

In This Issue

[Press Release](#)

[Other News](#)

[Technology Report](#)

[Previous News Releases](#)

About Us

- [Company](#)
- [Products](#)
- [Legal Notices](#)
- [Contact Us](#)

Join Our List

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NEWS RELEASE

October / Nov. 2009



[From the Desk of Ivan Vesely, Ph.D.](#)

Dear Colleagues

Best wishes to you and your family during the Thanksgiving Holiday!

For VXi, the highlight of October was the [European Association for Cardio-Thoracic Surgery](#), where VXi had a booth and showed off its new concept for a transapically implantable docking station. The meeting was a huge success for us, with the exchangeable valve being applauded by all that visited our booth. Most interesting were the countless visits by sales people wearing badges from other heart valve companies. After seeing our [poster](#), many noted that they are actually independent sales representatives and would rather sell our valve than that of the company on their badge. While this was quite amusing, it was nevertheless gratifying to see the excitement that VXi has created in the valve business.

In the technology report, I review the new transapically implantable docking station. With the bulk of physicians now appreciating the durability limitations of transcatheter valves, we are now ready to introduce a concept that will allow transapically implantable valves to have the same 15+ year durability of surgical valves, and an exchangeable leaflet set - the VXi Vanguard™ technology. This positions VXi at the forefront of the off-pump implantable valve revolution. Transapical valve technologies are currently limited to inoperable patients, and are destined to remain so due to their inherent durability limitations, The ValveXchange Vanguard™ technology will bring these advantages to the entire market, from pediatrics to geriatrics.

To support our new product line development efforts and our accelerated fund-raising activities, we have significantly expanded the content of our [web site](#). Our [Products](#) page now lists our entire portfolio of surgical and transapical valve technologies, and the associated tools for exchange and transapical access. The [Patients](#) page now reviews the options for valve

replacement, the range of technologies available, and the compromises that a patient must make when selecting a particular valve solution, be it surgical, transcatheter or Minimally Invasive - including VXi approaches. Although much of this information was already presented in my previous newsletters, it is now available in a more organized form on our web site. Coming soon to the web site is a greatly expanded "Physicians" page. Currently, that page has links to our Medical Advisory Board only. In the coming weeks, that page will be updated with scientific details that should be of interest to heart valve professionals.

We would also like to report that VXi has licensed a novel imaging technology from [Dr. John Carroll, Cardiology, University of Colorado Health Sciences](#). This technology enables the creation of patient-specific 3-D plastic models of the heart and its chambers. This technology will be invaluable for the training of physicians in the techniques of valve implant and exchange.

Finally, we are most excited to announce that [Dr. Antonio Calafiore](#) has joined the ValveXchange Medical Advisory Board. Dr. Calafiore is recognized internationally as an extremely talented and creative surgeon. He pioneered off-pump coronary artery bypass grafting, the "left anterior small thoracotomy procedure (LAST)", and the "Calafiore technique" of myocardial preservation. After a productive career at the University of Catania and the University of Chieti, both in Italy, Dr. Calafiore has recently moved to Riyadh, Saudi Arabia as the director of the Prince Sultan Cardiac Center.

For those new to this Newsletter, ValveXchange is an emerging technology company based in Colorado. We call ourselves "The Lifetime Tissue Valve Company" and are developing the first-of-its-kind "serviceable" bioprosthetic valve. By offering periodic, minimally invasive exchange of the worn-out leaflet set, young and physically active patients can avoid the use of a mechanical valve and the associated Coumadin® anticoagulation therapy. By adhering to the time-proven design tenets of conventional bovine pericardial valves, we believe that the ValveXchange system will offer the best combination of least-invasive techniques and greatest valve longevity and durability.

Press Release

Antonio Calafiore joins VXi Medical Advisory Board

October, 2009. Denver - ValveXchange Inc. is pleased to announce that Antonio Maria Calafiore, M.D., has joined the VXi Medical Advisory Board. Since May of 2009 Dr. Calafiore has been the Head of the Department of Adult Cardiac Surgery at Prince Sultan Cardiac Center in Riyadh, Kingdom of Saudi Arabia. From 1985, Dr. Calafiore was Associate Professor of Cardiac Surgery at the University of Chieti. He was Full Professor from 2001 until 2003. From 2003 to 2005, Dr. Calafiore was Full



Professor at the University of Torino, and from 2006 to 2009 he was Full Professor at the University of Catania. He was also the Chief of the Division of Cardiac Surgery at the University of Chieti from 1987 to 2003, at the University of Torino from 2003 to 2005, at the European Hospital in Rome from 2005 to 2006 and at University of Catania from 2006 to 2009).

