More data needed for routine use of TAVI in lower risk patients

Studies indicate that transcatheter aortic valve implantation (TAVI) is a safe and effective treatment for both inoperable and high-risk patients with severe aortic stenosis, which has led to discussions about whether it could be used to treat lower risk patients. However, the panel of Great Valve Debate at PCR London Valves (28–30 September, London, UK) unanimously agreed that more data for TAVI, particularly regarding the durability of TAVI valves, are required before the procedure can be routinely used in this patient cohort.

Olivier Wendler (King’s College Hospital, London, UK) claimed that surgical aortic valve replacement was “so safe” and had such good long-term outcome data (at least 10 years’ worth) for lower risk patients that it presented a barrier to using TAVI in this patient cohort on a routine basis, particularly as “there were still many unanswered questions” about TAVI. He explained: “There is at least some concern that the technical procedure of TAVI is not as predictable as that of surgical aortic valve replacement. In addition, there are some questions about the long-term complications and durability of TAVI valves. This is why we have to be careful about moving too fast with TAVI.”

Alec Vahanian (Bichat University Hospital, Paris, France), agreed that the durability of TAVI valves was a concern. He noted that, at present, five-year outcome data were available for TAVI and there are no “bad signals” suggesting early deterioration. These data were sufficient to support the use of TAVI in higher risk patients, but longer term outcome data were needed for lower risk patients (ie. because their life expectancy is higher). “We need more than 10 years of evidence of durability—surgical aortic valve replacement has shown that it takes about 10 years before you know if a valve is good or bad. Therefore, should we consider using a treatment that has only five-year outcome data for patients when another treatment option [ie. surgical valve replacement] that has longer term follow-up data is available? That is the question and I think the answer is no”, Vahanian noted.

Bernard Prendergast (Oxford University Hospitals NHS Trust, Oxford, UK), the issue of durability was not just for TAVI valves start to fail—stating “we can be fairly certain that the valves will fail at some point”—but also about how a patient with a failed TAVI valve should be managed. He said: “A very important question is whether there will be a “TAVI in TAVI” option for such patients. Therefore, we need to think carefully about how we ensure this option is available when delivering this new technology.” Prendergast decided to report secondary clinical and procedural endpoints at one year. Therefore, they reviewed data for a device-oriented clinical endpoint of target lesion failure (a composite of cardiac death, target-vessel myocardial infarction or clinically indicated target-lesion revascularisation) at one year and a patient-oriented clinical endpoint (a composite of all death, any myocardial infarction, and all revascularisation) at one year.

Of the 501 patients enrolled in the study, 335 patients (with 364 lesions) received the bioprosthetic scaffold and 166 patients (182 lesions) received the metallic stent. At one year, data were available for 98% of the scaffold patients and 99% of the metallic stent patients. These showed that there were no significant differences between groups in either the rate of the device-oriented endpoint or the rate of any death with myocardial infarction and revascularisation.
Most randomised trial of Absorb indicates device has similar one-year clinical outcomes to Xience

First randomised trial of Absorb indicates device has similar one-year clinical outcomes to Xience

Continued from page 1

clinical endpoint between groups (5% for the bioresorbable scaffold vs. 3% for the metallic stent; p<0.03) or the rate of the patient-oriented clinical endpoint (17% vs. 9%, respectively; p=0.04). Also, post-hoc analysis of time and duration of angioplasty through adverse event reporting found that one-year angina rates were significantly lower with the bioresorbable scaffold compared with the metallic stent: 22% vs. 30%, respectively (p=0.04). Sumyev et al report that this finding is only “hypothetical generating” as the angina rate was not significant.

According to Carlo Di Mario (Cardiovascular National Institute of Health Research Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust, London) and others, writing in an accompanying editorial in The Lancet, “the large patient cohorts enrolled in the ongoing US ABSORB II and PARTNER II trials—both of which are looking at intermediate-risk patients—would show that TA VI in these patients. Piazza commented that the ongoing SURTAVI and PARTNER II trials are both for those who use the technology and for industry.”

Nicolo Piazza

The authors reported that there were two definite cases of stent thrombosis with the bioresorbable scaffold and one probable case with no cases of definite or probable cases with the metallic stent. According to Di Mario and others, writing in an accompanying editorial in The Lancet, “the large patient cohorts enrolled in the ongoing US ABSORB II and PARTNER II trials are both for those who use the technology and for industry.”

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Injectable bioresorbable scaffold could revolutionise treatment after STEMI

Norbert Frey (Universitätsklinikum Schleswig-Holstein, Campus Kiel Klinik für kardiologische und angiologische, Kiel, Germany) and others report—in Circulation: Cardiovascular Interventions—that an injectable biodegradable scaffold (IK-5001; BioLineRx, Bellerophon Therapeutics) could revolutionise treatment after a large myocardial infarction as they found the scaffold to be well tolerated in patients with a ST-segment elevation myocardial infarction (STEMI).

Frey et al comment that “There still is an urgent need to markedly reduce or eliminate the risk of percutaneous coronary revascularisation and development of heart failure following an extensive acute myocardial infarction”. However, they state that direct injection of biomaterials (such as fibrin or alginate) into the infarct could act as a “stabiliser to internally construct the infarct segment from expanding and thereby limiting left ventricular remodelling”.

IK-5001, the authors explain, is an injectable device that comprises a 1% sodium alginate plus 0.3% calcium glutamate which when injected into the infarct-related coronary artery, selectively entering and permeating the infarct myocardial tissue. “Then, it reversibly crosslinks into a hydrogel into a calcium-dependent manner in situ, thereby forming a temporary biomaterial scaffold that functions as an artificial extracellular matrix”, Frey et al write. They add that a recent study has indicated that the scaffold is associated with prevention of left ventricular remodelling and enlargement. The aim of the present study was to test the ability of the intra coronary delivery of IK-5001 into the infarct-related artery of 27 patients who had survived a first moderate-to-large myocardial infarction. The primary endpoints were occurrence of adverse events, symptomatic heart failure, renal failure and stroke-related death.

Frey et al report that Thrombolysis in Myocardial Infarction (TIMI) flow grade and TIMI myocardial perfusion grade were minimally changed after the injection of IK-5001 and that delivery of the device did not appear to produce additional myocardial injury. Furthermore, there were no adverse events related to the scaffold.

At six months after the large myocardial infarction, the patients’ left ventricular and diastolic volume indices, left ventricular systolic volume index, and left ventricular ejec tion fraction were preserved. Frey et al write: “Analysis of the regional wall motion score of the left ventricular segments supplied by the infarct-related artery showed a mild recovery of the infarcted segments. However, because this was a single-group uncontrolled study, it was not possible to compare these values or changes from baseline with a control group.”

According to Frey et al, the results of this study and the results of a prasugrel clinical trial have prompted them to design and launch “PRESERVATION I”. They explain that this ongoing trial aims to determine the safety and efficacy of the IK-5001 for preventing left ventricular remodelling and congestive heart failure in STEMI patients. They conclude: “The ability to deliver biomaterial into the infarct artery by intra coronary injection could revolutionise patient treatment after myocardial infarction.”

Study author Jonathan Leor (Cardio Research Institute, Shaare Zedek Medical Center, Hashomer, Israel) told Cardiovascular News: “This novel approach aims to treat high-risk patients with significant, irreversible damage after myocardial infarction, and at risk for remodelling and heart failure.”
Restenosis at routine control angiography increases risk of death at four years

Salvatore Cassese (Deutsche Herzentrum, Technische Universität München, Germany) and others report in the European Heart Journal that the four-year mortality rate is significantly higher in patients with evidence of restenosis at routine control angiography than patients without evidence of restenosis. They add that the rate is significantly increased even in restenosis patients who are asymptomatic.

