

Your subscription to **Electroceuticals: Drug-Like Effects, Without The Drugs** is expiring.

[View My Account To Renew](#) | [Remind Me Later](#) | [Don't Show This Again](#)

START-UP

This copy is for your personal, non-commercial use. For high-quality copies or electronic reprints for distribution to colleagues or customers, click [here](#) or call +1 (908) 547-2200.

Printed by **Mr. Michael Carusi MBA, Advanced Technology Ventures (ATV)**

Cerebral Embolic Protection For TAVR: Start-Ups Compete

By Jenny Blair (Contributor) / [Email the Author](#) / [View Full Issue](#)
 Feature Articles / Word Count: **4593** / Article # **2015900196** / Posted:
December 22 2015 8:00 AM

Executive Summary

With minimally invasive left-heart procedures like transcatheter aortic valve replacement becoming increasingly safe and commonplace, attention has turned to procedure-associated brain injury from showers of emboli. Several medtech start-ups are developing devices that could protect patients' brains during not only TAVR, but also surgical aortic valve replacement, atrial fibrillation ablation and other left-heart procedures.

- Transcatheter aortic valve replacement (TAVR) could become a \$7.4 billion industry by 2025, but concerns about associated brain injury or stroke are rising, with some researchers concerned that large clinical trials of TAVR greatly underreport stroke.
- TAVR and other left-heart procedures can liberate microemboli made of calcified material, thrombus or device fragments that can travel to the brain and cause injury. Such microemboli don't necessarily cause clinically obvious stroke, but they are associated with important neurological and cognitive effects and downstream consequences nonetheless.
- Start-up companies are developing brain-protection devices with approaches that include deflecting emboli away from brain vessels and toward the periphery, catching and removing emboli from the body, and creating a pressure gradient in the blood column that diverts emboli.
- Some industry insiders say such protection will soon become standard of care

Related Articles: 1

Claret Targets TAVR Stroke Risk With Sentinel Embolic Filter Device

["The Gray Sheet" Oct. 17, 2014](#)

Related Deals: 3

Strategic Transactions

[Click a deal headline for more information](#)

Series B generates \$14mm for Keystone Heart

Series A lands \$3.5mm for Claret Medical

Claret Medical gets \$18mm via Series B

Topics Covered in this Article

[Click a keyword for related articles.](#)

Industries

[Medical Devices](#)
[Interventional Devices & Techniques](#)

Therapeutic Area(s) of Focus

[Cardiovascular](#)

Companies

[Keystone Heart Ltd.](#)
[Claret Medical Inc.](#)
[Medtronic PLC](#)
[Yale University](#)
[CardioLogical Solutions](#)
[Allium Medical Solutions Ltd.](#)
[Edwards Lifesciences Corp.](#)

– as it already is in carotid stenting – and point to the potential risk of not using such a device if clinical data show it to be effective.

With transcatheter aortic valve replacement (TAVR) becoming a mainstream procedure, worth a predicted \$7.4 billion by 2025, attention is turning to the associated stroke risk. Cerebral embolic protection devices show promise in prevention, and some start-ups predict they will become standard of care for TAVR and other left-heart procedures. Some estimate a billion-dollar market potential for such ancillary devices.

Across recent large randomized trials of TAVR, the reported stroke rate is about 2.8%. However, recent studies in Europe and the US that examine post-TAVR patients with MRI have found that 68% to 100% of patients suffer new brain lesions after TAVR, even if they don't show obvious signs of stroke. When checked for clinical signs by neurologists, 15% to 28% of these patients do show new deficits. Moreover, even small brain injuries like these can raise the risk for future dementia and stroke.