Professor Calafiore is internationally recognized as an extremely talented and creative surgeon. He pioneered (i) off-pump coronary artery bypass grafting, (ii) the LIMA to LAD via a left anterior small thoracotomy (LAST) operation, (iii) the use of intermittent antegrade warm blood cardioplegia for myocardial preservation which is now referred to as the "Calafiore technique", (iv) strategies for using all the arterial conduits (internal mammary arteries, radial artery, epigastric artery and gastroepiploic artery) in single or composite grafting, (v) multiple vessel revascularization on a beating heart, (vi) left ventricular surgical remodeling, and (vii) surgery for functional mitral and tricuspid valve regurgitation.

After a productive career at the Universities of Chieti, Torino and Catania, all in Italy, Prof. Calafiore has recently moved to Riyadh, Saudi Arabia as the director of the Prince Sultan Cardiac Center. He is Vice President of the Italian Society of Cardiac Surgery and Member of the European Society of Thoracic and Cardiovascular Surgery, Society of Thoracic Surgeons and American Association of Thoracic Surgeons.

ValveXchange Licenses Imaging Technology from Denver Cardiologist, Dr. John Carroll.

November, 2009. Denver - ValveXchange Inc. recently executed a license agreement with the University of Colorado for a process to transform cardiac imaging data into high-quality three-dimensional models used for heart valve product development, clinician training, and pre-procedure planning.

Based on the work of John D. Carroll and Shih-Yung (James) Chen, both of the University of Colorado Denver School of Medicine (Department of Cardiology), this technology converts data from routine medical imaging of soft tissues (ultrasounds and CT and MRI scans) into 3D models, which are then transformed into physical models using 3D printers. ValveXchange will use the technology in conjunction with its implantable heart valve program. ValveXchange is developing a novel artificial heart valve that has all the advantages of today's tissue-based heart valves, but can be implanted and replaced through a small incision between the ribs. This approach is expected to replace traditional open-heart surgery for many heart valve procedures.

The licensed 3D Heart Modeling Technology offers a unique opportunity to develop the valve technology using patient-specific heart anatomy examples, and later to train physicians in implant techniques in a highly realistic manner. Cardiovascular diseases, particularly heart attacks and strokes, are responsible for the death of seventeen million individuals worldwide annually. Improved valve designs coupled with more advanced clinician training and patient-specific procedure planning are expected to

significantly improve both treatment and quality of life of patients requiring these implants. *"We expect this advance in 3D heart modeling to provide ValveXchange with a real advantage in the market space,"* said ValveXchange CEO Larry Blankenship. *"By being able to work with a model of the specific patient's heart before the heart valve replacement procedure, physicians are expected to be able to decrease procedure time and increase success rates. This will be one more reason for them to select the advanced heart valve technology being developed by ValveXchange."*

"The models are a powerful tool for procedure planning and physician and patient education, and they will complement ValveXchange's expertise in medical device development," added Paul Tabor of the University of Colorado Technology Transfer Office. *"We are hopeful the marriage of these technologies results in a leap forward in the design, testing and performance of implantable heart valves."*

Other News

Heavy Fibrotic Tissue Overcome in Latest Leaflet Exchanges

We have recently done another open exchange procedure in the sheep model, this time at the 3-month time point. At this stage, the valve is heavily fibrosed - much more that is typically observed in humans (see image right). Again, we were able to remove the fibrosed-in leaflet set and snap a fresh one onto the docking station, which remained in the sheep. As our design intended, and our previous studies confirmed, the new valve seating area was clean and free of tissue ingrowth, and



accepted the new leaflet set properly with no perivalvular leakage. We have thus increased the challenges associated with our valve exchange experiments - this time, overcoming significant fibrotic tissue overgrowth - and now have another sheep alive and well with an exchanged leaflet set.