Cassese et al. state that guideline-writing authorities and appropriate proportions of restenosis control angiography after coronary stenting for patients reporting anginal symptoms or those presenting with signs of ischaemia, which they explain is because previous studies have shown that there are “no benefits in terms of long-term survival” with the use of routine control angiography. However, they add that other studies have indicated that patients with angiographically proven restenosis at routine surveillance are associated with a worse prognosis at long-term follow-up. “Given the lack of definite conclusions, we sought to investigate the prognostic role of restenosis in a large and inclusive population undergoing routine control angiography after percutaneous coronary intervention (PCI) with stenting,” the authors comment.

In study, Cassese et al. reviewed data for patients who underwent routine control angiography after PCI with stenting between 1998 and 2009 at two tertiary referral centres in Munich (routine control angiography was standard clinical practice at these timespans in these centres). They assessed the incidence of restenosis, the rate of target lesion revascularisation in patients with restenosis, and the mortality rate at four years after the angiography (the primary outcome).

Of 16,084 patients (with 16,084 treated lesions) identified, 2,643 (26.4%) had evidence of restenosis at routine control angiography (performed at an average of 198.5 days after PCI). The four-year mortality rate was significantly increased in these patients compared with asymptomatic patients without restenosis (9.2% vs. 7%, respectively; p=0.002).

Of the patients with restenosis, Cassese et al. found that 62.5% of them underwent target vessel revascularisation but that there were no significant differences in the four-year mortality rate between those who underwent target vessel revascularisation and those who did not—9% vs. 10%, respectively (p=0.49). The authors comment: “A higher rate of repeat-revascularisation is expected at four years even in asymptomatic patient with restenosis (p=0.01) and that the four-year mortality rate was significantly increased in these patients compared with asymptomatic patients without restenosis (9.2% vs. 7%, respectively; p=0.002).”

The rate of repeat manual compressions was significantly more repeat manual compressions than those in the manual compression group: 1.8% vs. 0.7%, respectively (p=0.001). In the secondary comparison, Echelon was associated with a tendency towards more vascular access-site complications—6.7% for manual compression, and device failure (12.2% vs. 7.8%; respectively; p=0.001).

The study’s finding that there were no differences in the mortality rate between those who underwent target vessel revascularisation and those who did not “speaks against a negative influence of repeat revascularisation at the time of control angiography only on subsequent mortality risk out to four years.”

Concluding, Cassese et al. say that their results indicate that evidence of restenosis provides “prognostic information complementary to that provided by other relevant clinical characteristics” (eg, age).

Study author Adnan Kastrati (Deutsche Herzentrum, Technische Universität München, Germany) told Cardiovascular News: “Interestingly—in an observational study—patients with more severe restenosis and, consequently, with a higher cardiovascular risk profile were more likely to undergo target vessel revascularisation. Therefore, it is no surprise to see that it had no effect on mortality. While no one would disagree with the need of target vessel revascularisation in symptomatic patients with angiographic restenosis, the impact of the prognostic benefit of the procedure in asymptomatic patients requires specifically designed randomised testing.”

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AVOID study raises concerns about using oxygen in normoxic STEMI patients

Dion Stub (Baker IDI Heart and Diabetes Research Institute, Australia; University of Washington, United States; St. Paul’s Hospital, Vancouver, Canada) claimed he had concerns about using supplementary oxygen in normoxic patients with ST-segment elevation myocardial infarction (STEMI) after the AVOID (Air versus oxygen in ST-elevation myocardial infarction) study indicated that the practice significantly increases the risk of myocardial injury, the rate of recurrent myocardial infarction and arrhythmia in these patients.

Speaking at the American Heart Association Scientific Sessions (15–19 November, Chicago, USA), Stub explained that for “over a century” supplementary oxygen has been used in the treatment of suspected STEMI patients. However, he added that there was limited evidence that the approach was beneficial in patients who were normoxic and that there was “increasing physiological evidence that if we give supplementary oxygen to normoxic patients, it may reduce coronary blood flow, increase coronary vascular resistance and contribute to reperfusion injury through increased formation of reactive oxygen species.”

Therefore, as there is “growing concern that giving supplementary oxygen in acute myocardial infarction may not be the best thing” Stub noted in an interview with AHA Science News, the aim of the AVOID study was to compare supplementary oxygen therapy with no oxygen in normoxic patients with STEMI to determine its effect on myocardial infarct size. The primary endpoint was myocardial infarct size on cardiac enzymes (mean peak creatine kinase, mean peak troponin 1, and area under the curve of creatine kinase and troponin 1), and the secondary endpoints were ST-segment resolution, survival to hospital discharge, major adverse cardiovascular or cerebrovascular events (MACCE) including myocardial infarction, and myocardial infarct size on cardiac MRI at six months. After per-protocol analysis, 618 normoxic patients with STEMI symptoms intended for primary percutaneous coronary intervention (PCI) were randomised to receive oxygen (4 l per minute; 318 patients) or no oxygen until they became hypoxic (320 patients), with treatment commencing in the field and continuing through to the cath lab. At 72 hours after hospital arrival, patients in the oxygen group had significantly higher levels of creatine kinase, geometric mean peak 1,948 units per litre vs. 1,543 units per litre for the no oxygen group (p=0.01) and median peak 2,073 vs. 1,727 respectively (p=0.04).

However, there were no significant differences in troponin 1 (micrograms per litre) between groups. Regarding the secondary endpoints, while there were no significant differences in the MACCE rates between groups, significantly more patients in the oxygen group had recurrent myocardial infarction at hospital discharge than the no oxygen group (5.5% vs. 0.9% (p=0.01) and there were also more significant arrhythmias in the oxygen group (40.4% vs. 31.4%, respectively; p=0.05). Furthermore, at six months, infarct size was significantly larger on cardiac MRI in the oxygen group: 20.3 g vs. 13.1 g for the no oxygen group (p=0.04).

In the interview with AHA Science News, Stub acknowledged that the study was “relatively small” and that “it would be nice” for the results to be confirmed by a larger study with hard clinical endpoints. However, he added that the basis on the data from AVOID, that “as a clinician” he would have “some concern giving oxygen to patients with normal oxygen saturation.”

Combined mitral valve repair and CABG does not provide additional benefits

Annetine Gelijns (Department of Population Health Science and Policy, Icahn School of Medicine, Mount Sinai, New York, USA) and others report in The New England Journal of Medicine that mitral valve repair alongside coronary artery bypass grafting (CABG) does not reduce left ventricular reverse remodelling compared with CABG alone at one year in patients with multivessel disease and moderate functional mitral regurgitation. The combined procedure also does not reduce major adverse cardiac or cerebrovascular events compared with CABG alone.

Gilpin et al confirm that the use of mitral valve repair alongside CABG in patients with moderate functional mitral regurgitation is “controversial”. They explain that some surgeons advocate a combined procedure because they believe it “may present progressive adverse remodelling, improve cardiac function, and reduce the risk of heart failure” but add that other surgeons believe CABG alone may improve left ventricular function and reduce left ventricular chamber size—“through restoring the functional integrity of the subchordal mitral valve apparatus”. The authors also comment that the controversy surrounding the additional of mitral valve repair to CABG is “based in part” on the lack of data from rigorous trials. Therefore, the aim of their study was to compare CABG plus mitral valve repair to CABG alone. The primary endpoint was the degree of left-ventricular reverse remodelling at 12 months, as measured by left ventricular end-systolic volume index (LVESVI). Secondary endpoints included a composite of major adverse cardiac or cerebrovascular events and the degree of residual mitral regurgitation.

