Type 1a endoleak appears to be effective. In this one-year report, no new Type 1a endoleaks > 30 days were reported. What's more, the persistent endoleak incidence at one year was encouragingly low (one Type Ia endoleak and one Type II endoleak).

"As with endovascular aneurysm repair [EVAR] in its infancy, one would expect complications and key learnings to emerge during this early maturity phase of EVAS. However, despite the learning curve (both institutionally and globally) the results are comparable to those reported with EVAR, achieved in a complex patient cohort with no prospective screening."

With these promising results to hand, the Nellix system clearly has great potential going forward. As such, could EVAS be a 'game changer' for the field? "Now that we have entered into the mid-term phase of the EVAS FORWARD Global Registry, we see trends that may support EVAS as a durable therapy for AAA patients," said Professor Thompson, adding that the applicability of endovascular therapy for patients with AAA has been enhanced both on- and off-IFU (Instructions For Use).

"The endoleak rate at a year is very low, and a 0.7% limb occlusion rate at one year is also impressive. Nellix has the ability to successfully exclude large iliac aneurysms while preserving the hypogastric artery, another challenge with traditional EVAR. Interestingly, the 95% freedom from all-cause mortality with a low rate of cardiovascular-related adverse events offers a glimpse of a signal that is worth watching."

Taking a moment to touch upon the limitations of EVAS at the current time, Professor Thompson first noted that there is indeed a learning curve for the device that must be considered. "In our experience at St. George's Vascular Institute, we first became familiar with the fundamentals of EVAS prior to attempting challenging anatomies and off-IFU applications such as EVAS with parallel grafts, revision for failed EVAR, or EVAS in acute AAA," he said. "As previously mentioned, we've identified optimal sealing techniques and safe use of pressure during endobag filling that have since been adopted."

> "Now that we have entered into the mid-term phase of the EVAS FORWARD Global Registry, we see trends that may support EVAS as a durable therapy for AAA patients."
>
> Matt Thompson

He went on to stress that another critical consideration with EVAS is imaging surveillance. Particularly, given that EVAS is a new and different method of AAA repair, normal postoperative imaging has unique appearances that change with time, and complications (such as endoleaks) also have specific appearances that differ from conventional EVAR. It is therefore paramount that a sound knowledge of what constitutes 'normal' appearances and complications is established for centres performing EVAS in order to avoid misdiagnoses (e.g. attributing appearances of contrast in the endobags for endoleak) and misperceptions that the endobags prevent visualisation of endoleaks.

However, as Professor Thompson described, there are emerging resources that can help in this imaging surveillance: "Published this month in the Journal of Endovascular Therapy is a consensus document by Holden et al. on imaging findings after Nellix EVAS, based on the collective experience of the sites involved in the Nellix EVAS Global Forward Registry and the US Investigational Device Exemption Trial."

In his closing remarks, Professor Thompson looked to the future of EVAS, first commenting on new data that is anticipated. "As we continue to follow the EVAS FORWARD Global Registry patients for five years, additional key findings are expected to emerge that may be applied to the practice of EVAS," he said, adding that improvements in device design will also pave the way for enhanced procedural success, while maintaining the principles of EVAS.

He continued: "We also are interested in evaluating the applicability of EVAS for other indications. Based on proof of concept testing and on the acceptable early clinical results among a sub-cohort of patients treated with Nellix and parallel grafts, we recently initiated the ASCEND registry (Aneurysm Sealing in Complex Anatomies: Evaluation of Nellix Durability). This is a physician-initiated, open-label, single-arm multi-centre study of Nellix with parallel grafts in juxta-renal, opera-renal, and supra-renal AAA. We plan to enrol up to 200 patients from 10 international centres with five-year follow-up and endpoints typical of EVAR therapy in complex AAA."

Professor Thompson will present the latest data from the Nellix EVAS FORWARD Global Registry during Thursday's session 'Unmet Clinical Needs in the Treatment of Abdominal Aortic Aneurysms', held at 2:30 – 3:45 pm.

VERVE DAILY NEWS

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Session III: Current Strategies … Treatment of Calf Artery Disease & CLI Thursday **4:00–6:00pm**

‘Room for expansion’
DCBs below-the-knee

The ‘Australian experience’ with drug-coated balloons (DCBs) will be exhibited on Thursday afternoon, with Ian Spark (Flinders Medical Centre, Adelaide, Australia) sharing his thoughts on the ins and outs of DCB use below-the-knee (BTK).

VERVE Daily News caught up with Professor Spark to chew over some of the important points in DCB use in the BTK region, as well as finding out just what messages he will be keen to share with the audience.

Perhaps we can begin by framing the core issues in the comparison of DCBs. Would you agree that different devices, data sets and interpretations/endpoints mean that comparisons can be difficult?
There are still comparisons available to be made, but what is clear is that there are significant differences in the outcomes between various devices, which raises the question of the absence of a class effect. Lack of standardisation of technique and factors such as inflation times and antiplatelet regimens may be more relevant to the outcomes than we think.

What are your thoughts on the potential of more rigorous comparative trials between one DCB and another? They would surely be expensive and require a massive patient population, but could they hold key value?
I do think more randomised trials are needed, in particular head-to-head comparisons. A lot of the early trials were for device approval and hence don’t often reflect ‘real world’ experience. It has been shown that the data are positive for DCBs for short-to medium-length lesions in non-severely calcified vessels that can be dilated. So this is where the strength of the registries lie, as long as we collect the appropriate outcome measures.

There are an increasing number of drug coated balloons coming onto the market, again with short duration (six-month follow-up) safety trials supporting them, but we do lack long-term data.

What components stand out most in terms of how DCB designs differ? Aside from drug choice, what are your perspectives on (for example) drug delivery, construct of the balloon, and open/closed/folded setups? Have we learnt important lessons along the way?
I think we are still learning. The current balloons have the same drug, but differ in their coating, which can result in an uneven covering, downstream drug loss during balloon transit and inflation, and a less uniform dose delivery. Various excipients (urea, citrate, sorbitol) are also being used, and they play a significant role in drug transfer and release rate, but the ideal solution is still awaited.

What will you bringing to the table during the session in terms of the ‘Australian experience’? Are there aspects you are particularly keen to share?
We are trying to start an Australian/New Zealand collaboration, and one option we hope to initiate is an Australian/New Zealand registry for the use of DCBs in the SFA and popliteal arteries. Currently we have 180 patients from our own site and hope to be able to present our experience.

> “Lack of standardisation of technique and factors such as inflation times and antiplatelet regimens may be more relevant to the outcomes than we think.”
>
> Ian Spark

What do you feel the future should hold in terms of further study/design, and crucially, should the message that DCBs are indeed not equal be more prominent on the minds of their users?
I think the selection criteria for which DCB to use should be based on the available evidence we have. As to when to use them, there is evidence to support the use of DCBs in short- to medium-length lesions in non-severely calcified lesions. For the future we need more long-term data, with the results of DCBs in longer, more complex lesions.

Professor Spark will present ‘An Australian Experience with Drug Coated Balloon BTK Interventions: Not All DCB are Created Equal’ during the session ‘Current Strategies for the Treatment of Calf Artery Disease and Critical Limb Ischaemia’, held at 4:00 – 6:00 pm on Thursday afternoon.

Session IV: CTO Crossing and Tibiopedal Access with the Experts Friday **7:45–9:30am**

Angiosome concept rewards revascularisation of tricky wound-related arteries

Despite the inherent difficulty, tackling a challenging vessel that feeds directly into a wound area is worth the effort, delegates will hear on Friday morning during a presentation that places the angiosome concept front and centre.

By delineating body tissue into three-dimensional blocks that are fed by specific arterial and venous sources known as ‘angiosomes’, the concept hopes to improve revascularisation of ischemic tissue lesions, with limb salvage as a central component.[1] “It is still trying to achieve a healed viable limb for the patient, but the philosophy of revascularisation is different,” Shannon Thomas (Prince of Wales Hospitals, Randwick, NSW, Australia) told *VERVE Daily News* ahead of his presentation.