Several start-ups are looking to prevent such injury; those that have gained the most attention are [Keystone Heart Ltd.](#) and [Claret Medical Inc.](#), both of which are testing catheter-based protection devices. Keystone is about to begin an IDE trial after concluding an observational study in the US of embolic brain injury during unprotected TAVR. Claret is over a year into its pivotal IDE study

EXHIBIT 1

Select Start-Ups In Cerebral Embolic Protection

Company	Product Name and/or Approach	Select Milestones
Keystone Heart	TriGuard; deflects emboli peripherally, away from all three aortic branches that lead to the brain	2013: CE mark for TAVR 2015: CE mark extended to all transcatheter heart procedures 2015: DEFLECT III-protected group more likely to be free of new brain lesions post-procedure 2015: Neuro-TAVR: 94% of unprotected patients with microemboli on MRI End of 2016: Completion of pivotal IDE trial REFLECT 2017: 510(k) submission
Claret Medical	Montage and Sentinel; captures and removes emboli from two of three aortic branches that lead to the brain	2013: CE mark 2014: CLEAN-TAVI: protected group's MRI lesions fewer and smaller 2015: MISTRAL-C: protected group trended toward fewer new MRI lesions and

		lower chance of neurocognitive deterioration Ongoing: Pivotal IDE trial SENTINEL Late 2016: FDA approval
Innovative Cardiovascular Solutions	Emblok: Protects entire aorta from emboli	Early 2016: CE mark and first-in-humans
Stroke Protection Systems	Stroke Prevention System: Creates temporary pressure gradients in carotid arteries using an inflatable cuff around patient's neck	Ongoing: Clinical study with transcranial Doppler Late 2015: 510(k) submission Early 2016: FDA approval
Transverse Medical	POINT-GUARD: Deflects, filters, captures and removes emboli via undisclosed technology	Late 2016: First-in-humans and initiate clinical trial

Company reports

A successful cerebral embolic protection device for TAVR could penetrate other procedures too, including surgical aortic valve replacement (SAVR), atrial fibrillation ablation and left atrial appendage closure. (Testifying to the potential need for cerebral protection in procedures besides TAVR is the FDA's 2011 decision that the risks of [Medtronic PLC's Ablation Frontiers](#) device did not outweigh the benefits owing to elevated rates of cerebral microembolization in a pivotal trial for atrial fibrillation.)

Younger patients receiving TAVR, in whom the consequences of brain injury may be even more devastating than in older patients, may drive demand for cerebral embolic protection too.

"In aortic valve procedures, more often than not the very reason you're there is because the valve is calcified and stenosed, [and if you] crunch into that, you liberate a bunch of materials," says Vince Burgess, venture partner with Orbimed Advisors LLC, a major investor in start-up Keystone Heart. "We couldn't conceive of a way for valve companies to design a valve that kept debris from being showered into the brain."

"Stroke may effectively be the Achilles' heel of percutaneous valves," says Fred Khosravi, chairman of the board of directors at Claret Medical and managing director of Incept LLC, a major Claret investor.

What Counts As Stroke? It Depends

In TAVR, as the replacement valve is maneuvered into place and deployed, it breaks open the old, calcified valve, sending showers of emboli, valve material and other debris through the aorta and down its branches. This debris is blamed for most strokes that occur during or shortly after the procedure.

There is more than one way to define stroke. It could be something as obvious and disabling as weakness on one side of the body. It could be a subtler disability that