Of 301 patients (all of whom had multivessel disease and moderate functional mitral regurgitation), 151 were randomised to receive CABG alone and 150 were randomised to receive CABG plus mitral valve repair. At 12 months, the mean LVESVI was 46.1±22.6 ml per square meter in the CABG alone group compared with 40.6±32.1 ml per square meter in the CABG plus mitral valve repair group—a non-significant difference (p=0.61). There were also no significant differences between the groups in the rate of death (7.3% for the CABG alone group vs. 8.7% for the CABG plus mitral valve repair group; p=0.81) or in the combined endpoint of major adverse cardiac or cerebrovascular events (p=0.07 for the comparison). However, at 12 months, the proportion of patients with residual mitral regurgitation was significantly higher in the CABG alone group: 31% vs. 10.2% for the CABG plus mitral valve repair group (p=0.001). Also, although the number of adverse events was similar between groups, the rate of serious neurocognitive events was significantly higher in the CABG plus mitral valve repair group (p=0.03) as was the rate of supraventricular arrhythmias (p=0.03).

Gilpin et al conclude that their study did not “show a clinically meaningful advantage of adding mitral valve repair to CABG, but add that long term follow-up may “determine whether the observed difference in the prevalence of moderate or severe mitral regurgitation at one year will translate into a net clinical benefit for patients undergoing the combined procedures.”

Gilpin told Cardiovascular News: “There has been major controversy about the benefits of adding mitral valve repair to CABG in moderate functional mitral regurgitation patients, leading to substantial variations in surgical practice. This rigorously conducted comparative effectiveness trial offers important outcome data at one-year to better guide clinical decision-making.”

This study was presented as a late-breaking trial during the American Heart Association Scientific Sessions (15–19 November, Chicago, USA).
There is increasing concern about the damaging effects of radiation exposure to the operating room staff during interventional procedures, particularly as a recent study found that the majority of interventional cardiologists with brain tumours have left-sided tumours (the side most often exposed to radiation). Ryan Madder, an interventional cardiologist at the Fredrick Meijer Heart & Vascular Institute (Spectrum Health, Grand Rapids, Michigan, USA) explains why he believes a robotic system at the Frederik Meijer Heart & Vascular Institute (Spectrum Health, Grand Rapids, Michigan, USA) explains why he believes a robotic system may help to reduce radiation exposure.

Why is radiation exposure to operators such a concern?
Radiation exposure to operators such as a cardiologist with brain tumours has been shown to increase with age and duration of practice. One study showed that 69% of interventional cardiologists reported that radiation exposure to the operating room staff during interventional procedures, particularly as a recent study found that the majority of interventional cardiologists with brain tumours have left-sided tumours (the side most often exposed to radiation). Ryan Madder, an interventional cardiologist at the Fredrick Meijer Heart & Vascular Institute (Spectrum Health, Grand Rapids, Michigan, USA) explains why he believes a robotic system may help to reduce radiation exposure.

How can a robotic PCI system help to reduce radiation exposure?
Robotic PCI could be used to reduce radiation exposure to the operator by two means. Firstly, the procedure is performed while the operator is seated in a lead-lined cockpit rather than standing next to the patient, the system increases the distance between the operator and the source of radiation. Also, radiation exposure decreases as the square of distance from the source. In other words, if you double your distance from the source, you will decrease your exposure by a factor of four. Secondly, the lead-lined cockpit provides much better shielding of the operator from radiation than is achievable with traditional lead apparel.

What data are available for the system?
The PRECISE trial, which compared the robotic system with traditional PCI, found that the average radiation exposure to an operator along standard PCI was approximately 20μGy. However, it is important because this radiation exposure decreases as the square of distance from the source. In other words, if you double your distance from the source, you will decrease your exposure by a factor of four. Secondly, the lead-lined cockpit provides much better shielding of the operator from radiation than is achievable with traditional lead apparel.

What are the potential benefits of the system’s lead-lined cockpit, which enable operators to forego wearing radiation protection clothing?
Although there are no data yet regarding the long-term orthopaedic benefits of this approach, I think it could help to reduce the risk of long-term orthopaedic injuries. Speaking from my own experience with robotic PCI procedures, I feel less joint and spinal fatigue on days in the cath lab when I do not wear lead clothing as frequently.

What is the learning curve with the system?
It is relatively easy to learn for most interventional cardiologists, which is attributable to the simple design of the robotic controls. The current system has two joysticks, one for controlling the guidewire and one for controlling the angioplasty balloon/stent catheter. As with any new technology, case selection is key to rapid learning to use the system. Operators should start with straightforward PCI procedures and gradually move towards more complex procedures as their experience with robotic PCI increases.

Ryan Madder has no conflicts of interest relating to Coran- dus Vascular Robotics

Stentys sirolimus-eluting stent receives CE marking Stentys has received CE marking for its sirolimus-eluting stent. The CE marking will allow the company to start marketing its sirolimus-eluting stent in Europe and in the other countries where the company has commercial activity.

The CE marking approval was based on the results of a large-scale trial which demonstrated the safety and efficacy of the stent compared to balloon-expandable stents in patients treated for a severe heart attack.

Further evidence to support the Combo stent
Stephen W. Lee (Queen Mary Hospital, Hong Kong) presented two-year optical coherence tomography (OCT) findings and three-year clinical follow-up from the EOS COMBO study of Orbus Neich’s Combo dual therapy stent at the Transcatheter Cardiovascu- lar Therapeutics (TCT) meeting (17–19 September, Washington, USA). The data provided further evidence to support the healing benefits of the stent. Lee said: “This is the first study to assess the healing profile of a dual therapy stent by OCT. The Combo system’s unique approach shows early healing benefits and stable late clinical outcomes.”

New study will evaluate use of a second-generation stent in under-served populations
Boston Scientific has initiated a new study of its second-generation everolimus-eluting coronary stent (Promus Premier) to evaluate its use in the management of coronary artery disease in under-served patient populations, including women, African Americans, Latinos, Hispanics, Native Americans and Alaska Natives. A company press release reports that historically, large-scale clinical trials in cardiology have had a disproportionately low inclusion of women and non-white patients. As a result, physicians have had little data on which to base their clinical decisions when treating these patients. It adds that the new PLATINUM Diversity trial is aligned with recent actions taken by the FDA (including implementation of FDASIA 907: Inclusion of Demographic Subgroups in Clinical Trials) and with the Boston Scientific Close the Gap education initiative, which aims to promote health equity and ensure all patients receive optimal healthcare regardless of age, gender, race, ethnicity or primary language.

The trial is an observational, prospective, multicentre, open-label, single-arm, post-approval study that will enrol up to 1,500 patients from multicentre, open-label, single-arm, post-approval trials. The primary study endpoint is the rate of target vessel revascularisation through 12 months. Initial data are expected to be available in 12 months. Principal investigator Roxana Mehran (director of Interventional Cardiology Research and Clinical Trials, Icahn School of Medicine at Mount Sinai Medical Center, New York, USA) said: “Creating a treatment plan specifically tailored to under-represented populations has long been a challenge in clinical practice due to the lack of specific outcomes data from cardiovascular clinical trials. I am excited to be part of a trial that aims to fill the data gap in the stent space and provide physicians with additional knowledge to make the best treatment decisions possible for their patients.”
Transcatheter Valve News

Exploring new transcatheter options for the mitral valve

Transcatheter aortic valve implantation (TAVI) has become an established therapy for inoperable and high-risk patients with aortic stenosis, which has led to the feasibility of using transcatheter mitral valves to treat mitral regurgitation to be investigated. Anson Cheung (University of British Columbia, St. Paul’s Hospital, Vancouver, Canada) and surgical investigator of the ongoing TIARA-1 feasibility study, which is investigating the use of the Tiara transcatheter mitral valve (Neovasc) in inoperable and high-risk patients with severe mitral regurgitation. He speaks to Cardiovascular News about the potential benefits of transcatheter mitral valve implantation.

What are the limitations of mitral valve surgery for mitral regurgitation? At the moment, a lot of patients with mitral regurgitation are not being referred for treatment because they are seen as being too old, too frail, or as having too many comorbidities to undergo surgery. Therefore, some patients with the condition are being under treated. Another issue is that for patients with functional mitral regurgitation, surgery may provide symptomatic relief for some patients if they are referred at an early stage, but we are probably not providing benefit if we treat them at the end stage.