“The previously-accepted philosophy of revascularisation was to pursue any vessel you could get down to the ankle – if you could revascularise it then the limb will be saved. But there is increasing evidence showing that might not be enough. If you can achieve that one vessel to the ankle, there are still patients that lose their legs because that wound hasn’t healed – and that’s where the angiosome concept comes in.”

> “There are still patients that lose their legs because [a] wound hasn’t healed – and that’s where the angiosome concept comes in.”
>
> Shannon Thomas

Dr Thomas went on to stress that at its core, the angiosome concept is all about ‘wound-directed’ arteries, i.e. working to revascularise the artery feeding the wound in question, rather than picking the easiest route. Looking to the evidence supporting the concept, he added: “There are

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Session IV: CTO Crossing and Tibiopedal Access with the Experts Friday **7:45–9:30am**

Angiosome concept rewards revascularisation of tricky wound-related arteries

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a couple of papers out there: recently there was a meta-analysis as well that seemed to be supporting this hypothesis – that if you get blood flow into that wound-related artery then you get a higher rate of wound healing, and the wound seems to heal quicker."

He added: "[The meta-analysis] looked at a total of around 10-12 papers, each of which were basically single centre prospective cohorts, and they pooled all of the patients to do their analysis. They found that there was concordance between having direct revascularisation, and quicker healing of the wound, and limb salvage."

However, taken as a whole, evidence to date is not robust, which means there are still sceptics of the angiosome approach: "That makes it difficult to apply to all centres around the world. But it is rapidly emerging over the past 10 years," said Dr Thomas.

"One of the problems in this area is that the definitions are so loose. Everyone is using different definitions when they are publishing their papers, so to try and combine all of that into something that is meaningful is difficult. But the evidence is building, and there are more and more papers suggesting that this works.

"Yes, there are papers out there where people have not used an angiosomal approach, and still have very good limb salvage, and that is what a lot of the critics point to. But certainly when you look specifically at angiosomal versus non-angiosomal approaches, the evidence for the number of patients treated successfully is building."

Commenting on the types of patients who may not be suitable for an angiosome-first approach, Dr Thomas underlined that factors such as high-level proximal disease (a blocked iliac and SFA, for example), may benefit enough from revascularisation of those vessels, without further need for angiosomal intervention. "Whereas the other situation is when you've got someone who has diabetes, and has tissue loss, ulcerations – recalcitrant tissue loss as well," he said, adding: "If there, for instance, you have a heel ulcer, yet there is an anterior tibial artery coming down into the foot, then I would say that anterior artery doesn't really supply the heel [sufficiently]. And a lot of patients end up losing their foot because of that.

> "If you get blood flow into that wound-related artery then you get a higher rate of wound healing, and the wound seems to heal quicker."
>
> Shannon Thomas

"Certainly our experience here at the Prince of Wales is that if you can get the posterior tibial and peroneal artery going … then you can revascularise the heel and save the limb. So I think that is the context where I see a place for this concept: it is in those situations where you are dealing with wounds in very specific territories, and where there is [insufficient] blood supply into those territories."

One aspect that has garnered intrigue in the wider angiosomal field is the balance between limb salvage and healing, i.e. is there room for improvement in how we define a successful revascularisation in the short- and long-term, and could follow-up be a crucial tool to understanding how well that salvaged limb is actually performing? "My personal opinion is that limb salvage may be too crude a measure," said Dr Thomas. "For instance if you salvage the limb, but it's not a usable limb – i.e. the patient cannot walk on it because there are ongoing wound areas, or ongoing pain in the leg from incomplete revascularisation – then that is useless. It is not just limb salvage, it is functional limb salvage."

With this in mind, Dr Thomas was keen to stress that an overhaul of revascularisation definitions may be a wise step forward, in particular tightening up concepts of wound healing, wound areas, and how a wound presents before revascularisation begins. "You can't really compare an entire gangrenous forefoot to a small gangrenous toe," he said. "The amount of healing required is completely different. And that is not reflected at the moment in most of the classifications that we use to define wounds before revascularising them."

> "My personal opinion is that limb salvage may be too crude a measure … It is not just limb salvage, it is functional limb salvage."
>
> Shannon Thomas

He continued: "The SVS [Society for Vascular Surgery] came up with the definition of major adverse limb event (MALE), which is amputation or need for second revascularisation after a primary revascularisation surgery. And I think that is a new concept. We need to have these definitions that we all use in a standardised fashion for these angiosomal-type studies. And then use these definitions as we follow patients up."

Looking to the future, Dr Thomas is hopeful that as technology and skills improve, more and more people will be doing pedal and wound-related arterial revascularisation techniques. Indeed, just in terms of his own centre's experience, adoption of the angiosome concept has been a great success: "Here at the Prince of Wales – and we have data to back it up – the amputation rate has just fallen through the floor," he said. "And I think that is what we are going to see: more units adopting the philosophy, and beginning the see the results. I would hope that major amputation really becomes a thing of the past."

He concluded: "At the moment, I get a lot of patients who have seen other people who've said they need their leg amputated, but then we will do an anterior tibial or dorsalis pedis [revascularisation] down to the wound, get that region healed, and then patients are really happy. They were told initially that their leg would be removed, but then they go back home and their wound is healed. So I am hoping that when people see the results of this [angiosome concept], it really spreads."

Dr Thomas will explore the angiosome concept in more detail during the session 'Session IV: CTO Crossing and Tibiopedal Access with the Experts', held at 7:45 – 9:30 am on Friday morning.

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1. V Alexandrescu , M Söderström, M Venermo. Angiosome theory: fact or fiction? Scand J Surg. 2012;101(2): 125-31

Session VI: Treatment of Thoracic Aortic Dissection and Arch Aneurysms Friday **11:00–12:30**

Uncomplicated type B aortic dissection
Some are more equal than others

Mortality rate is much lower in patients with type B aortic dissection compared to their type A counterparts, with 70% presenting with uncomplicated dissection.[1] Yet evidence suggests that this uncomplicated type B cohort includes a sub-group at high risk of rapid progression – the so-called 'initially uncomplicated' group of patients.

With a discussion of the balancing act surrounding decisions to treat such cases, as well as the urgent need to address the question formally, Michael Dake (Stanford University School of Medicine, CA, USA) spoke to *VERVE Daily News* ahead of Friday's session on the treatment of thoracic aortic dissection and arch aneurysms.

"'Initially uncomplicated' implies that there is a group of patients who clearly will progress," said Professor Dake. "The challenge is to determine who these are."

Complicated type B aortic dissection involves a rupture or symptomatic branch vessel occlusion.[2] Those patients who remain uncomplicated are so labelled because they do not necessarily dilate their false lumen, and such cases are treated with optimum medical therapy, explained Professor Dake: "Clearly that frequency of false lumen dilatation to the point of being aneurysmal occurs in only about 30% to 40% of patients. That means that the majority don't go on dilating. They may die from something else, but they don't have the problem with the false lumen."

The evidence that an at-risk subgroup exists – comprising initially uncomplicated type B patients – lies in key anatomical features and dissection characteristics, and possibly other factors. Some of these are well known, explained Professor Dake, while others are not. "There is the recognition that there are features that may place a certain subgroup of that uncomplicated group at risk of early progression of disease or complications.

"We don't really know what all of these criteria are, but a number of the features are now well established. There are multiple corroborating articles in the medical literature that suggest that not necessarily one or two factors may prognostically determine who is at risk – but certainly, working kind of like a jury with the preponderance of the evidence, we could determine that this patient, who does not have a rupture or does not have branch vessel compromise or ischemia, is still at risk of progression of disease and therefore might benefit from early intervention."

There is still uncertainty, though, in whether or not a particular patient would indeed benefit, as Professor Dake cautioned. "There are complications from any intervention, so we have to weigh the risk in there too. The main risk would be the potential for retrograde type A dissection, or some complication from the stent graft or the procedure itself.