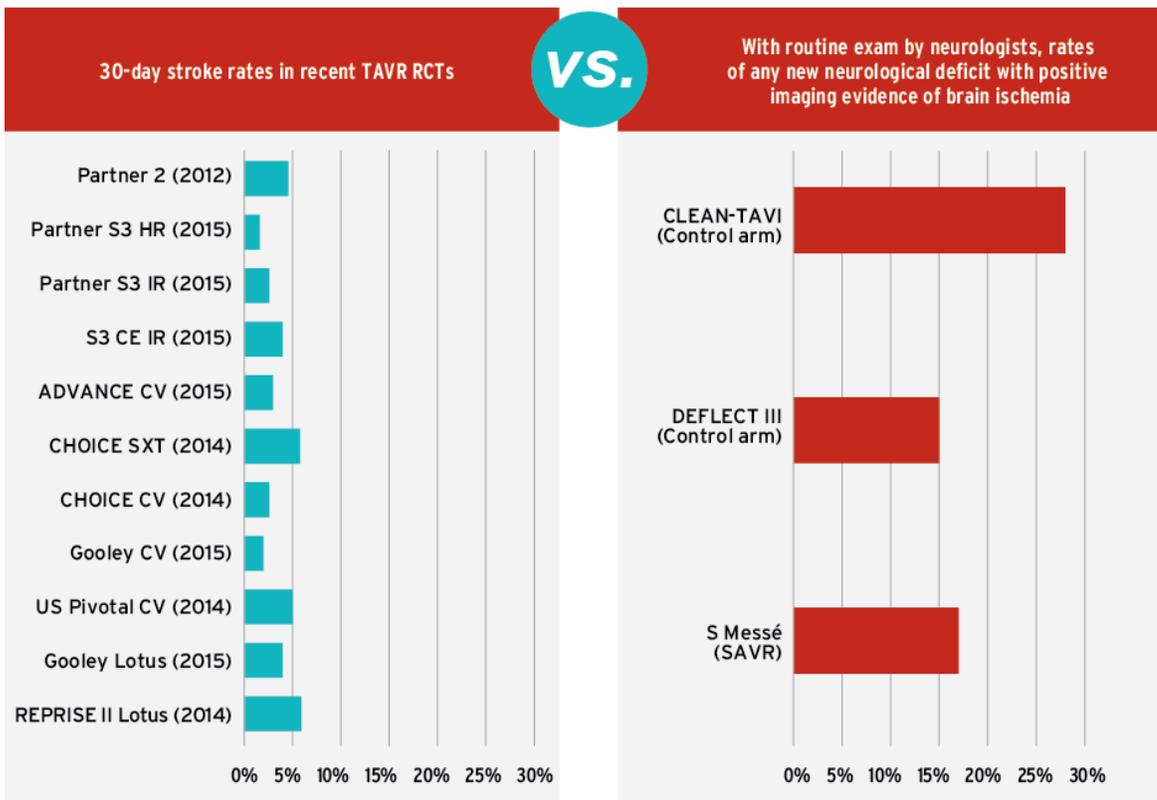
shows up only on neurological testing by a specialist. Or it could be bright spots suggesting emboli on diffusion-weighted MRI (DW-MRI), an imaging technology that is sensitive to early stroke and that can highlight new infarctions down to millimeter-scale resolution.

In 2013, the American Heart Association/American Stroke Association (AHA/ASA) released revised stroke guidelines in which stroke was defined as *any* objective evidence of neurological infarction, such as MRI findings, with or without acute clinical evidence of such injury. That means that many small infarcts once thought to be clinically “silent” are now considered stroke by these criteria. Such infarcts are known to be associated with adverse consequences, including increased risk for dementia and future stroke and a threefold mortality rate.

Those studies that go looking for these infarcts in post-TAVR find them – in a whopping 68% to 100% of patients. Moreover, most TAVR patients with infarcts have several of them. (See Exhibits 2 and 3.)

EXHIBIT 2

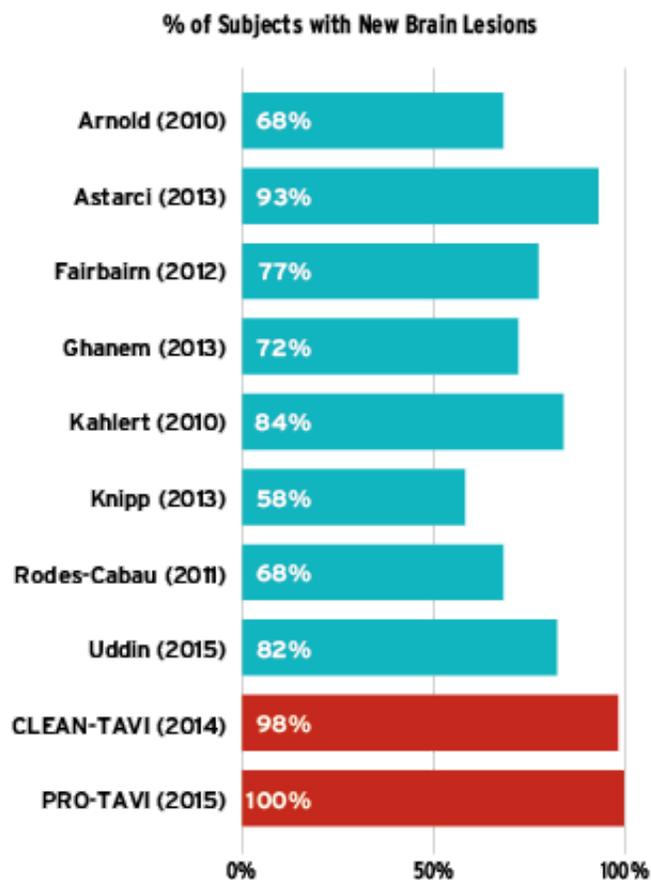
Clinical Stroke Rates May Be Under-Reported