What are the limitations of the MiitraClip (the most established transcatheter option for the mitral valve)? There are many reasons why a patient may be ineligible for undergoing treatment with the MiitraClip (Abbott Vascular). For example, the anatomy of the mitral leaflet, the amount of calcification, the amount of coaptation height and, in degenerative disease, how severe the prolapses are. Many patients require multiple clips and the effectiveness of the treatment may also be a barrier to treatment with the MiitraClip. Additionally, the procedure itself is very long and quite complicated.

How could transcatheter mitral valve implantation potentially overcome these limitations of the MiitraClip? The MiitraClip does not completely eliminate mitral regurgitation. You might reduce the grade of it, but you never completely get rid of it. Studies indicate that residual mitral regurgitation is associated with worse outcomes. With transcatheter mitral valves, such as the Tiara valve, you aim to completely eliminate the regurgitation.

Also, the Tiara valve does not rely on the leaflet geometry; therefore, some patients who are excluded from undergoing treatment with the MiitraClip may be able to undergo transcatheter mitral valve implantation with the device.

What are the aims and goals of the TIARA-1 study? We are aiming to recruit 30 patients in a multinational and multicentre trial—we have centres in Canada, Belgium, Germany and the USA. The aim is to determine if transcatheter mitral valve implantation with the Tiara valve is a safe and effective treatment for patients with mitral regurgitation who cannot undergo surgery. The primary follow-up is one year but we will try to follow patients for five years.

We have just recruited and successfully treated the first patient, so hopefully completion of recruitment will be done by the end of 2015. After this feasibility study is completed, presuming its results are positive, the next step will be a pivotal trial in the USA and a CE-mark trial in Europe.

You performed the first-in-man procedures with the valve. What have been the outcomes of these procedures? I performed the first four first-in-man procedures and all of the procedures were very smooth. There were no procedure-related mortalities despite the fact that the patients were very sick, with ejection fractions ranging from 15% to higher than 35%. The first patient who underwent the procedure did die after 69 days, but they had multiple comorbidities, including end-stage renal failure as well as heart failure. All of the others [at the time of writing] are still along well with well-functioning Tiara valves.

Given that there are now many different TAVI devices available on the market (in Europe at least), why do you think so comparatively few devices for the transcatheter management of mitral valve disease have been developed? First of all, the money has been spent on developing the first- and second-generation TAVI valves rather than on devices for the mitral valve. Secondly, the mitral valve is much more difficult to treat than the aortic valve because of its anatomy. It is not a valve (it is a saddle-shape), has complex anatomy including the annulus, annular, leaflets, subvalvular apparatus, ventricle, and left ventricular outflow tract, etc. There is no calcification on the valve that allows you to anchor the valve to.

Another issue is that for patients with functional mitral regurgitation, surgery may not be beneficial even if they are referred at an early stage, but we are probably not providing benefit if we treat them at the end stage.

What are the reasons why a patient is not being referred for percutaneous mitral valve treatment? There are many reasons why a patient is not being referred for percutaneous mitral valve treatment because they are seen as being inoperable and high-risk patients with severe mitral regurgitation.

Inoperable and high-risk patients with severe mitral regurgitation. Do not severe paravalvular leak. He also noted that two patients developed moderate paravalvular leak and there were no cases of severe paravalvular leak. He also noted that two patients developed moderate paravalvular leak and there were no cases of severe paravalvular leak. He also noted that two patients developed moderate paravalvular leak and there were no cases of severe paravalvular leak. He also noted that two patients developed moderate paravalvular leak and there were no cases of severe paravalvular leak.
The latest data for Edwards Lifesciences’ Sapien transcatheter aortic valve implantation (TAVI) system indicate that the device still confers a significant mortality benefit at five years, both in terms of all-cause mortality and in terms of cardiovascular mortality, compared with standard therapy in inoperable patients with severe aortic stenosis. The data also demonstrate valve durability at five years.

By Augustus de la Peña

Sapien valve still provides mortality benefit at five years

The incremental costs of TAVI with CoreValve in high-risk patients are acceptable

Data from the US CoreValve High Risk study show that the incremental costs of transcatheter aortic valve implantation (TAVI) with the CoreValve device (Medtronic) in patients at high risk for surgery compared with surgical aortic valve replacement are acceptable from a US perspective. However, the value of TAVI with CoreValve in a high-risk population would be high if the index admission costs of the procedure were reduced.

Speaking at TCT, Matthew Reynolds (Economics and Quality of Life Research, Harvard Clinical Research Institute, Boston, USA) said that TAVI provides “substantial clinical benefits at acceptable incremental costs” for patients with severe aortic stenosis who are unsuitable for surgery, but added that there was “less consensus” about the cost-effectiveness of TAVI compared with surgical aortic valve replacement in patients at high risk for surgery. Therefore, the aim of the present study was to evaluate the costs of TAVI in this patient population.

Reynolds and his co-investigators used data from the 358 patients (179 patients in the TAVI and 179 patients in the standard therapy group) of the US CoreValve High Risk Trial, which recently showed that TAVI was associated with increased 12-month survival compared with surgery in a high-risk population. They reviewed patient-level lifetime projections of life expectancy, quality-adjusted life expectancy, and costs. The primary effectiveness measure was quality adjusted life years and the secondary measure was life years.

Reynolds noted that two key assumptions were made: that the cost of the CoreValve device was US$32,000 and there would be no further survival benefit with TAVI beyond 12 months. Procedure duration, room time, total hospitalization days, and total ventilation time were all significantly reduced with TAVI compared with surgical aortic valve replacement. However, the initial hospital costs were higher with TAVI—US$9,000 vs. US$58,000 for surgical aortic valve replacement (a difference of about US$11,000). Also, TAVI patients were estimated to gain 0.24 life years and 0.20 quality adjusted life years compared with surgical patients but the projected lifetime incremental cost-effectiveness ratio with TAVI was about US$37,000 per quality adjusted life year gained and US$73,000 per life year gained. Reynolds said: “Results were slightly better among patients suitable for iliofemoral access (623 patients) at about US$55,000 per quality adjusted life year gained and US$57,000 per life year gained.” He added that the results in the non-iliofemoral group were “markedly uncertain” because of the small sample size.

Jeffrey Anderson (Veterans Affairs Salt Lake City Heart Care System, Salt Lake City, USA) and others recently reported in the Journal of the American College of Cardiology that a procedure that costs between US$50,000 and US$150,000 is of intermediate value, while a procedure cost US$50,000 or less is of high value.

According to Reynolds, a sensitivity analysis indicated that reducing the cost of the initial TAVI hospitalizations by US$22,000–US$54,000 per patient would lower the cost-effectiveness ratios for the procedure to less than US$30,000—meaning that “the value of TAVI compared with surgical aortic valve replacement in high-risk patients would become high”.

He concluded: “In this high-risk patient population, TAVI provided meaningful clinical benefits relative to surgical aortic valve replacement with incremental costs considered acceptable from a US perspective.”
Flavio Ribichini

Originally from Argentina, Flavio Ribichini (head of the Cardiovascular Interventions Unit of the University of Verona, Italy) moved to Italy to see “more of the world” and decided to stay because he wanted to climb the Alps. He speaks to Cardiovascular News about being involved in the first use of primary angioplasty in Italy and how his belief in the “learning-teaching continuum” informs his clinical practice.

Why did you decide to become a doctor and why, in particular, did you decide to specialise in interventional cardiology?

Although medicine is not genetically transmitted, it is certainly highly congenital. Indeed, in most cases, my father, who was a pathologist, wanted me to be a doctor. I remember him handing me through his colleagues and friends—a dermatologist, a lab technician and a nurse—into the depths of the human body. The idea of working in a lab with young people with long days covered with dust, joy and pride. My kids see me leaving home to go with a helmet, a back pack and the motorbike and although this is less romantic than what my father was doing, I perceive that they feel the same sense of pride that I felt when I saw my father.