> "There is the recognition that there are features that may place a certain subgroup of that uncomplicated group at risk of early progression of disease or complications."
>
> Michael Dake

"The consensual feeling right now is that we are poised to move into an era where we will be addressing these initially uncomplicated (but high risk of progressing to complications) patients with early intervention. This doesn't necessarily mean acutely within the first few hours, but perhaps within the first month to three or even six months. That would have to undergo some sort of clinical trial to determine whether that makes sense or not."

Optimal medical therapy for uncomplicated type B dissection effects an 8% to 9% 30-day mortality rate. And it is not known whether earlier treatment might mitigate that risk, noted Professor Dake, explaining that procedural

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Session VI: Treatment of Thoracic Aortic Dissection and Arch Aneurysms Friday **11:00–12:30**

Uncomplicated type B aortic dissection
Some are more equal than others

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risks are not to be sniffed at with retrograde type A dissection occurs in as many as 2% to 3% of cases.

"Most people would say that we need to let this dissection 'season', and stabilise the septum and the aorta itself," he continued. "Maybe we would then have less risk of a retrograde type A dissection if it wasn't done in the hyper-acute phase, but was done later on. But when does later on mean? One, three, six months? The problem is that, if we wait that long, we basically give away the chance that we might influence that early mortality of the dissection itself which might be reduced if we were to treat it. So there is a balance, and I don't think anyone really knows the best answer.

"Most people think it is worth waiting some period of time to avoid the complications of the hyper-acute phase. When you get to nine months, certainly some of the patients won't have the potential to remodel the aorta as completely as if they were treated more acutely. Individually though, some may. When you get to that stage, there are individual patient characteristics that influence whether you can get the desired ideal result."

Difficulty lies in knowing that, with each passing month, a small number of patients will experience some kind of event. In addition to this, said Professor Dake, patients can be lost to follow-up, possibly turning up only when they experience a rupture. While clinical decisions are reasoned based upon best available evidence, knowing more precisely how to identify those patients at greater risk can only come from more detailed study.

"That is going to be the next step once people get to that level of comfort," said Professor Dake, "and when there are interested parties who want to test whether or not early treatment can benefit some patients."

But this is always a matter of funding, he concluded, especially when competing with other large research projects that affect a larger proportion of the population: "In many cases now a lot of interest in medical trial funding (that is not industry related) would be from people trying to answer big questions like back pain, cancer, diabetes.

"Dissection, although very interesting and catastrophic, still does not affect enough of the population that people are willing to spend five million dollars to study it. The alternative is to get industry to co-fund it, and that has pluses and minuses, with the potential for bias to get introduced. Working through a situation that is more than 'how would you do a trial?' but actually, and more importantly, 'how would you fund the trial?' is an ongoing process. A lot of different groups are focussed on this, because this is right now one of the most interesting and (arguably) relevant questions that we could answer."

> "Working through a situation that is more than 'how would you do a trial?' but actually, and more importantly, 'how would you fund the trial?' is an ongoing process."
>
> Michael Dake

Dr Dake presents, 'Is There a High-Risk Sub-Group of Patients With Initially Uncomplicated Type B Aortic Dissection?' during 'Session VI: Treatment of Thoracic Aortic Dissection and Arch Aneurysms' taking place on Friday between 11:00 and 12:30.

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Session V: New Horizons in Carotid Intervention Friday **9:30–10:40am**

New findings on asymptomatic carotid artery disease

Michael Jaff (Harvard Medical School / Massachusetts General Hospital, Boston, USA) is a professor of medicine specialising in vascular medicine, including peripheral arterial disease, venous thromboembolic disease and aneurysmal diseases. He is the founder and medical director of the Vascular Ultrasound Core Laboratory (VasCore), which facilitates novel clinical trial strategies for peripheral vascular device and drug evaluation. *VERVE Daily News* caught up with Professor Jaff before Friday's 'New Horizons in Carotid Intervention' session in which he will give a comprehensive update on trials investigating asymptomatic carotid artery disease.

The serendipitous discovery of cerebrovascular pathology brings certain dilemmas to patients: on one hand the severity of the pathology, but, on the other hand the risks of surgical treatment, so the benefit may seem hypothetical. Professor Jaff explained how to inform patients of their risk of severe events using clinical evidence to help with decision-making. "When we consider management strategies in patients with extracranial carotid artery disease, we first determine if the patient has symptoms related to the carotid artery stenosis.

"Once that has been determined, we confirm the severity of the stenosis of the internal carotid artery. If the stenosis exceeds 70%, this prompts further discussion about invasive therapy. Next, we then consider the general health of the patient, such as co-morbid conditions that may influence disease management, and also whether we believe that the patient has a likelihood of surviving five years from the time of invasive therapy."

There are three options for patients with extracranial carotid artery stenosis: medical therapy[1], carotid endarterectomy [CEA] and carotid artery stent [CAS] deployment. Most experts believe that optimal medical therapy, (including daily administration of aspirin, clopidogrel and, in some patients, antihypertensive agents, as well as management of various risk factors such as blood pressure, cholesterol, weight etc.,) is the foundational therapy for all patients with carotid artery stenosis.

> "Medicare will only reimburse for carotid stents performed on patients with severe carotid stenosis who has symptoms from the stenosis and is determined to be high risk for CEA."
>
> Michael Jaff

The decision to perform surgery depends on symptom status: carotid endarterectomy or carotid artery stent deployment should be considered if the carotid stenosis exceeds 70% and there is reasonable likelihood of the patient surviving for five years or more; if the patient has no serious medical condition (such as active coronary artery disease, advanced chronic obstructive pulmonary disease or chronic kidney disease); and if the anatomic situation is not high risk (for example, restenosis after prior carotid endarterectomy, contralateral internal carotid artery occlusion or tracheal stoma).

Professor Jaff highlighted a lack of cohesion between this clinical evidence and health insurance guidelines, "In the United States, our government health insurance plan, Medicare, will only reimburse for carotid stents performed on patients with severe carotid stenosis who have symptoms from the stenosis and is determined to be high risk for CEA[2]."

Professor Jaff described findings from very recent trials with which he was involved. The ROADSTER trial reported the lowest stroke rate (1.4%) for a multicentre clinical trial of CAS using a novel transcarotid neuroprotection system that provides protection against periprocedural embolisation[3]. Remarkably, these results were also observed when surgical teams had little or no prior experience of these techniques. He was also involved in a retrospective cohort study linking 30-day mortality with relative experience of physicians and hospital procedure volumes. Whilst previous studies indicate that provider proficiency can influence patient outcomes, this new data shows that patients undergoing carotid artery stenting by higher volume providers tended to be healthier patients and were associated with less co-morbidity and that there were smaller proportions of symptomatic or non-elective patients than lower volume providers, suggesting that the high volume providers also may employ different patient selection procedures.

Professor Jaff then went on to speak about the ACST-2 trial, "It is the largest trial ever conducted in patients with severe asymptomatic carotid stenosis requiring revascularisation; this on-going trial compares CAS with CEA, seeking to compare their benefit in preventing stroke. Interim data shows that contemporary carotid intervention for asymptomatic stenosis has a low risk of serious morbidity and mortality[4]. Another study, 'Carotid revascularization for primary prevention of stroke' (CREST-2) that is ongo-

ing in the USA consists of two independent multicentre, randomised controlled trials comparing any invasive therapy (CAS or CAE) with optimal medical therapy versus medical therapy alone in asymptomatic patients with carotid stenosis."

The CREST-2 study is particularly pertinent because the evidence supporting revascularisation over medical treatment is based on trials that recruited up to 30 years ago, yet since then medical treatment has improved considerably with respect to stroke prevention. Professor Jaff added: "It is challenging to presume that the results of early trials of CEA to optimal medical therapy are as accurate today, given that optimal medical therapy is far more comprehensive today that when, for example, the ACAS trial was published."