Alexandra Lansky, MD, from London Valve 2015 presentation "Neurologic Complications of Contemporary Unprotected Trans-Aortic Valve Replacement: Final Results of A Prospective Multicenter Study to Evaluate the Neuro-Embolic Consequences of TAVR in the United States (The Neuro-TAVR Trial)", citing AP Kappetein et al. EHJ (2012) 33:2403–2418 and Sacco et al. Stroke (2013) 44:2064-2089

EXHIBIT 3

Post-TAVR Brain Lesions Detected On MRI



Alexandra Lansky, MD, from London Valve 2015 presentation "Neurologic Complications of Contemporary Unprotected Trans-Aortic Valve Replacement: Final Results of A Prospective Multicenter Study to Evaluate the Neuro-Embolic Consequences of TAVR in the United States (The Neuro-TAVR Trial)", citing multiple sources; Medtech Insight

Recommendations for outcomes measurements in TAVR studies from the second Valve Academic Research Consortium (VARC-2) are that patients be evaluated for stroke by a neurologist; imaging data are optional. But in light of data showing high stroke rates on imaging studies, a new consortium called NEURO-ARC convened at the *Transcatheter Cardiovascular Therapeutics (TCT)* conference in San Francisco this October to discuss revising the guidelines to include these microinfarcts; the committee includes FDA representatives, according to Azin Parhizgar, PhD, CEO of Claret Medical.

"That by itself is a very good indicator of how the field is developing, and how embolic protection in the context of these types of procedures is being recognized as a definite clinical need," Parhizgar says.

"MRI data show us that over 90% of TAVR patients have new brain lesions after TAVR. These lesions are strokes, TIAs and other smaller events that were previously viewed as 'silent,' but we now know they can cause real brain injury and long-term neurocognitive damage," says James Eadie, MD, a partner at Santé Ventures and a board member for Claret Medical.

"Now that the TAVR community has tackled the challenges of paravalvular leak, vascular complications and repositionability, the new focus is on technologies that better protect the brain from procedural debris, such as Claret's technology, which is designed to make TAVR even safer," Eadie adds.

“We are very supportive of this great indication, which is transcatheter valve replacement – it’s a huge thing that medicine and science have made this leap forward,” says Shuki Porath, CEO of Keystone Heart, who predicts embolic protection for TAVR and other cardiac procedures will likely become as indispensable for safety as automobile air bags and seat belts. “[Keystone is only] trying to make it safer – we believe you should take care of your brain as much as you take care of the heart.”

Keystone Heart: Deflecting Emboli Downstream

Keystone Heart makes a device that deflects emboli away from the brain. The company was founded in 2004 under the name SMT Research and Development Ltd. by Dov Shimon, MD, a cardiothoracic surgeon intent on developing a device to protect the brain during cardiac surgeries like SAVR. Six years later, as venture capital firm OrbiMed Advisors LLC got on board, the company changed its focus and began to develop a brain-protection device for TAVR. To date, the 25-employee firm has raised \$29 million, most recently \$14 million from OrbiMed last May. [\[See Deal\]](#) A Series C fundraising round is underway, to be completed by second-quarter 2016. Keystone has patents and patent applications in the US, Europe, Asia Pacific and Israel.

Porath, who joined Keystone Heart in 2011, is a 19-year veteran of medical device management; previously, he was CEO of SeamVad Ltd. and ES Vascular Ltd. He also held executive positions at Biosense Webster, a Johnson & Johnson company.