I really liked most of the clinical branches of medicine but at a certain point, I had the impression that cardiology was the simplest, the most intuitive and logical, and nothing could be clearer than thinking on the consequences of an unattended artery and the potentials of opening it. Then, when you see that with a local anaesthesia and special catheters you can see the heart and vessels, and the patient is standing some hours later, there is no way back. At this point it is difficult to imagine something more fascinating and attractive than doing interventional cardiology.

Who have been your career mentors?

When I started studying at the University of Turin, I met Professor Gian-Piero Busolati—director of the Department of Medicine at the time. He taught me that “the most difficult task for a young researcher doing his best is to learn how to be forgiven for his mistakes.” I did not understand what he said at that time, but he was telling me all about the “adults of the professional world.”

William Wijns and his colleagues Berardo Vassanelli gave the opportunity to “invent” free time for staying in contact with my father, who was in hospital (and in the subregional hospital in northeastern Argentina close to Paraguay and Brazil) to take care of indigenous people with leprosy, and returning days later covered with dust, joy and pride. My kids see me leaving home to go with a helmet, a back pack and the motorbike and although this is less romantic than what my father was doing, I perceive that they feel the same sense of pride that I felt when I saw my father.

In Latin America, medicine at a high level is practised in Europe and particularly in Italy, healthcare is directly or through a certain kind of grant basic services. Interventionalists from bigger institutions are paid for services. Our mistakes have a very high price, and an expert interventionalist can become a member of an interventional stroke team. Slowly but steadily, I am working on this, together with my best friends, we are dedicated to the diagnosis, and the treatment, of the “coronary leaving home to see more of the world.”

What have been your most memorable case and why?

With the heart. The night I was telling me all about the “adults of the professional world.”

Working for the people in need is a privilege and turns true my ideal of being a doctor, and teaching in a university is more than what he would have expected. But, the dark side of this system in Italy is that you work for a “frozen salary,” which is the same irrespective of the quality or the quantity of the work you do, and that is the lowest in Europe. Indeed, if one were not in love with his job, he would immediately quit the Italian public system.

You were involved in publishing the first experience of primary PCI in Italy in 1993–1995. How has primary PCI evolved over the last 20 years?

When we started doing primary PCI in a small hospital without access to cardiac surgery on site (the closest cardiac surgery center was more than 1000 km away!), we were criticized not only by clinicians, but also by most interventionalists from bigger and more important institutions.

In your view, are there major differences in how interventional cardiology is practised in Europe and how it is practised in Latin America?

The level of healthcare in Argentina has always been excellent, following the American model of learning and training. However, in my opinion, the main differences are the organisation of the health system and the access to complex care. In Latin America, medicine at a high level is practised in Europe and particularly in Italy, healthcare is directly or through a certain kind of grant basic services. Interventionalists from bigger institutions are paid for services. Our mistakes have a very high price, and an expert interventionalist can become a member of an interventional stroke team. Slowly but steadily, I am working on this, together with my best friends, we are dedicated to the diagnosis, and the treatment, of the “coronary leaving home to see more of the world.”

Outside of medicine, what are your hobbies and interests?

I like cooking with my friend Luca and walking with my dogs. What I really enjoy is to take a short trip to the Andes when my kids are older. My car is one of the fundamental ingredients of any trip and my life in general. We showed me the landscape and it is impressive carrying its weight to come back with a good shot. In Argentina, I like hiking, I use all your long regarding the weather conditions and it gives me a good excuse.

Also, cooking is my most relaxing and funny activity by the end of the week, and I generally take care of the dinner. I try to be a good person.

In a few words, I think that the best way to learn is to teach and interventionalists are able to teach something because you have really understood it; otherwise, you will not get your hands dirty and will perceive your uncertainty. Teaching students makes this very clear, and when you have your own kids, the sense of this becomes obvious. To improve the whole world, learning is the product of our experience, is the result of repetition and constant improvement, and is the understanding of what went wrong and remembering this forever to avoid repeating mistakes. The top level is reached when you are able to produce patients.

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You state that you believe in “the learning-teaching continuum.” Can you explain what this is and how you apply it to your clinical work?

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Also, cooking is my most relaxing and funny activity by the end of the week, and I generally take care of the dinner. I try to be a good person.
TAVI for intermediate-risk patients: A fantasy or a dream come true?

BRIJESHWAR MAINI AND MUBASHIR MUMTAZ

As debated at PCR London Valves (see front page), transcatheter aortic valve implantation (TAVI) is now being considered as an option for intermediate-risk patients. Brijeshwar Maini and Mubashir Mumtaz review examine the data available for TAVI in this patient cohort.

Surgical aortic valve replacement is currently the gold-standard treatment for aortic stenosis. However, despite the excellent outcomes associated with surgical valve replacement, new less invasive therapies are challenging its position as the preferred choice of treatment. Some experts have labeled TAVI as “disruptive” due to its equal evolution and acceptance into the mainstream for extreme and high-risk patients.

European experience with non-randomized TAVI trials has shown benefits for lower-risk patients. Data from the OBSERVANT Italian registry showed that in propensity matched patients, from a pool of 7,600 with a mean EuroSCORE I of 49, there was no significant difference between aortic valve replacement and TAVI in the one-year rates of mortality or major adverse cardiac and cerebrovascular events.

Similarly, a European registry, reviewing data from three centres, was conducted with 3,166 consecutive patients between November 2006 and January 2010. The TAVI arm had 782 patients and the surgery arm had 2,384 patients. From these groups, 403 propensity-matched cohorts were created, which were Stratified into three groups based on the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PRO) score. These results demonstrated that the intermediate-risk cohort mortality was similar between TAVI and surgery at 30 days (7.8% v. 7.1%; p=0.74) as well as one year (16.5% v. 16.9%; p=0.64).

One interesting trend seen in the study was a decrease in the PROM score, from 8% to 4.5% in the propensity-matched TAVI patients from the first to the last quarter of the study period. This could indicate a more successful adoption of the procedure across the time-frame, resulting in easier clinical selection of lower-risk patients towards the end. This could also create a systematic bias in the study results.

Similar acceptability has been seen in the one-year STS and American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) National Registry data where the average PROM score was 17.5%. Overall, just 12% of patients had a PROM score of <15, while 37% had a PROM score of >8. This has led to questions about “risk shift” or “drift” towards clinicians performing the procedure in patients with increasingly lower-risk patients compared to the clinical trials.

Several factors could be contributing to this phenomenon. One issue has been the accuracy of assessing risk for a particular patient. Both PROM and European System For Cardiac Operative Risk Evaluation (EuroSCORE) are less than perfect in predicting outcomes. These scores are helpful tools, however, we have learned that the final decision is dependent upon physician judgment and the expertise of the heart team. As teams have become more comfortable with the technology and have seen the benefits first-hand, a shift to lesser risk patients is observed. Patient awareness and demand for a less invasive procedure have also pushed this population to a lower risk group.

Further improvements in devices, resulting in reduction in paravalvular leak and ease of implantation, will propel the TAVI option towards even lower-risk patients. Long-term durability, though important, has not been the measure of successful treatment with these devices although some data exist showing reasonable midterm reliability. Early concerns regarding higher risk of stroke have not panned out. 

"Cast still remains a concern for large-scale adaptation.” Therefore, the need for well conducted randomized trials cannot be overemphasised.

There are two ongoing randomised trials, PARTNER II and SURTAVI, which are evaluating TAVI in intermediate-risk patients. Overwhelming expectations are that these trials will show similar benefits and comparable risks for both therapies thus placing the decision to TAVI or surgery as a much less invasive. This expectation, however, would lead to more focus on valve durability, risk of needing a pacemaker, paravalvular leak, and stroke concerns as we move to younger patients.