> "It is challenging to presume that the results of early trials of CEA to optimal medical therapy are as accurate today, given that optimal medical therapy is far more comprehensive today."
>
> Michael Jaff

He continued: "I am worried that unless patients who absolutely would be considered for intervention (>80%) are not included, and if the mean stenosis severity is 60-70%, there will be no real comparison as these patients are commonly managed with medical therapy alone."

Looking to the future, Professor Jaff concluded by speaking briefly about VasCore, and potential methods for lesion selection and patient stratification, "Although carotid plaque imaging via duplex ultrasonography has not reliably predicted symptoms and outcomes of the various treatments for internal carotid artery stenosis, we hope future assessments with, for example, MRI-plaque imaging and FDG-PET imaging may be very helpful."

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Session V: New Horizons in Carotid Intervention Friday **9:30–10:40** am

Evidence-based medicine can improve CEA surgery

Carotid endarterectomy (CEA) reduces the risk for stroke in patients with internal carotid artery stenosis but the best surgical technique has been debated for a number of years. With this in mind, *VERVE Daily News* was fortunate to speak to experienced CEA surgeon, Bernard Bourke (Central Coast Area Health Service, Gosford, NSW, Australia), who is president-elect of the Australian and New Zealand Society for Vascular Surgery. The interview was in advance of Friday's presentation in which he will provide exemplary evidence-based recommendations on best practice.

He began: "Over the last 30 years I have carried out almost 2000 CEA operations. There are various methods that we have developed and published; I am going to talk about the methods which I've concluded are the safest."

Because most strokes from carotid plaques are from embolisation rather than flow reduction, Dr Bourke was keen to highlight that a key objective of CEA is preventing embolisation. "The aim of surgery is not only to remove the source of cerebral embolism but also to perform the procedure in such a way that you are not causing the embolism.

"This is under-appreciated because practitioners can get hung up on the degree of stenosis and perceived blood flow reduction, instead of being more concerned about what the plaque is doing. Carotid artery pathology usually manifests itself differently from arterial pathology elsewhere in the body – for example, in the leg where the degree of arterial stenosis is very important. With the carotid, we should be much more concerned about what the plaque is depositing in the brain."

Early distal control of the internal carotid artery (ICA) beyond the plaque during CEA allows the vessel to be isolated and clamped, therefore protecting the brain from particulate plaque embolism. In his 2002 publication in the Journal of Vascular Surgery, Dr Bourke demonstrated the effectiveness and feasibility of this technical approach[1], which has since been corroborated by others.[2] He explained: "At least 92% of anticoagulated patients can tolerate their ICA being clamped, and don't require ipsilateral blood flow support and, therefore, the clamp is really acting as a cerebral protection device from that point on. The vast majority of these 92% can have the ICA clamp applied without disturbing the plaque bearing segment at that early stage.

"So the problem is the 8% or so who can't tolerate the clamp, and in those patients you could potentially be causing strokes. We have to work out the best way of determining clamp tolerance; that is, which patients need ipsilateral blood flow supported with a shunt or be otherwise protected from the effects of cerebral ischaemia. Unnecessary use of shunts is a potential cause of preventable embolisation and cerebral ischaemia for reasons which will be outlined."

With regards to stratifying patients into groups for appropriate treatment, Dr Bourke is a keen advocate of CEA under local anaesthesia. This allows the operator to immediately and dynamically assess the patient's neurological status (motor, speech and higher cerebral functions), providing a continuous assessment of cerebral perfusion. Local anaesthetic also means the potential reduction in myocardial ischaemia and markedly fewer cardio-respiratory complications, while facilitating the selective use of shunts.

"We perform CEA under local anaesthetic as that's been proven to be the best way to assess whether a patient needs a shunt inserted[3-5]. In a series of almost 1500 patients under local anaesthesia, we have never had to convert to general anaesthesia during the procedure. We've had just one patient who panicked in the anaesthetic bay and had to have the procedure under general anaesthesia.

> "The aim of surgery is not only to remove the source of cerebral embolism but also to perform the procedure in such a way that you are not causing the embolism."
>
> Bernard Bourke

"There are other methods, such as EEG monitoring, Transcranial Doppler assessment of middle cerebral blood flow (TCD), somatosensory evoked potential (SSEP) or carotid artery stump pressure measurement. Stump pressure has been shown to be inferior to the assessment of awake patients, to EEG monitoring, to TCD and to SSEP to assess the need for a shunt to support ipsilateral carotid blood flow[3-5]. Although EEG is fairly accurate, it is still not as good as assessing the awake patient[4], and it involves expensive equipment and a dedicated EEG technician in the operating theatre. Intraoperative monitoring of the awake patients is the most sensitive and specific method to identify the least number of patients requiring shunt placement."

Dr Bourke is also interested in how to gauge the success of one CEA technique against another. The traditional primary endpoints have been stroke, death and more recently myocardial infarction, meaning that other subclinical but very important outcomes may be missed or go unreported.

He explained: "These days most experienced vascular surgeons operate within the 'accepted limits' of stroke and death. However, I believe that the endpoints of stroke or death or myocardial infarction are very gross. So we refined our endpoint to look at what is happening inside the brain, as determined by diffusion-weighted imaging [DWI], via magnetic resonance imaging."

Describing their recent study (currently in press in the European Journal of Vascular and Endovascular Surgery) using DWI to compare pre and post-operative images in patients who had

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Session V: New Horizons in Carotid Intervention Friday **9:30–10:40** am

Evidence-based medicine can improve CEA surgery

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received different procedures such as eversion CEA, longitudinal endarterectomy with vein patch and shunting[6], he said : "We measured new sub-clinical lesions as detected in the postoperative DWI scan. It's an important study because it showed, by logistic regression analysis, that shunting is a definite risk factor for these lesions – and therefore for possible perioperative and future stroke and possibly for future cognitive impairment. It also showed that the eversion technique has advantages over longitudinal endarterectomy.