Keystone Heart’s *TriGuard* is a collapsible nitinol frame and mesh inserted via a 9 French (9F) catheter through the femoral artery during TAVR, accessing the same artery used for the TAVR pigtail catheter. Visible on angiogram, the device expands into a sled-like shape for positioning over the three arteries exiting the aortic arch. TriGuard is designed to fit over all three, deflecting valvular debris away from vessels that lead to the brain. It can be used with any valve brand, according to Porath. The device earned a CE mark in 2013 for TAVR, then an extended-indication CE mark in 2015 for all transcatheter heart procedures.

Results from Keystone’s DEFLECT III, its multicenter randomized trial presented this March at the American College of Cardiology’s ACC.15, showed that TriGuard rendered patients more likely to be free of new brain lesions post-procedure. Protected patients also had a lesser volume of brain lesions compared with those whose procedures did not use TriGuard, and had a 10% absolute reduction in stroke rate. (Safety in both groups was comparable.) At the 30-day mark, the treated patients had one-fifth the number of new neurological deficits compared with controls.

The company also recently completed Neuro-TAVR, a study of MRI and clinical endpoints in unprotected US TAVR patients. Such data exist from European centers, but Porath says that key opinion leaders and industry representatives wanted to see US data owing to intercontinental differences in methodologies, expertise and patient populations.

Doing Neuro-TAVR was a “difficult and expensive decision,” says Burgess of OrbiMed Advisors, which led Keystone’s \$14 million Series B round last May. The aim, he says, was “to show the problem isn’t solved.”

The five-center US trial enrolled 48 TAVR patients for pre- and 30-day post-procedural neurocognitive clinical tests, as well as a post-procedural DW-MRI. In September, [Yale University](#) cardiologist Alexandra Lansky, MD, Neuro-TAVR’s principal investigator, presented the results at *PCR London Valves*.

Of 34 patients to complete the study, 32, or 94%, suffered new brain infarcts as a result of the procedure. The average patient had five lesions; almost 60% of lesions

measured 150 mm³ or more. There was also a statistically significant diminution of clinical neurocognitive function, with 14.8% of patients not lost to follow-up displaying diminished function at 30 days post-procedure by ASA/AHA criteria alone. Other clinical tests revealed post-procedure deficits in up to about half of patients not lost to follow-up. These results echo European results across multiple studies.

Next comes Keystone Heart's pivotal investigational device exemption (IDE) trial, REFLECT. After receiving an initial green light for the trial from the FDA, the company changed the protocol to include clinical outcomes as primary endpoints, in addition to DW-MRI findings as surrogate efficacy endpoints. The revised protocol was approved a month ago, and enrollment is expected to begin in early 2016. This safety and efficacy trial will enroll 280 European and US patients with 2:1 randomization to the company's third-generation device. The time line calls for completed enrollment around the end of 2016 and Porath estimates a 510(k) submission in about 18 months.

Porath says the firm's clinical data do not indicate downstream safety issues associated with the deflection of emboli. About 80% of blood and emboli flowing through the aorta already heads downstream, he points out, with TriGuard deflecting 15% to 20% more.

"We give added value [in] protecting the brain, but we're not adding any considerable risk [by] deflecting the extra debris downstream," Porath says. "Those organs downstream are quite capable of handling those."

Burgess estimates that if TriGuard is priced at \$2,500 to \$3,000, the TAVR-related market could amount to \$300 million annually. Including atrial fibrillation ablation and surgical aortic valve replacement, TriGuard's annual market could be \$800 million to \$1 billion.

As for the company's exit strategy, Burgess declines to discuss specifics, but says that because TAVR is performed at relatively few centers, a large sales force wouldn't be needed.

Claret Medical: Removing Emboli Entirely

Removing such debris from the body entirely is the approach taken by Claret Medical's flagship *Sentinel Cerebral Protection System*. Approaching through the radial artery of the right arm with a 6F catheter, the operator inserts a pair of cone-shaped polyurethane filters, deploying one in the brachiocephalic artery and the other in the left common carotid. Held against arterial walls with nitinol hoops, these filters remain in place during the TAVR procedure, catching released embolic debris, and are then removed from the vessels afterward along with the debris. This debris can include thrombus, chunks of heart muscle, valve tissue, foreign body and calcium.