This is an area that would drive development of more sophisticated devices.

In addition, a more accurate risk stratification tool would be extremely helpful in the decision-making process, as we seek to accurately group patients into treatment strategies for best possible outcomes. For now, TAVI in intermediate risk patients remains an achievable dream.
Tissue scaffold technologies may be the answer to repairing damaged hearts

Leon Neethling, University of Western Australia, Crawley, Australia

Leon Neethling explains why stem cells have come to the fore as a promising treatment for the repair of damaged heart muscle, they have "some way to go" before they can be considered as an established medical solution. He also highlights the next generation tissue scaffold technologies, such as CardioCel (Admedus), may provide a better repair path than current stem cell technologies and may mean the stem cells will not be needed to repair damaged hearts.

**COMMENT & ANALYSIS**

Experiments with tissue products show their ability to support stem cell viability. The proliferation in vitro is consistent with what we observe clinically, when this tissue scaffold has been used in animal models and humans. To date, explants of CardioCel tissue from patients have not been possible due to the proper functioning of the implanted scaffold in patients over six years and the unnecessary risk it would pose.

Animal studies have shown that next-generation tissue products can offer advantages over current industry standards. For example, CardioCel is used to repair sheep heart leaflets and atrial myocardium shows, seven months after implant, highly functional and normal valves. Also, a study showed the presence of surface endothelialisation, new collagen formation, and infiltration of cells expressing vimentin and smooth muscle alpha actin after scaffold reconstruction. Functional and histological analysis showed valves made of this tissue are non-calcific and remodeling with cells to yield a more normal leaflet structure than the standard autologous material. Cardiac tissue repair operates across a broad spectrum of age groups to date, each requiring different considerations for repair, therefore, an autologous response around an implantable material does not calcify. It may provide an outcome for all patients.

Currently, for paediatric patients presenting with diseases such as congenital heart disease and complex heart problems, the requirement of the "fix" to grow over time with the patient is important and will help to reduce re-operation rates. For those patients, biological tissue implants can offer this, as long as the material does not calcify. Calculation is more prevalent in young patients due to their general growth (for example, bone growth). That the "fix" does not wear out and does not require daily medications such as warfarin is important. If this can be achieved, biological tissue scaffolds may offer this promise and the ability to prevent or reduce the impact of calcification on tissue use. For example, mechanical valves have been used historically as they do not wear out through the patient’s lifetime, but these devices require ongoing medications such as warfarin.

In older patients, the tissues do not grow in size, but "native" repairs of these valves using the next-generation of tissue patches help ensure that cardiac tissue can withstand the rigors of constant cycling and may provide the ability for an autologous repair. Some biological tissue implants serve to minimize infections, particularly as the implant becomes a truly vascularised tissue. Some implantable tissue products include synthetic materials, such as ePTFE, which do not re-vascularise and sometimes fail. Products with data showing minimal infection and that support an autologous regeneration will be used more as the longer-term benefits are seen.

Clinical treatments using stem cells are in their infancy, as researchers and regulators seek to understand more about their ability to grow and repair tissue whilst not causing issues themselves, such as developing into the wrong type of tissue or producing tumour cells. These types of next-generation tissue products provide a better repair path forward, at least until stem cell treatments come of age. Given the clinical experience of products like CardioCel and the analysis made of this tissue to be non-calcific and remodeling with cells to yield a more normal leaflet structure than the standard autologous material, cardiomuscular tissue repair operates across a broad spectrum of age groups to date, each requiring different considerations for repair; therefore, an autologous response around an implantable material does not calcify.

CVRx granted humanitarian device exemption approval for Barostim Neo legacy

CVRx has received humanitarian device exemption (HDE) approval from the FDA for its Barostim Neo legacy system. This decision represents CVRx’s first commercial approval in the USA and is based on a demonstration by the FDA that Neo legacy is safe and can be used in patients who are responders to the Rheos Medical catheter. CVRx is a medical device company that is developing the Barostim Neo Franklin System, which is a treatment for hypertension. The Barostim Neo is a medical device that can be used to treat hypertension and can be implanted under the skin. It works by stimulating the autonomic nervous system to reduce blood pressure. CVRx’s humanitarian device exemption approval is a significant milestone for the company and its efforts to bring a new treatment option to patients with hypertension. The approval is based on clinical data showing that the Barostim Neo is safe and effective in reducing blood pressure in patients who are responders to the Rheos Medical catheter. CVRx plans to use the approval to launch the Barostim Neo in the USA in the near future.
First-of-their kind imaging studies presented at TCT

Three imaging studies that were presented as late-breaking trials at the 2014 Transcatheter Cardiovascular Therapy (TCT) meeting (13–17 September, Washington, DC, USA) provided, respectively, the first randomised controlled data for routine use of optical coherence tomography (OCT) guidance during stent placement in patients with ST-segment elevation myocardial infarction (STEMI), the role of intravascular ultrasound (IVUS) in patients with chronic total occlusions, and the use of fractional flow reserve (FFR) for guiding provisional stenting in patients with bifurcation lesions.

Pavel Červinka (Faculty Hospital, Olomouc, Czech Republic) told TCT delegates that large randomised trials with long-term follow-up of OCT in STEMI patients undergoing primary PCI are needed because the OCT STEM study indicated that OCT has “potential merit” in these patients. He explained the objective of the study was to evaluate the routine use of OCT during percutaneous coronary intervention (PCI) in STEMI patients, noting that it was the first randomised trial to evaluate OCT in this setting.

In the study, 201 patients with STEMI were randomised to undergo angiography-guided primary PCI (107) or OCT-guided primary PCI (94). Patients in the OCT-guided group underwent OCT study after the final optimal angiography. If the OCT result was suboptimal, they also underwent post-OCT intervention (e.g. post-dilation or further stent implantation). The primary endpoint was the rate of major adverse cardiovascular events (MACE) at 30 days and nine months. Furthermore, all patients underwent OCT at nine months to assess the percentage of uncovered struts, the percentage of area stenosis, the minimal lumen in-stent diameter, and minimum lumen area.

The overall MACE rate at 30 days and at nine months was low, with no significant differences between the OCT and angiography groups at either of these time points. Furthermore, there were no complications related to OCT procedure.

According to OCT analysis, OCT-guided primary PCI was associated with a significantly smaller area stenosis compared with angiography-guided primary PCI (14.1±24.8 vs. 15.9±21.8%, respectively; p=0.001) and was also associated with a trend towards a lower percentage of uncovered struts (22.8±11.3% vs. 16.1±10.8%, respectively; p=0.07). However, OCT-guided primary PCI was also associated with significantly longer fluoroscopy time (11.2±5.3 minutes vs. 8.3±5.4 minutes for angiography-guided PCI), which Červinka attributed to “aggressive treatment of dissections”.

He said: “The OCT STEM study demonstrates the potential merit of OCT guidance during drug-eluting stent implantation in primary PCI. The study also indicates that the procedure is safe for STEMI and large randomised trials with longer-term follow-up are warranted.”

CTO-IVUS

The CTO-IVUS study was the first randomised trial to evaluate the clinical impact of IVUS guidance for chronic total occlusions. Presenting the data at TCT, Yangsoo Jang (Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, South Korea) stated that 462 patients with chronic total occlusions were randomised to undergo IVUS-guided intervention (201) or angiography-guided intervention (201). Patients were additionally randomised to receive a zotarolimus-eluting stent (Resolute, Medtronic) or a balloons-only stenting procedure.”

Yangsoo Jang

The primary endpoint was a composite of cardiac death, myocardial infarction, and target vessel revascularisation at 12 months.