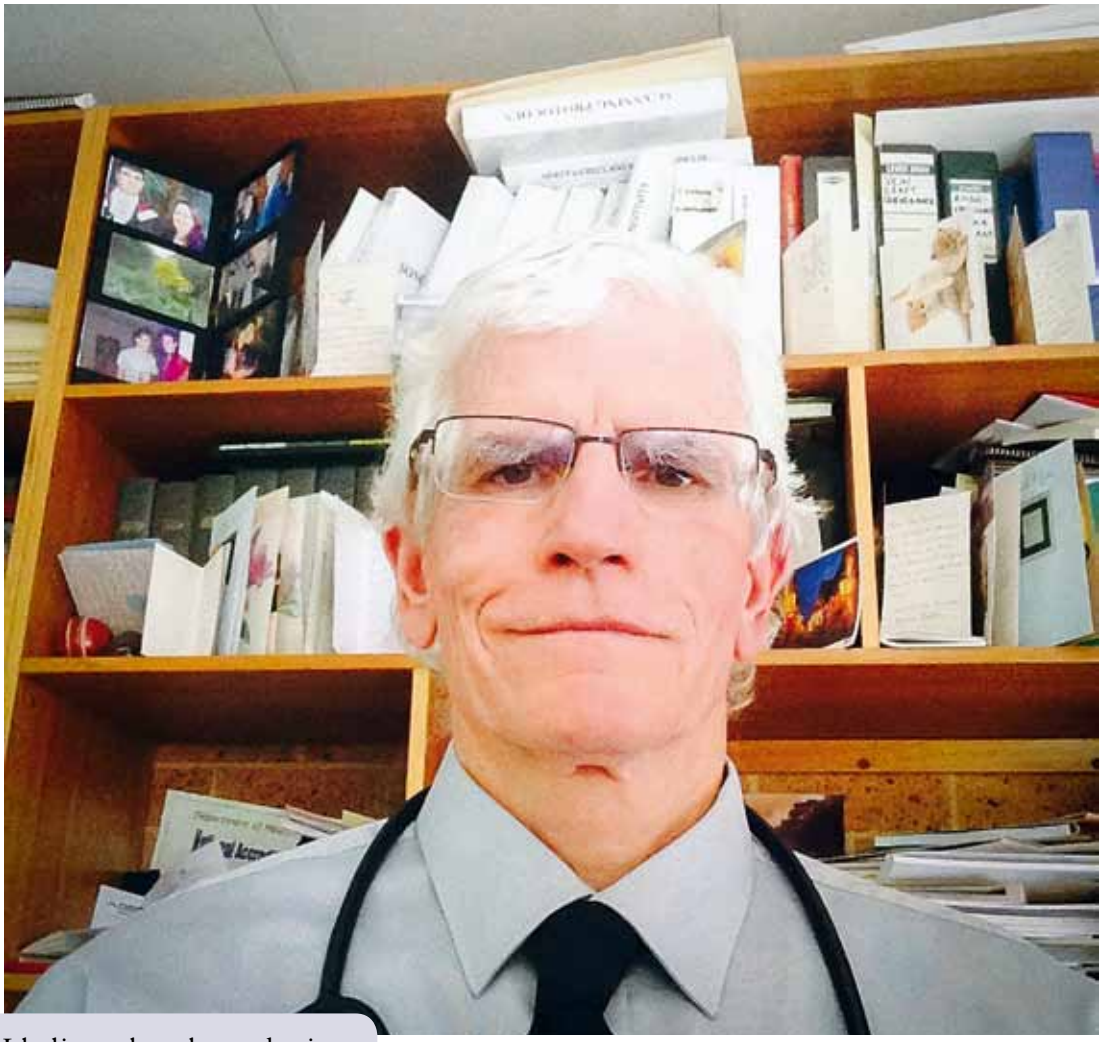
"The reason we need to use these finer endpoints is that CEA is being challenged by so-called 'Best Medical Therapy' and by Carotid stenting [CAS]; we need better endpoints to demonstrate any differences which may occur between major therapies and within major therapies. In addition, others may argue that asymptomatic patients should be treated with drugs or stenting but in future, using these refined endpoints, we may be able to show that these latter strategies lead to significantly more DWI changes which have been incriminated in the development of vascular-related dementia and the development of future stroke. We've shown that it is possible to use these more refined endpoints to demonstrate important differences in outcome using varying techniques."

Dr Bourke then talked about his experience performing eversion surgery for CEA. "I thought it would speed the procedure up, which is good for patients when they're awake especially when you are training future vascular surgeons. Just like when I first used CEA under local anaesthesia, I have never turned back after my first eversion CEA. My intention now is that when I do a CEA I aim to always perform eversion CEA.

"The only time I don't do that is if I have to use a shunt and in that case, I revert to longitudinal endarterectomy and vein patch, and would very rarely use a synthetic patch because of the risk (albeit, rare) of infection. The argument against vein patches is the perceived risk of aneurysmal change but in my experience of 1500 or so vein patches, this has only occurred once, and I was able to fix this."

Moving on to CAS, Dr Bourke admitted that while he once used to speak out against it in the early days when it was used for wrong indications and with poor techniques and equipment that he now uses it in certain situations particularly if there are likely to be physical difficulties accessing the ICA surgically such as a patient with a very short neck with a high carotid bifurcation, scar tissue from say laryngectomies or other previous neck surgery, or if a patient is too breathless to lie flat. He considers it a valuable adjunct in the armamentarium of the vascular surgeon when used with the correct technique and for the correct situation.

"I'm more likely to use a stent in patients who have plaques that are not all that stenotic but are symptomatic because in those cases you don't need to balloon the plaque. The stent is used to contain the plaque and then to cause the plaque to remodel and stabilise. It's more a physical reason. There's no medical contraindication to CEA under local anaesthesia except the rare patient who can't lie flat, I suppose. My CAS series is approaching 230 cases since 2005."



> "I believe that the endpoints of stroke or death or myocardial infarction are very gross. So we refined our endpoint to look at what is happening inside the brain."
>
> Bernard Bourke

He concluded by emphasising the importance of preoperative, intraoperative and postoperative medical management: "All patients should be on maximal medical treatment, including antiplatelet agent / agents, a statin and should have adequate blood pressure control. The other important thing I do, and I've been using it routinely for over 30 years, is to use a perioperative infusion of dextran 40 (immediately preceded by a bolus of dextran 1 to prevent a rare anaphylactic reaction)[7]. Although we didn't realise its exact mechanism of action in the early days (but we still used it), TCD techniques have subsequently shown dextran reduces the rate of embolisation, both intra- and post-operatively. This is an important part of patient management in CEA surgery in my view."

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Session VIII: Current Concepts in Embolisation Therapies Friday **2:30–3:45pm**

Embolisation for visceral trauma: **What is the best approach?**

Data now indicates that trauma is a leading cause of death in young people, with 30-40% of trauma deaths being caused by uncontrolled bleeding[1]. Therefore dealing with any traumatic injury is time-critical, and when complex embolisation surgery is required, a very focused approach to diagnosis and patient stratification is paramount. *VERVE Daily News* caught up with Gerard Goh (Monash University, Melbourne, Vic, Australia) ahead of his presentation on embolisation treatment for visceral trauma. Dr Goh began by broadly describing how systematic management of trauma embolisation can deliver a timely and clinically effective service, and he also emphasised the importance of diagnostic tests such as computed tomography angiography (CTA), angiography, patient selection, referral pathways as well as the actual materials and methods involved in embolisation procedures.

The success of embolisation treatment in trauma is time-critical with respect to the development of severe coagulopathy amongst other complications, so it is imperative that patients are assessed rapidly. A multidisciplinary team is involved in decision-making when trauma has occurred. Dr Goh explained: "Ideally, we would like to have the patient in the angiography suite as soon as possible after diagnosis.

"Our diagnostic radiology colleagues phone through the results of an active haemorrhage immediately after the scan has been reported, then the trauma team, surgical team and interventional radiologists review the images before making a joint decision as to whether to refer the patient for embolisation."

Dr Goh then described how the diagnoses may lead to various embolisation approaches. "Because most trauma patients who are referred for embolisation have haemorrhages in two or fewer systems/viscera, stabilisation is not required before transfer. This means that the patient can be rapidly transported, with resuscitation continued in the angiography lab. In this case, the embolisation will stabilise the patient. If a patient needs an urgent laparotomy or other surgical procedure then the trauma surgeons must achieve operative haemostasis."

Dr Goh went on to talk about other challenging situations, for example whether to perform permanent embolisation in visceral organs with poor collateral blood supply. "The degree of contraindication depends on the clinical scenario and each case has to be assessed individually for benefit versus detriment. Permanently embolising selected small areas of the kidney is acceptable as the kidneys have large functional reserves in most patients, however in the liver this is associated with high levels of complications."

> "The degree of contraindication depends on the clinical scenario and each case has to be assessed individually for benefit versus detriment."
>
> Gerard Goh

"In an emergency trauma situation with uncontrollable haemorrhage it is completely acceptable to perform permanent embolisation in end organs or large arteries. For example, in some cases of pelvic arterial exsanguination we may embolise the entire internal iliac artery if it means saving the patient's life."

The type of embolisation device – for example permanent embolisation device (coils or plugs) versus a temporary agent (gelfoam) – depends on both the individual trauma patient as well as the practitioner. "Gelfoam embolisation has a slightly higher rate of re-perfusion than permanent embolic agents[2] but is useful for 'scatter embolisation' where a slurry is introduced to embolise multiple small bleeding branches at once," said Dr Goh.

> "In an emergency trauma situation with uncontrollable haemorrhage it is completely acceptable to perform permanent embolisation in end organs or large arteries to save a patient's life."
>
> Gerard Goh

Another potential complication in trauma embolisation is vessel spasm, and this is a particular problem in the younger trauma population. In addition to the general reduction in peripheral and central perfusion, it can make angiography and embolisation technically very difficult. Spasms cause access problems for both arterial sheaths and smaller vessel catheters and can also hide active extravasation.