"When you can capture it effectively and remove it efficiently, why deflect [debris] to the kidneys and mesenteric arteries to create another problem downstream?" asks Claret's Azin Parhizgar. The one-size-fits-all Sentinel also achieves good apposition to vessel walls, reducing the chance that debris will float past, according to Parhizgar, and remains out of the way of TAVR catheters and devices during the procedure to reduce any chance of interference – "a key safety differentiator," she says.

CE marked in 2013, Sentinel is now in its fourth generation. As of November it had shipped about 2,200 devices in the EU. With respect to valve brands, it is platform-agnostic, and Parhizgar says it can be used in other left-heart procedures that produce embolic showers.

Claret Medical was founded in 2009 by Randall Lashinski, an engineer and

entrepreneur who had previously helmed Allure Medical and Direct Flow Medical and had been a VP at Medtronic. Neurosurgeon Leo Nelson Hopkins, MD, and interventional cardiologist Eberhard Grube, MD, PhD, provided clinical leadership by defining clinical need, according to Parhizgar. Claret closed a Series A round of \$5 million in August 2009, and its Series B was announced last August for up to \$18 million, from Santé Ventures, Lightstone Ventures, Easton Capital and Incept. [\[See Deal\]](#)[\[See Deal\]](#) The company has 39 employees. Parhizgar joined Claret in 2013 after co-founder Lashinski stepped down. Previously, she was chief operating officer of Conor Medsystems, which Johnson & Johnson acquired for about \$1.4 billion in 2007.

As noted earlier, the Sentinel covers the brachiocephalic and the left common carotid arteries. It does not cover the left subclavian artery, the third major vessel to take off from the aortic arch. The main branch of the left subclavian feeds the left arm; a smaller one forms the left vertebral artery. The left and right vertebral arteries unite via crossover circulation at the circle of Willis at the base of the brain, where they go on to supply many regions of the brain. Because the Sentinel does protect the right vertebral artery and because of this commingling in the circulation, the left vertebral artery is partially protected, according to Parhizgar.

“A number of publications as well as internally generated data illustrate that the left vertebral artery contributes about 5% to 7% of the cerebral circulation,” Parhizgar says. As a two-vessel protector, the Sentinel CPS is a simple and quickly deliverable device with a high efficiency of debris capture that does not risk becoming entangled with or dislodged by TAVR equipment, she says.

“Everything that has been published with fluid dynamic studies with respect to the blood flow to the brain shows that the contribution of embolic debris toward the left vertebral artery is small,” Parhizgar says. “The majority of anything that goes to the left subclavian artery is going to go down the arm. For that reason also, the thought process was that leaving the left vertebral artery partially protected is not going to be significant. In fact, our pivotal European trial, CLEAN-TAVI, has demonstrated this very fact.”

“The 5% to 7% that we’re not protecting fully, we will revalidate from the Sentinel clinical studies in the US if that is significant or not,” Parhizgar adds.

The Sentinel CPS was tested in CLEAN-TAVI, a prospective randomized controlled trial of cerebral embolic protection in high-risk AS patients undergoing TAVR. One hundred patients being fitted with a Medtronic CoreValve underwent pre- and post-procedural MRI using highly sensitive 3-Tesla MRI. In patients randomized to the Sentinel, the study found a clinically significant reduction in the volume and number of DW-MRI-detected lesions shortly after TAVR. A trend toward fewer neurological events was noted in the protected group. This “compelling” trial was among the factors that attracted Santé Ventures to invest in the technology, according to James Eadie.

Claret’s multicenter double-blinded European trial, MISTRAL-C, was presented at TCT in October. This study randomized TAVR patients to Sentinel protection or no protection, with pre- and post-procedural 3-Tesla DW-MRI and neurological and neurocognitive assessments. Fifty-four patients were needed for an adequately powered trial, but only 37 received the second MRI. In those patients there were trends toward fewer new brain lesions and a lower chance of neurocognitive deterioration, according to the principal investigator, cardiologist Nicolas M. Van Mieghem, MD, PhD.