ValveXchange expands its International Presence at the EACTS Meeting in Vienna

The EACTS conference was by far the most successful for VXi. Larry and Ivan were accompanied by [Dr. Gerard Guiraudon](#), our special advisor and inventor of the Guiraudon Universal Introducer (GUCI™), that VXi is developing for transapical access to the heart for valve implantation and exchange. With all the traffic at the booth, we barely had time to take a photo of the booth (see below). Dr. Guiraudon is shown at left and Mr. Blankenship, our CEO, is shown at right. A copy of the poster that was presented at the meeting can be downloaded [here](#).



The VXi booth was close to that of St.Jude and Sorin, and that may have contributed to the high amount of traffic. Nevertheless, the EACTS meeting in general had greater physician presence in the exhibits area than observed in other meetings. Besides the [poster](#), we also had a running computer display showing features of our technology, such as the transcatheterally implantable docking station of our new Vanguard™ valve. The positioning of the Vanguard™ technology in the marketplace is discussed below in the Technology Report. Besides interested physicians, we also had a huge interest by sales people wearing badges from other heart valve companies. We naturally thought that this was part of the competitive intelligence gathering process. However, after seeing our poster, most of these people approached us and said to the effect,

"Although my badge may say Valvetronic Life Sciences, I am actually an independent sales rep. I would really like to sell your valve instead of what I am selling now. Do you have a European distributor?"

While this was quite amusing, it was nevertheless gratifying to see the excitement that VXi is creating in the valve business. These sales reps would then leave and bring over a key physician client of theirs for a second opinion on the ValveXchange technology. All left with smiles on their faces. If VXi completes its fundraising in early 2010, VXi expects to begin first-in-man studies by the end of 2010 or early 2011.

Besides meeting future customers and industry partners, the EACTS meeting was also very useful in obtaining information about competing products. Having a lot of valves on display at the various booths is great PR if done right. Conversely, it can also clearly display their deficiencies. Our new web site includes examples of such deficiencies. Conferences such as EACTS are thus invaluable in helping evaluate our progress compared to others. The evidence is now more convincing than ever that transcatheter devices will remain limited primarily to the inoperable patient population as consistency of deployment in the native aortic valve cannot be assured, and the valves will have markedly reduced durability as compared to conventional surgical valves. The new, collapsible,

transapically implantable VXi Vanguard™ will be the first, best hope for an off-pump, transapically implantable valve with the full durability of conventional surgical valves and the added benefit of exchangeable leaflets.

Technology Report

As noted in the Reality Check section of the [previous newsletter](#), concerns about the long-term durability of transcatheter valves have suddenly come to the forefront. In particular, in his opening address to the transcatheter valve session at last month's TCT meeting, [Dr. Martin Leon made a comment to the effect](#) that '*Transcatheter valves should be limited to inoperable patients until their durability has been established*'. Thank you! This is exactly what we have been saying all along. The good news is that the VCs have been listening also... if not to me then perhaps to Dr. Leon. Indeed, during the past two VC conference calls, I was hurried through my detailed explanation of why transcatheter can't last more than 5-7 years with words like "Yes, we understand why they can't last. Now what are you doing about it?"

In this month's Technology Report, I would like to introduce you to the VXi Vanguard™. The on-line Webster dictionary defines "[Vanguard](#)" as "*the forefront of an action or movement*". With the introduction of the transapically implantable docking station, we intend to lead the movement to translate the non-surgical approach to valve implantation to the operable patient. While we applaud the transcatheter valve companies for developing new ways of treating the inoperable patient, the larger goal of obsolescing heart valve surgery cannot be realized until such devices measure up to the durability of established surgical valves. Further, the larger goal of obsolescing heart valve surgery must also include a solution for the younger patients who are candidates for mechanical valves. This will require a "lifetime tissue valve" solution - please see the ValveXchange logo.