However, with expertise and experience, Dr Goh stressed how these demanding situations can be tackled. "Dedicated anaesthetic support is vital in ensuring adequate blood pressure, as well as blood and fluid filling to avoid vascular spasm and shut down. Intubating and paralysing a patient also helps counteract vasoconstriction.

"As an endovascular specialist I can directly hand-inject drugs such as glyceryl tri-nitrate or calcium channel antagonists into catheterised vessels to 'open up' the artery. In extreme cases where the bleeding areas cannot be identified, we can introduce heparin or fibrinolytic agents (e.g. r-TPA) to promote bleeding. This is obviously an extremely advanced technique that requires high-level training and anaesthetic support."

Dr Goh concluded by emphasising the importance of teamwork and high-level training of this multidisciplinary trauma team in determining whether embolisation is required after arterial injuries, and also how the communication between team members is key in managing these events.

"At the Alfred hospital [at Monash], our emergency trauma unit and trauma surgeons receive special training in dealing with major trauma. We hold various education and skills workshops for all staff in all specialities from consultants, junior doctors, nurses, radiographers and ancillary staff. This includes all specialities such as emergency, trauma, anaesthetics, surgery and radiology.

"Training situations such as mock trauma calls, mock major incident hospital-wide training and live training during real-life trauma cases and are all provided so that our staff stay at the cutting edge of major trauma. In addition, our trauma unit is involved in research; one of the current studies we are performing is the use of the REBOA (resuscitative endovascular balloon occlusion of the aorta) technique in selected trauma cases."

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Session I: Challenges and Unmet Needs in the SFA & Popliteal Artery Thursday **13:00–14:30**

TIGRIS continues to impress over the knee

Later generation stents boast increasing aptness in mimicking the every stretch and bend of blood vessels around the knee, thanks to critical developments in their design and material construction. In this way, we have made significant advances towards meeting the demands of critical limb ischemia in the longer term.

The TIGRIS stent (Gore Medical, USA) is one such stent dealing with the problematic popliteal segment: long and heavily-calcified lesions in this region are particularly vulnerable to stent fracture and restenosis, compounded by forces of flexion, compression and extension that describe normal leg movement.

In conversation with *VERVE Daily News* ahead of his discussion of a two-year analysis of the use of TIGRIS in occlusive disease of the popliteal, John Hardman (Southmead Hospital Bristol and Royal United Hospital Bath NHS Foundation Trust, UK) described the stent's dual components that separates it from its nitinol-only counterpart: "It uses the clinically-established nitinol stent frame that other competitors have," he said. "But instead of interlinking the stent with more nitinol wire, it is interlinked with a fluoro-polymer connection. That is then covered with a heparin bonded surface. This essentially allows the stent to compress and elongate as the popliteal artery flexes and extends."

> "Certainly the patency up to two years is much higher than other studies."
>
> John Hardman

Dr Hardman will discuss the latest results on TIGRIS on Thursday afternoon, as part of a broader session looking at the challenges and unmet needs in the SFA and popliteal artery. These two-year follow-up data are a welcome addition to the body of evidence in support of the TIGRIS's efficacy; Piorkowski et al. published positive retrospective analyses of experience with the stent in 32 patients, reporting a primary patency rate of 91.7 ± 8.0% at six months, and 85.5 ± 6.0% at 12 months.[1,2]

Earlier this year at the Leipzig Interventional Course in Germany, Martin Werner evidenced good medium-term efficacy in a retrospective analysis of 73 patients who underwent stenting in the femoropopliteal segment, demonstrating clinical improvement in 82% of cases after a mean follow-up of one year.[3] More recently, Parthipun et al.

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TIGRIS continues to impress over the knee

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analysed data from a prospective registry of 48 patients (50 limbs, of which 74% were chronic total occlusions, with stented lesion length 114.2 ± 36.9mm), reporting primary patency of 69.5 ± 10.2% with an 86.1 ± 5.9% freedom from TLR and 87 ± 5.0% amputation-free survival.[4]

Dr Hardman will be presenting his analysis of 69 patients, the majority of whom had critical limb ischemia typified by gangrene, ulceration or rest pain. "Over half of these cases were popliteal occlusions," he noted and the majority occurred within the P2 and 3 segments of the popliteal artery, which is the area that bends the most.

"We are describing the patients that require popliteal stents following simple angioplasty. In the majority of patients, you can't get an optimal angioplasty result so they will go on to have a stent put it. We try and open up as many of the crural vessels below to try to optimise the outflow. So a lot of the patients have extensive crural angioplasty at the same time as in the popliteal artery recanalisation. And then they will go on to standard dual antiplatelet therapy for six weeks."

The patency rate at one year was found to be just under 80%, Dr Hardman explained, adding that although only a limited number of patients were included in the two-year study, all of those stents have remained patent. "Certainly the patency up to two years is much higher than other studies," he stressed.

"And TIGRIS is fairly similar to the SUPERA stent [IDEV Technologies, Inc/Abbott Laboratories, Inc, USA], which is also very flexible and can be used in the popliteal artery. I think the reason we use the TIGRIS is that it is very easy and simple to use – there are lots of us doing the interventional procedures. I think it is probably simpler to use than the SUPERA stent, very easy and accurate to deploy."

> "The reason we use the TIGRIS is that it is very easy and simple to use."
>
> John Hardman

Describing the difficulties of maintaining a follow-up regime in this class of the population, Dr Hardman pointed out that the average patient age was 73, with most being frail and having multiple comorbidities. "By one year [post-stenting], 12 of those had died," he said. "This reflects the population.

"There is a challenge to keep these patients followed up, because they are often elderly and don't want to continue coming back to hospital, and often have other health complaints. So the challenge is to keep following them past two years."

"Although we haven't got that many patients out to two years, I think this data adds to the literature that this stent is easy to use, flexible, and that it does give improved patency and clinical results compared to the use of standard nitinol stents across the knee joint. The whole SFA-popliteal stenting is a bit up in the air – comparisons of the different stents or atherectomy or drug-eluting balloon are a bit unclear."

While the number of patients included in this registry continues to grow, with longer term follow-up anticipated, Dr Hardman reflected on the impact that this latest generation of stents will have for patients: "The flexibility of the stent will hopefully reduce occlusions, stent fractures and stent separations," he said. "And certainly, in terms of important outcomes to the patient, [we have found that] the amputation-free survival is fairly high."

Dr Hardman presents, 'Two-Year Results Using the Tigris Stent for Occlusive Disease of the Popliteal Artery,' as part of Thursday afternoon's symposium, 'Session I: Challenges and Unmet Needs in the SFA & Popliteal Artery,' taking place between 13:00 and 14:30.

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Session I: Challenges and Unmet Needs in the SFA & Popliteal Artery Thursday 13:00–14:30

Brains versus brawn

Chemical and mechanical barriers for SFA ISR

The discussion of the challenges of the SFA and popliteal arteries takes place on Thursday afternoon, with Koen Deloose (AZ Sint Blasius Hospital, Dendermonde, Belgium) comparing the data on different solutions to in-stent restenosis (ISR) in the region of the SFA. ISR occurs in up to 25% of cases of native lesions in the SFA and popliteal artery in the year following treatment with modern nitinol stents. While ever-improving technologies are paving the way for increasingly minimal treatment of native lesions, the burden of ISR in the meantime remains a significant one to patients and healthcare systems.

Dr Deloose explained how metallic implants can play a direct role in the precipitation of ISR: "The SFA and popliteal are very flexible arteries that are elongated, compressed and twisted in the human leg," he said. "These are very prone to physical irritation by the presence of metal.