In October 2014, Claret launched its pivotal IDE trial, SENTINEL. This US multicenter randomized controlled trial will study Sentinel’s safety and efficacy in 296 patients receiving “some of the latest US approved” transcatheter valves, in Khosravi’s words, using as its primary endpoint the reduction in median new brain lesion volume as

measured by two types of MRI sequences. Patients will also be clinically tested for neurological and cognitive deficits. (See "[Claret Targets TAVR Stroke Risk With Sentinel Embolic Filter Device](#)" — "[The Gray Sheet](#)," Oct. 17, 2014.) The trial is being closely watched, not only by reimbursement bodies but also potential future innovators and investors, Khosravi says.

Eadie expects the SENTINEL study to be completed in the first half of 2016, and FDA clearance by the end of 2016.

Parhizgar says the company is working with estimates of a global TAVR market of \$3.5 billion by 2020, but declines to speculate on cerebral protection's potential degree of penetration before IDE data are in. However, she adds, if efficacy is proven, "I would say this will become a mandatory use for the device."

She is noncommittal about potential pricing, and says Claret will consider acquisition among other possible strategies after IDE results are in, including raising a Series C round to continue as an independent company. Parhizgar is also discussing reimbursement with the Centers for Medicare and Medicaid Services, and the company plans to submit an ICD-10 application in July 2016.

Other Companies' Approaches

Keystone deflects emboli downstream to other parts of the body, while Claret protects just two of three arteries leading to the brain. **Innovative Cardiovascular Solutions LLC** (ICS) has developed a windsock-like nitinol and polyurethane filter device called the *Emblok Embolic Protection Catheter*, which deploys circumferentially in the ascending aorta to protect not only the cerebral but also the visceral and peripheral blood vessels from liberated embolic debris. Founded in 2012 by interventional cardiologist William Merhi, DO, the company is helmed by CEO R. Kevin Plemmons. ICS has raised \$6.5 million from angel investors, with the most recent round scheduled to close in early 2016. The Emblok device is a 12F system introduced into the femoral artery opposite the one admitting the TAVR device. The company anticipates obtaining CE mark and performing first-in-man in first-quarter 2016.

The father-and-son team behind the start-up **Stroke Prevention Systems** hope to be the first to win FDA approval with a non-invasive device, the *Stroke Prevention System (SPS)*, which fits around the neck much like a blood pressure cuff. When inflated during TAVR, the SPS' purpose-designed bladders briefly occlude both carotid arteries, creating a pressure gradient to deflect potential embolic debris downstream from the cerebral circulation. The deflection of cerebral emboli can be observed in real time with transcranial Doppler ultrasound. The maneuver can be repeated whenever embolic release is expected. Michael Zhadkevich, MD, PhD, a cardiothoracic and vascular surgeon who developed the SPS, is the firm's CEO, while his son, Alexei Zhadkevich, MD, is the company's chief operating officer. The firm has made five US and European patent applications.

"The mere insertion of any catheter or a device inside the aorta or a head artery to prevent embolic events may actually produce additional trauma and generate additional embolic particles and stroke," Alexei Zhadkevich says, explaining their choice to develop a non-invasive alternative. They say the device is easily mastered and could be used in addition to invasive protective options, or as stand-alone cerebral protection in TAVR and other heart procedures.

According to Michael Zhadkevich, the device would initially be reserved for patients who are free of carotid plaque, but he adds that the pressure needed to compress the artery and deflect emboli is low and unlikely to disturb plaque. One advantage of this non-invasive approach, he adds, is that protection can be offered to all patients, not

merely those deemed at higher risk for brain injury.