I recently came across a second publication that reports on the non-circularity of deployed transcatheter valves. The first was the work of [Zegdi](#) from Paris, who reported direct, intraoperative visual evidence of non-circular deployment. The second is by [Schultz](#) from Rotterdam. Schultz et al. analyzed 30 patients implanted with the CoreValve system using multislice computed tomography. In that manuscript, they report the incidence of non-circularity and non-apposition at various level of the Nitinol cage. Schultz et al. report that "*none of the frames reached the nominal dimensions*", with the mean cross sectional area of the valve being 24% lower than that of the patients annulus. This suggest some residual stenosis. More importantly, only 5 of the 30 patients had symmetrical expansion of the CoreValve cage at the critical leaflet coaptation level. In most cases, the CoreValve cage expanded to an elliptical shape with a major-axis/minor-axis diameter difference of 2.3 mm. For the two valves sizes that were designed to have a 22 and a 24 mm diameter at the critical leaflet coaptation region, the mean minor axis diameters were 20.0 and 20.8. indicating significant underdeployment in

both valve sizes. The authors also noted that there was incomplete apposition of the valve in 61% of the patients, although *"it remains to be elucidated whether incomplete apposition is associated with a higher risk of thromboembolism"*. Both non-circularity and underdeployment lead to the malpositioning of the leaflets that has historically been linked to early valve failure. For example, in the Ionescu-Shiley valve, poor leaflet geometry contributed to an [8-year failure rate of 71%](#). Indeed, even slight leaflet asymmetry can cause a good pericardial valve to fail as early as 3 years. For example, the valve shown at right failed from single leaflet prolapse at 3 years.



Note that the free edges of the left and right leaflets (arrows) sit below that of the posterior leaflet (*).

As reported last month, non-circularity and incomplete expansion is a huge problem for pericardial tissue valves. Both lead to leaflet [wrinkling](#), [pinwheeling](#) and elevated stresses, and ultimately to early valve degeneration and failure. This has been established through the historical evolution of surgically implantable valves.

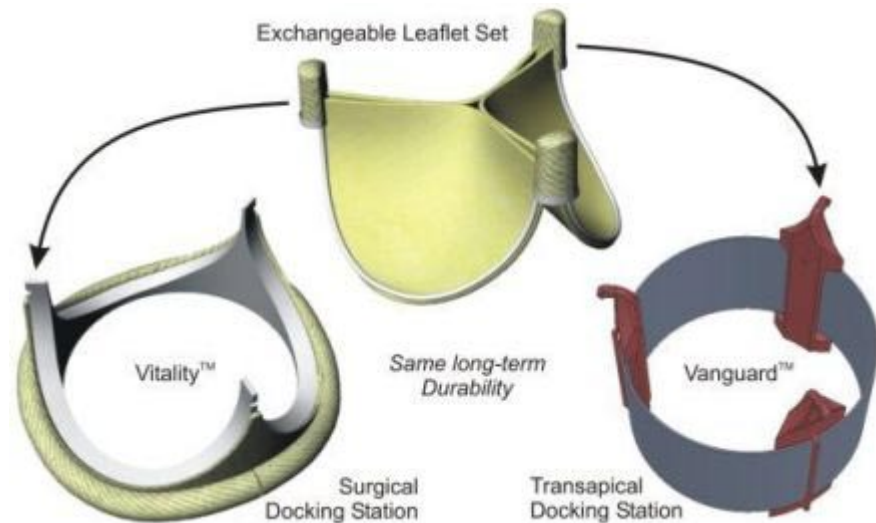
How does one then ensure that a new valve concept follows the three tenets of good valve design:

- (i) Flexible stent posts
- (ii) Precise central gap between mating leaflets
- (iii) Absolute leaflet symmetry and circularity when deployed,

yet still be collapsible? Let's revisit the collapsibility requirement. Does it really need to be collapsible? If so, then by how much? If it needs to be collapsible for transcatheter delivery, what is an acceptable route? Is transfemoral really any better than transapical? The difficulty that the early pioneers of transcatheter valves got themselves into by making the valve so small, is that they had to compromise the principles of good valve design by making the valve highly collapsible. If we were to relax the collapsibility requirement somewhat and use a transapical only approach, these critically important valve design features could be retained. This is exactly how we have designed our products.