"Based on this irritation, there is a chronic inflammatory response between the vessel wall and the metal. This leads to smooth muscle hyperplasia, creating intimal hyperplasia and ISR. Of course, there are several grades of ISR or reocclusion, and if you look carefully at the literature there is only one [paper] that describes this in a more-or-less correct way – the Tosaka classification.[1]"

The 2012 study by Tosaka et al. examined the relationship between angiographic patterns of ISR and the frequency of refractory stenosis. ISR lesions were distinguished into one of three classes, describing focal (>50mm in length) ISR, diffuse ISR (>50mm length), and totally occluded lesions. Multivariate analysis was then carried out in order to determine predictive factors that might be useful prognostically.[1]

"Tosaka I are those that are quite easy to treat," noted Dr Deloose. "And Tosaka II are still not the most complex, as you can easily pass with a wire. Tosaka III, where you have an in-stent reocclusion, is of course one of the most challenging situations concerning femoropopliteal disease, because you are not always sure that you can enter with a wire, a catheter, or whatever other device. In the stent and in the occlusion, we notice that in a lot of cases there is a trend for our wires and catheters to go subintimally. Then of course you have a big problem, because you are in between the vessel wall and the stent – so these are very difficult to pass and treat."

> "I don't know if the solution is in adding more metal – more stiffness and rigidity. That is why I am so enthusiastic about the DCB."
>
> Koen Deloose

Dr Deloose will discuss the two distinct approaches to smooth muscle hyperplasia and intimal hyperplasia during the session: the chemical approach, with drug-coated balloon (DCB) or drug-eluting stent (DES); and the mechanical approach, via the implantation of a covered stent

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which creates a mechanical barrier between the blood and the vessel wall. Both mechanisms can be defended, he explained, with scientific argument based on relevant clinical studies.

In evaluating such clinical studies, Dr Deloose emphasised that, while the most evidenced outcome is primary patency, freedom from TLR is also an important outcome from the clinical perspective: "If the patient is treated in a good way, then even if there is some restenosis after a few months or one year, its impact depends on whether the patient is symptomatic or not. So there are different ways to judge. My preference is to judge both primary patency and freedom from TLR. But in discussions with colleagues, I prefer to discuss primary patency rates."

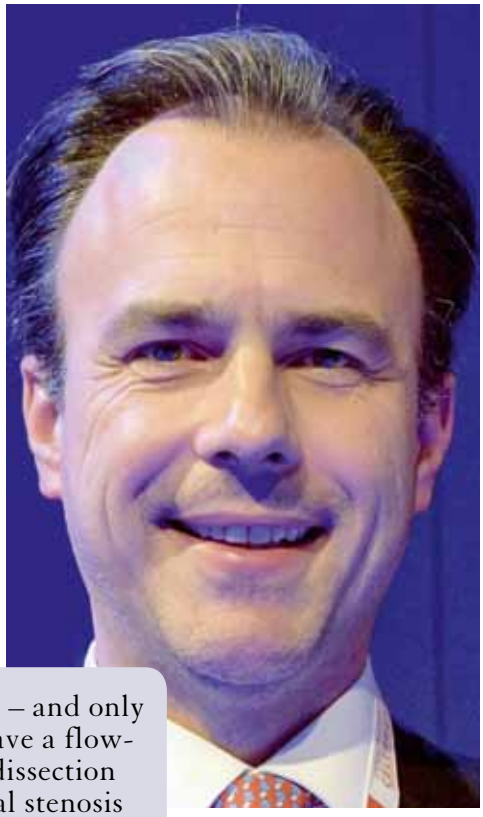
The safety and efficacy of DCB compared to plain old balloon angioplasty (POBA) has been evidenced by a number of trials, he continued. These include the single-centre study of Stabile et al, which saw the primary endpoint of primary patency at one year reached in 35 (92%) of its 39 patients.[2] Another study, PLAISIR, demonstrated a 90% primary patency after one year.[3] The DEBATE-ISR trial of Liistro et al found that recurrent restenosis and repeat angioplasty was lower in the DCB arm of a study of 44 diabetic patients versus historic POBA patients.[4]

"What is, in my opinion, one of the most important trials (because it is bigger, multicentre, and randomised controlled) is the FAIR trial of Krankenberg et al," said Dr Deloose. "We have randomised DCB versus PTA, where DEB had a primary patency of 70.5% after one year and freedom from TLR of almost 91% after one year.[5]"

In addition, Dr Deloose cited the multicentre, randomised, prospective COPA-CABANA trial (demonstrating freedom from TLR of 90%)[6], and the recently presented ISR sub-cohort of IN.PACT GLOBAL (with primary patency of around 90%).

"These are for me sufficient argument that DCB work in this area of ISR," he summarised of the body of evidence, adding: "Beside this, we have another solution as a chemical block – the Zilver PTX stent [Cook]"

Zilver PTX is a drug-eluting stent tailored to SFA anatomy; data published in 2013 pertaining to 119 ISR lesions as part of the broader Zilver-PTX global registry[7] found primary patency after one year to be 79% and freedom from TLR 81%.[8] Commenting on the concept and the place of such devices in general, Dr Deloose said: "I mentioned that one of the causes of ISR is the mechanical irritation of the metallic implant to the very flexible and difficult SFA. I don't know if the solution is in adding more metal – more stiffness and rigidity. That is why I am so enthusiastic about the DCB; you treat with paclitaxel but you don't add more metal as you do with the Zilver PTX. But in any case, the results are there, and 79% primary patency at one year is not bad at all."



> "DCB first – and only when I have a flow-limiting dissection or residual stenosis of more than 30% do I add some metal support."
>
> Koen Deloose

It may be that the incidence of ISR will diminish with the expected era of 'leaving nothing behind' – in which drug-elution will play a significant part: "Of course this is another topic, in terms of the treatment of native atherosclerotic lesions," commented Dr Deloose on the concept. "But definitely DCB is number one for all kinds of lesions in the SFA. It is DCB first – and only when I have a flow-limiting dissection or residual stenosis of more than 30% do I add some metal support."

Mechanical solutions, therefore, are sometimes needed, especially in poorer vessels. Dr Deloose noted the Viabahn covered stent (Gore Medical, USA) as a particular candidate; the results of the RELINE trial, which compared Viabahn and POBA, found primary patency of 75% in the Viabahn group at 1 year versus 28% in the POBA group. Freedom from TLR was 80% after 1 year with Viabahn and 28% with POBA.[9]

Describing the two-year results, Dr Deloose continued: "After two years with Viabahn we have a primary patency of 58%. Not bad but not fantastic. But compare this to the 11% with POBA, which is nothing. This trial gives us some opportunity for the treatment of ISR with Viabahn.

"Based on this, we have some rationale to say that for Tosaka I and II, we perform a chemical solution with, by preference, a DCB, and if necessary a DES. For Tosaka III, we use a covered stent."

Dr Deloose presents, 'Which is Best? A Mechanical or Chemical Barrier for In-Stent Restenosis of the Femoral Artery,' on Thursday afternoon as part of Session I, 'Challenges and Unmet Needs in the SFA & Popliteal Artery', taking place between 13:00 and 14:30.

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Session IX: Techniques for Resistant CTOs and Extensive Calcification Friday **4:00–6:00** pm

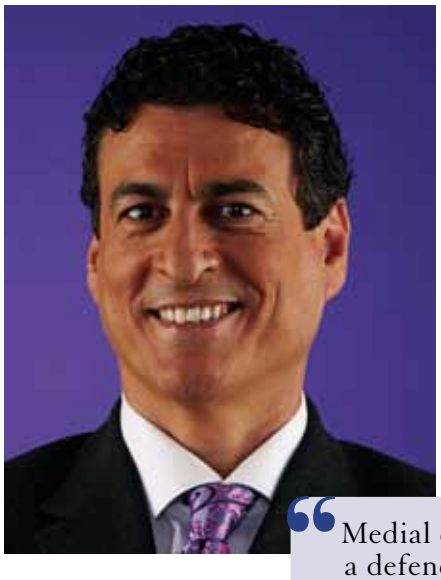
Infrainguinal calcification: Identification, characteristics and treatment

Calcification is a major factor in revascularisation strategies for PAD patients, increasing the risk of adverse events during balloon angioplasty. To that end, Jihad Mustapha (Metro Health Hospital, Wyoming, MI, USA) will step-up to the podium this afternoon to relay his experience with infrainguinal calcification in particular.