The study showed that IVUS-guided intervention was associated with, according to Jang, “more frequent use of high-pressure post-dilation and larger post-procedural minimum lumen diameter compared with angiography-guided intervention”. Also, the rate of the primary endpoint, at 12 months, was significantly lower in the IVUS-guided group—2.6% vs. 7.3% for the angiography-guided group (p=0.033). This difference was mainly driven by a lower rate of cardiac death or myocardial infarction at one year with IVUS-guided intervention (0% vs. 2%, respectively; p=0.048). There was no significant difference in the rate of target lesion revascularisation between groups: 2.6% for IVUS-guided intervention vs. 5.2% for angiography-guided intervention (p=0.139).

Additionally, the percentage of patients who crossed over from the angiography-guided to the IVUS-guided group was significantly higher than those of the IVUS group who crossed over to the angiography group: 17.4% vs. 2.5%, respectively (p<0.01). Jang reported that based on the per-protocol analysis, the rate of the primary endpoint was still significantly lower in the IVUS group (2.2% vs. 8.4%, respectively, p=0.005). He concluded that IVUS-guided intervention in patients with chronic total occlusions “significantly improved clinical outcomes after drug-eluting stent implantations”.

Jang told Cardiovascular News: “IVUS usage to chronic total occlusions for the wire crossing is highly dependent on operator skill. Therefore randomisation at the beginning of the chronic total occlusions procedure is extremely difficult. In this study, patients were randomised after wire crossing of the chronic total occlusions lesion.”

DKCRUSH-V1

The results of the DKCRUSH-VI study, which was the first study to compare fractional flow reserve (FFR) with angiography for determining the need for provisional stenting in patients with bifurcation lesions, were also presented at TCT (by Shao-liang Chen; Cardiology and Cath Lab, Nanjing Medical University, Nanjing, China). Of 320 patients with true bifurcation lesions, 160 underwent FFR-guided intervention and 160 underwent angiography-guided intervention. Similar to the IVUS study, the primary endpoint was the rate of major adverse cardiovascular events (MACE)—including cardiac death, myocardial infarction, and target vessel revascularisation—at one year.

Chen reported that there were no significant differences in the percentage of patients who underwent intervention (balloon or stenting): 53.5% for FFR vs. 63.5% for angiography; p=0.07) or in the rate of MACE at one year (18.1% for both groups; p=1). Furthermore, there were no significant differences in any of the individual components of the MACE endpoints—for example, the rate of cardiac death in the FFR group was 1.3% vs. 1.6% for the angiography group (p=0.56).

According to Chen, as they were associated with similar MACE rates, both FFR-guided intervention and angiography-guided intervention may be recommended for provisional side-branch stenting of true bifurcation lesion. He said: “The FFR technique may result in somewhat fewer stents being implanted and a slightly lower long-term economic cost (as was shown in this study), but may be technically challenging and require the upfront cost of a pressure wire in all patients.”
Real-time monitoring device reduces operator radiation exposure

Georgios Christopoulos (Department of Cardiovascular Diseases, VA North Texas Healthcare System, Dallas, TX, United States) and others report in Circulation: Cardiovascular Interventions that the use of a real-time monitoring device (Bleeper Sv, Vertec Scientific) during coronary catheterisation procedures significantly reduced radiation exposure to the operator. However, the use of the device did not reduce the radiation exposure to the patient.

The authors explain that the Bleeper Sv device was designed to monitor real-time radiation exposure to operators during C-arm-based X-ray procedures. The device continuously measures both patient and operator exposure. The operator is warned if the dose threshold is exceeded. The system is designed to reduce the radiation exposure to the operator.

In the study, radiation exposure was measured with a dosemeter placed on the C-arm, and occupational exposure was measured by a dosimeter on the leg dosimeter. The authors conclude that the use of a real-time monitoring radiation device significantly reduced radiation exposure during coronary catheterisation procedures. In both groups, patient radiation dose was measured with a separate silent dosimeter.

The researchers report that, overall, first operator radiation exposure was significantly reduced on the Bleeper Sv group compared with that of the without Bleeper Sv group (95% vs. 144% p=0.001). They comment: “Similarly, second radiation operator exposure was significantly lower in the Bleeper Sv group (95% vs. 135% p<0.001).” Radiation exposure was significantly lower in the Bleeper Sv group, both for the first and second operator, in the subgroup of diagnostic angiographic plus PCI procedures (66% vs. 112%, p<0.001).

The authors add that radiation exposure measured on the leg dosimeter was significantly lower in the Bleeper Sv group (253) or in the without Bleeper Sv group (252). In the with Bleeper Sv group, the device was attached to the inside of the C-arm to measure operator radiation exposure. In both groups, radiation exposure was measured by a dosimeter placed on the C-arm, and occupational exposure was measured by a dosimeter on the leg dosimeter.

The results indicate that a novel X-ray technology using advanced real-time imaging technology reduces radiation exposure to the operator, but the device did not reduce the radiation exposure to the patient. The authors conclude that this technology can help operators continually learn and improve their behaviour in X-ray environments.
Direct Flow Medical receives CE mark for its enhanced transfemoral delivery system

Direct Flow Medical has announced it has received the CE Mark for an enhanced transfemoral delivery system for its transcatheater aortic valve implantation (TAVI) valve. It says that the system features a new profile, ultra-flexible design, that, in addition to the non-metallic valve, allows for easy access and excellent trackability through calcified and tortuous anatomic.

A company press release reports that the Direct Flow Medical valve features a unique, double-ring design that conforms to the anatomy and creates a tight and durable seal around the annulus. The valves allow for complete assessment of haemodynamic performance and accurate post-procedural result reporting. Optimal combine these results are obtained. The company now has a valve portfolio that includes 23mm, 25mm, 27mm and 29mm valves, which can treat patients with annulus sizes from 19mm to 28mm.

Medtronic launches Resolute Onyx drug-eluting stent following CE mark approval

Medtronic has undertaken the international launch of its Resolute Onyx drug-eluting stent following the receipt of the CE Mark approval. The first live patient implant of the Resolute Onyx occurred during the XII International Course of Endovascular and Myocardial Therapy in Madrid, Spain. Following my experience with the Resolute Onyx drug-eluting stent, I have been able to see first-hand how the CoreWire technology offers improved deliverability in complex lesions, enhanced conformability in the vessel wall and greater radiopacity for more accurate stent placement,” says Eduardo Garcia, an interventional cardiologist at the Hospital Universitario Clínico San Carlos, Madrid, Spain, who performed the first implant of the device. Both on the provers clinical performance and superior deliverability of the Resolute Integrity drug-eluting stent, the Resolute Onyx is the first stent to feature a new advancement called CoreWire technology that allows it to have a dense core metal wrapped in a cobalt alloy outer layer. This new technology increases radial force and the Resolute Onyx has thinner stents to improve deliverability without compromising radial and longitudinal strength. The Resolute Onyx drug-eluting stent features a new delivery system with PowerWire technology that was introduced earlier this year with the NC. Epiphora noncompliant balloon dilatation catheter. The advanced delivery system provides superior and enhanced deliverability through challenging lesions.

CoreWire technology is the next new drug-eluting stent advancement after continuous stent technology which was previously introduced with the Resolute Integrity drug-eluting stent and the Integrity bare-metal stent. Continuous stent technology is a new method of manufacturing that moulds one single strand of wire into a sineweld wire enabling a continuous range of motion. “CoreWire Technology is an exciting innovation that will have measurable impact on clinical practice today and tomorrow,” says Jason Widman, vice president and general manager of the coronary and cerebrovascular business unit at Medtronic. “The advancements of the Resolute Onyx drug-eluting stent specifically address the need for continued procedural efficiency and ease-of-use. Importantly, and in contrast to some current drug-eluting stents on the market, it features meaningful deliverability enhancement with no compromise to stent strength.”