The self- and angel-funded company is currently conducting a non-blinded prospective randomized study at Self Regional Hospital in Greenwood, SC, where the elder Zhadkevich practices, using transcranial Doppler to monitor emboli. At the same time, a study of the device in Germany is about to begin, which will use pre- and post-procedural DW-MRI as well as transcranial Doppler. A planned study at Emory University is awaiting institutional review board approval. Assuming the US Doppler data show a reduction in observed emboli, the founders plan to submit a 510(k) application to the FDA in December for potential quick approval, without claiming that the device outright prevents stroke. MRI data may allow for a future PMA submission, Alexei Zhadkevich says. FDA approval will lead them to seek a strategic exit. They estimate a price of \$400 to \$500 per device.

Transverse Medical Inc.'s POINT-GUARD is designed to deflect, filter, capture and remove debris during TAVR and other procedures through an undisclosed technology. It would also protect all three arteries, according to CEO Eric Goslau, who adds that the device "conforms to the [aortic] arch anatomy using a dynamic double-edge sealing technology" to eliminate residual flow around the protection device. The privately funded company was founded in 2011 and has filed PCT and US patent applications; it aims for a first-in-humans experience and initial regulatory trials in the latter half of 2016.

Cardiogard Medical Ltd. received 510(k) FDA approval in January for its device, the CardioGard Cannula, which both delivers blood and removes debris from the aorta.

CardioLogical Solutions is the product of a 2013 merger between VasoStitch Inc. and embolic-protection device company Emboline Inc. [\[See Deal\]](#)

In January 2013, **Allium Medical Solutions Ltd.** acquired Gardia Medical Ltd.'s CE-marked stand-alone filter, the WIRION Embolic Protection System, which can be connected to the operator's guidewire of choice. In June of this year, the WIRION earned FDA approval for use in carotid stenting procedures.

Edwards Lifesciences Corp. was initially a front-runner alongside Claret and Keystone with its Embrella for TAVR. However, it released results of a pilot trial in 2013 at EuroPCR, PROTAVI-C, in which all 54 patients, 42 of whom received the device, showed evidence of new ischemic lesions on post-procedural MRI. Edwards spokesperson Sarah Huoh confirms that at this time the company is not pursuing Embrella, though the device remains a part of the Edwards portfolio. "The main driver of this is the latest SAPIEN 3 data, which has demonstrated excellent results, in particular with very low rates of stroke," Huoh says.

Market And Business Considerations

At this time, despite many promising trials, clinical data do not yet exist to definitively prove that embolic protection improves neurological outcomes. But companies are talking to reimbursement agencies and discussing how the devices might be offered. At present, Eadie says, hospitals offering these devices are eating the cost as part of a bundled procedure payment, reducing their short-term profit margins. But if trials show benefit, Burgess says, strategics offering valves could opt to package them with cerebral protection devices, a tactic he says may offer relatively inexpensive differentiation as well as forestall price competition.

Positive results from SENTINEL, Khosravi says, will lead to plenty of meaningful competition among neuroprotective devices. That'll be fine, in Eadie's view. "The opportunity to reduce brain injury is so large across endovascular and left-heart

procedures, the market can handle multiple technologies," Eadie says.

Eadie points out that there is an increasing awareness of brain injury amid recent news about football and battlefield head traumas. The public now recognizes that brain injuries "can be immediately devastating, in the form of an acute stroke, or devastating over the long term from the cumulative effect of repetitive smaller injuries," he says. "This is the next evolution that we're going to witness in interventional cardiology."

Growing public awareness of embolic stroke during cardiovascular intervention – and of the risk of not protecting the brain – may drive market penetration of protective devices, some insiders say. "If we can prevent stroke, shouldn't we do it in every patient?" asks Michael Zhadkevich.

This copy is for your personal, non-commercial use. For high-quality copies or electronic reprints for distribution to colleagues or customers, click [here](#) or call +1 (908) 547-2200.

Printed by **Mr. Michael Carusi MBA, Advanced Technology Ventures (ATV)**

Copyright (c) 2015 Informa Business Intelligence, Inc., an Informa Company. All rights reserved. No part of this article may be reproduced in any form or incorporated into any information retrieval system without the written permission of the copyright owner. Online/print subscriptions, reprints, and web posting and distribution licenses are available. Contact us at (888) 670-8900, +1 (908) 547-2200, or custcare@informa.com.