Infrainguinal calcification involves the femoral, popliteal, or infrapopliteal arteries and can vary according to location along the vessel, location within the vessel and also in its form. The lesion characteristics are very different depending on whether they are located above-the-knee (ATK) or below-the-knee (BTK). Speaking to *VERVE Daily News*, Dr Mustapha briefly explained the findings from a recent large-scale preclinical cadaveric study. "Above-the-knee vessels tend to have much higher intimal calcification with noticeable variable densities. Many of the eccentric lesions created a large positive remodelling with extensive intimal calcium invasion into the vessel wall. In the past it was referred to as medial calcification, today it is referred to as invasive intimal calcification with variable densities and positive remodelling.

"BTK vessels, on the other hand, have a significantly higher concentration of medial calcification and, surprisingly, demonstrate negative remodelling. The location of negative remodelling, referred to as the JENALI gap, does not possess calcium and appear to have lost its vasculature layers. BTK medial calcification is highest in concentration at the level of the ankle strap."

With regard to the characteristic locations of calcium deposition i.e., intimal deposits in the proximal end and medial deposits in distal end, Dr Mustapha suggested how these may be indicative of different disease pathologies or progression, "We feel that medial calcification is a defence mechanism that tibial vessels develop to cope with different stages of disease and stressors, whereas intimal calcification is a natural progression of evolving plaque."



> "Tibial medial calcification is a friend for endovascular therapy as it allows modest vessel dilatation without significant risk of deep wall dissection or frank perforation."
>
> Jihad Mustapha

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> Jihad Mustapha

The intrinsic adaptability of the tibial artery has evolved to cope with the tremendous pressures placed on it, however, this plasticity is lost due to calcium deposits. Dr Mustapha explained: "Using extravascular ultrasound (EVUS) to evaluate calcified tibial vessels, we found them to have lost the majority of their intrinsic plasticity. Interestingly, some of the plasticity returned after aggressive revascularisation, including orbital atherectomy[1]."

Sometimes patients present with combined intimal and medial calcium deposits at the level of the medial tibial arteries, this particular scenario is extremely challenging due to difficulties is separating the chunks of calcium, Dr Mustapha said, "This is absolutely a cumbersome combination. If the lesion is located ATK, directional or rotational atherectomy is the best form of therapy. For BTK, orbital atherectomy seems to work best[2]. Of course, both require adjunctive balloon angioplasty."

Dr Mustapha illustrated his own research into severely calcified tibial vessels and in-stent restenosis and how this has led to potential solutions, "After reviewing the macropathology and histopathology of the tibial vessels we saw a great opportunity for structured algorithmic therapy. In fact, tibial medial calcification is a friend for endovascular therapy as it allows modest vessel dilatation without significant risk of deep wall dissection or frank perforation.

"Also, we have learned to push the therapy until we see adventitial staining which usually indicated a successful interruption of the usual circumferential tibial medial calcification. Insistent restenosis-type plastic tissue is notorious and is a very effective barrier. In clinical practice, we have evolved into debunking with atherectomy first, followed with drug-coated balloon (DCB) angioplasty. Direct DCB most likely will have some difficulty penetrating the unwoven structure of hyperplasia."

Fluoroscopic imaging for detecting ossification is routinely performed when calcium deposits are suspected, as Dr Mustapha expanded: "It should be done using high-resolution cine, preferably rotating [to] place the vessel away from the bone. Medial calcification shows itself most of the time as straight or semi-straight plates of calcium, whereas intimal calcification tends to show itself as islands of calcium with much higher density than medial calcification."

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Session IX: Techniques for Resistant CTOs and Extensive Calcification Friday **4:00-6:00pm**

Improved outcome by BioMimics stent due to increased swirling flow

On Friday afternoon at The VERVE Symposium, Thomas Zeller (Universitäts-Herzzentrum Freiburg, Bad Krozingen, Germany) will relay results from the Mimics randomised control trial – a pilot trial to compare the BioMimics 3D helical structured nitinol stent (Veryan Medical, UK) with a standard slotted tube nitinol stent.

Speaking to *VERVE Daily News*, Professor Zeller explained that initially the data was to be used as a basis for a power calculation for a bigger global evaluation on the performance of the biomimic stent concept. "Interestingly, what we found after a two-year follow-up was that even though the study was not powered for a significant difference in a technical endpoint of primary patency, and clinical endpoint of freedom from target lesion revascularisation [TLR], in terms of patency and freedom from TLR, there was a significant advantage for the BioMimics 3D stent as compared to the control stent in terms of patency and freedom from TLR."

Preclinical studies with the BioMimics 3D stent have shown statistically significant reductions in neointimal thickness after 30 days and cadaver studies have demonstrated superior curvature allowing improved femoropopliteal shortening during leg flexion as compared to the standard straight stent. Another finding of the Mimics study was superior fracture resistance in a test setup replicating adductor canal / proximal popliteal fossa.

Another key feature of the BioMimics 3D stent is the promotion of vascular curvature in order to promote swirling flow in the stented segment, assimilating non-planar curvature throughout the vascular system.

Swirling flow elevates wall shear stress (WSS), which is an important aspect of vascular homeostasis[1].

> "There was a significant advantage for the BioMimics 3D stent as compared to the control stent in terms of patency and freedom from TLR."
>
> Thomas Zeller

Swirling flow is compromised in the superior femoral artery by the vessel length, anatomy and disease, and straight stents used in this setting promote laminar flow, rather than swirling flow.

Due to the performance of DEBs over the last few years, the biomimetic stent is not considered the first-line strategy in the treatment of stenosis of the femoropopliteal artery[2]. Restenosis after DEB angioplasty is easier to manage than in-stent restenosis so stents are generally considered a second choice or 'bail-out' indication.

With research showing that stent length can impact on primary patency, and that spot stenting is associated with more favourable outcomes[3], Professor Zeller weighed up the best treatment to very long total occlusions of the femoropopliteal artery, based on this clinical evidence. "What we previously believed was that with long superficial femoral artery occlusions, the patency would be better if the entire lesion length was covered with a stent (when there was a stent indication).

"But our strategy has changed to stenting only if the DEB outcome is insufficient, with a preference for spot-stenting, whereby we simply cover the areas of recoil or severe dissection with stents (instead of the entire lesion length)."

He added: "For this purpose the biomimetic stent may be a very attractive stent device. What we saw in the Mimic trial was that the significant benefit of the biomimetic stent starts between one to two years. So there seems to be a long-term protection of restenosis effect that arises from changes within the vessel attributed to the helical stent design.

"And that's why, in my opinion, the combination of a drug-eluting balloon (which prevents short-term development of restenosis) along with a helical stent (which offers long-term advantages) might be a very attractive option."

While new resorbable polymeric materials claim to be promising candidates for the next generation of stents, Professor Zeller commented on their feasibility, "I don't believe that will become a commercially viable technology in the next 5-10 years, for two reasons. Firstly, the actual mechanisms are still problematic. It is very difficult to find the right balance between the timely degradation of this device whilst achieving enough scaffold in the acute and subacute phase.

"Secondly, the outcomes for DEB are so outstanding that it is hard to improve on these. We need to bear in mind that these discussions are driven by those who pay for such treatments, such as medical insurance companies. Cost effectiveness is a very important topic in conjunction with new technologies, and I don't believe that a bioabsorbable device can be produced for the same price as compared to a DEB, particularly if they do not perform as well."

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> "The combination of a drug-eluting balloon (which prevents short-term development of restenosis) along with a helical stent (which offers long-term advantages) might be a very attractive option."
>
> Thomas Zeller

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