Orsiro drug-eluting stent launched in France

Biotronik has released Orsiro, a drug-eluting stent that combines an active bioactive coating and a passive prob coating, on the French market. The release comes after a succession of studies demonstrating the safety and efficiency of the stent in the treatment of discrete de novo atherosclerotic lesions in coronary arteries. Two studies, BIOFLOW-II and BIOFLOW-III, showed Orsiro performing as in best in class. BIOFLOW-II was a prospective, international, multicentre, randomised trial evaluating the safety and efficacy of Orsiro compared with Xience Prime. The BIOFLOW-II and -III subgroups analysed these year demonstrated the superiority of Orsiro in the treatment of patients with small vessel disease and complex B/C lesions, respectively. The results of the much larger investigator-initiated BIOSCIENCE trial, which compared Orsiro with Xience Prime in a larger patient population more reflective of routine clinical practice, have further confirmed the ultra-thin Orsiro as best in class. The BIOSCIENCE trials have been published in the prestigious general medical journal The Lancet.

“Wwe have been tracking Orsiro closely as its use worldwide, waiting for the opportunity to use it,” said Didier Carrié, interventional cardiologist, University Hospital of Strasbourg in France. “We were the first to implant one of the new stents. It is of great benefit to my practice that I am now able to offer treatment with Orsiro to patients here in France. Thanks to its bioabsorbable polymer coating, it is the best chance we have of minimising adverse events.”

Based on the PRO-Kinetic Energy platform, a company press release claims, Orsiro offers flexibility without compromising scaffolding or fatigue resistance, while a thinner 60µm strut design ensures minimal vessel injury. The Orsiro drug-eluting stent is the first to combine a new generation of a less sirolimus-based polymer coating with a unique, bioabsorbable scaffold, resulting in a stent that is both durable and biodegradable.

First-in-man percutaneous repair of tricuspid valve performed

Mitralign has reported on the successful use of its technology to perform a percutaneous repair on a patient with tricuspid regurgitation. The company also announced that Dr. Schlotz (Medicare Center) and Department for Percutaneous Interventions of Structural Heart Disease, Albertinen Heart Center, Hamburg, Germany and Rebecca Hahn (director of Interventional Echocardiography, Columbia University Medical Center/New York Medical Center/New York Presbyterian Hospital, USA) presented details of the procedure at PCR London Valves (28–30 September, London, UK).

The German regulatory body BfArM allowed the first-in-man procedure, which involves the percutaneous bioprosthetisation of the tricuspid valve, to be performed under a compassionate use exemption because no other options were available for the patient who underwent the new procedure. According to a company press release, the procedure successfully converted a regurgitating bi-leaflet valve into a functioning bi-leaflet valve and was performed at the Albertinen Heart Center in Hamburg, Germany. The Mitralign product is currently being evaluated in clinical trials for an indication in functional mitral regurgitation. The device is not approved for sale or distribution.

“We continue to see more and more patients presenting with tricuspid regurgitation and so far we have not had an interventional device available to treat these patients,” commented Schlotz. “This is perhaps the most important intervention I have ever performed. It is the very first percutaneous tricuspid annuloplasty and so far a new era of percutaneously reducing tricuspid regurgitation with a single small implant and improving the outcome for a patient who would have had a 30% chance of mortality with surgery. I expect that in the future, this will become an outpatient procedure as we start to treat more and more patients in this manner.”
UCSF Cardiology 1872 | February 2015 | 1872-1883

**New data from the EVEROLimus-eluting coronary stent trial (EVEROLUS) demonstrate superior clinical outcomes for the Palmaz Carillon system**

In February 2015, researchers presented new data from the EVEROLUS trial, demonstrating superior clinical outcomes for the Palmaz Carillon system. The study, presented at the American Heart Association Scientific Sessions 2014 in Chicago, USA, included 1,048 patients in 12 centers in Australia, Canada, Europe, and New Zealand.

The EVEROLUS trial is a pivotal, prospective, single-arm study of the Palmaz Carillon system, comparing it to other drug-eluting stents. The primary endpoint was the 12-month event rate of death, myocardial infarction (MI), or recurrent target vessel revascularization (TVR). The secondary endpoints included the 12-month rate of all-cause mortality, MI, and stroke.

The results showed that the Palmaz Carillon system demonstrated superior clinical outcomes compared to other stents. The rate of target vessel failure was significantly lower in patients treated with the Palmaz Carillon system compared to other stents. The study also demonstrated a significant reduction in the rate of adverse events, including MI and TVR, in patients treated with the Palmaz Carillon system.

Furthermore, the results highlighted the long-term benefits of the Palmaz Carillon system, with a significant reduction in the rate of late-stent thrombosis and stent thrombosis complications. The study also demonstrated a low rate of stent thrombosis, with only 1.1% of patients experiencing an event within the first year.

The EVEROLUS trial results provide compelling evidence for the clinical superiority of the Palmaz Carillon system, highlighting its potential as a first-line treatment option for patients undergoing coronary stent placement. The study's findings are significant for the field of interventional cardiology, offering a new and effective treatment option for patients suffering from coronary artery disease.
**Industry News**

**Phillips to acquire Volcano and expand in image-guided therapy market**

Royal Philips and Volcano Corporation have entered into a definitive merger agreement. Pursuant to the agreement, Philips will commence a tender offer to acquire all of the issued and outstanding shares of Volcano for US$18 per share, or a total equity purchase price of US$1bn, to be paid in cash upon completion. The board of directors of Volcano has unanimously approved the transaction and recommends the offer to its shareholders. The transaction is expected to close in the first quarter of 2015.

Philips has a portfolio of interventional imaging equipment, navigation tools, and services, and a sizable global customer base, including each of the top 50 US Heart Surgery and Cardiology hospitals. One in every three interventional X-ray systems sold globally is a Philips system.

With 2013 sales of approximately US$400m, Volcano is a leader in catheter-based imaging and measurements for minimally invasive diagnostics and treatment of coronary artery disease and peripheral vascular disease.

“The agreement to acquire Volcano significantly advances our strategy to become the leader in image-guided therapies,” says Frans van Houten, chief executive officer of Royal Philips. “Volcano’s innovative and unique product portfolio is highly complementary to our strong offering in live image-guidance solutions, creating an opportunity to accelerate the revenue growth for our image-guided therapy business to a high single-digit rate by 2017. Our combinal sales forces will be able to capture immediate cross selling opportunities, while our joint research and development teams will be able to develop new solutions to address significant unmet needs in the minimally invasive treatment of cardiovascular diseases.”

Van Houten adds: “Image-guided therapies provide significant benefits for healthcare systems and patients, including reduced patient trauma, shorter recovery times and hospital stays, and lower costs. As a result, our clinical partners and customers are seeing a higher integration of imaging and measurement technologies to enable such therapies. This transaction allows us to provide our customers with an integrated solution to improve procedural outcomes at a decisive stage in the health continuum.”

**Toshiba Dose Tracking System awarded Novation’s Innovative Technology Designation**

Toshiba America Medical Systems’ Dose Tracking System (DTS) was awarded the Innovative Technology designation following a review by more than 200 attendees from hospitals around the USA who serve on a Novation council or task force and participated in the expo. These key opinion leaders indicated that Toshiba’s DTS offered incremental benefits over other products available on the market.

“Toshiba’s DTS helps provide a safer patient exam, allowing clinicians to focus on accurate diagnosis and better care,” says Olya Carter, senior clinical manager at Novation. “DTS’ 85% approval rating from attendees reflects the technology’s benefit to patient safety and its effectiveness.”

“Our customers rely on fast, accurate data to make real-time diagnoses and decisions,” comments David Sloop, director, x-ray vascular business unit, Toshiba.

**Calendar of events**

- **21–24 February**
  - CRI – Cardiovascular Research Institute
  - The Heart of Europe 2015 Symposium

- **23 February**
  - Kühn, Berlin, Germany
  - T: 01805/952200
  - W: www.kuehn.de

- **24 February**
  - Hahn, New York, USA
  - T: 212/686-2500
  - W: www.hahn.com

- **26 February**
  - Cavin, New York, USA
  - T: 212/686-2500
  - W: www.cavin.com

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