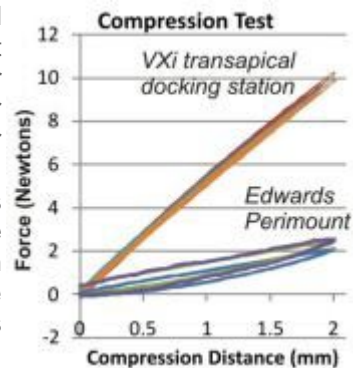
To provide a superior option to transcatheter valves that maintains the three principles of good valve design, we have conceived of a collapsible, transapically implantable docking station. The VXi two-part valve concept lends itself well to the transapical implant approach because the leaflets can be delivered after the docking station is in place and do not need to be pinched within the collapsed metal frame. This means that the leaflets can be of the appropriate thickness and therefore do not violate the "Triad of Dimensions, Load and Materials" introduced in [last month's newsletter](#). Indeed, the same leaflet set can be used for both the solid docking station of the Vitality™ valve and the collapsible docking station of the Vanguard™ (see image below). Both docking stations are circular, both

maintain 120 degree leaflet symmetry, and both have a fixed, non-variable diameter that preserves the important central gap between the coating leaflets.



All current transcatheter valve designs are a single unit. That is, the leaflets are mounted to the cage that is collapsed and then re-expanded inside the calcified native aortic valve. This has two limitations. The first is that the leaflets need to be folded, crimped or somehow wrinkled up inside the collapsed cage. This means that the leaflets have to be thinner, and great care has to be taken to not damage the leaflets during valve collapse. The second is that having the leaflets as an integral component of the supporting cage limits the ways in which the cage can be collapsed. Separating the leaflet set from the docking station, as done in the VXi valve, frees the docking station from the design constraints of collapsibility in the presence of fragile leaflets. It enables a collapsing mechanism that is topologically very different from that possible with the leaflets attached. In the Vanguard™ design, we use a metal band on which the three stent posts slide as the band is wound up, much like a watch spring or the lid of a can of sardines is wound or unwound. This type of mechanism for collapse and expansion cannot be used in conventional valve designs where the leaflets are rigidly fixed to the metal cage.

A further advantage of the sliding metal band is that it can be a solid piece without any holes or struts that need to stretch or collapse. Being solid gives it far greater torsional and compressive resistance. For example, even in its first prototype phase, the Vanguard™ docking station was already 5 times stiffer than the base of the Edwards Perimount valve, when compressed from a circle to an ellipse (see graph at right). This means that when it is deployed in the calcified valve, it will be



round, it will remain round, and it will remain at the deployed diameter. When the leaflets are snapped on, they will have the intended diameter, the central gap will be preserved and leaflet geometry will remain as precise as in the one piece, surgically implanted Vitality™ valve. Stent post flexibility will be identical to that of the Vitality™ because the Vanguard™ uses the same stent posts and the same leaflet anchoring mechanism.

With the emergence of the Vanguard™ technology, VXi has crossed a major threshold in the evolving heart valve technology marketplace. We conceived the original Vitality™ because we believe that a surgical valve with an exchangeable leaflet set is the best solution for patients - it provides the greatest effective orifice area because it is implanted after the native calcified leaflets are excised, it does not depart from the principles of good valve design and hence can offer the longevity that patients have grown accustomed to, and its serviceability provides a lifetime tissue valve solution. This has been the foundation of the exchangeable valve concept and the origin of the VXi Vitality™. We continue to believe that a single surgery Vitality™ option with off-pump exchanges later in life is indeed "best for the patient". A secondary option is important for patients of all ages who have the need to eliminate the first open, on-pump procedure. For those patients who are candidates for surgery, but who are willing to have their calcified leaflets "pushed aside" rather than surgically excised, we are developing the Vanguard™ transapically implantable docking station. The Vanguard™ ensures the same long-term leaflet durability as the Vitality™, but without the first open-heart surgery. With the Vanguard™ technology, ValveXchange is thus at the forefront of a movement to offer completely non-surgical approaches for the treatment of valvular disease for patients of all ages. We are the only valve company whose off-pump valve technology conforms to the three critical tenets of durable valve design and the only valve company with exchangeable leaflets.

(i) Flexible stent posts to cushion leaflets during closing

(ii) Central gap to accommodate leaflet extension and prevent wrinkling

(iii) Absolute circularity of frame and precision of 120° leaflet symmetry



As noted on the main page of our revised web site - ValveXchange is developing The Future of Heart Valve Therapy - **WITHOUT COMPROMISE!**

With our ongoing success in leaflet exchange in the hyperfibrotic sheep model, ValveXchange continues to push the limits of Minimally Invasive Valve Technologies. We are particularly pleased with the continued expansion of our Medical Advisory Board, which now rivals that of established valve companies. With the emergence of the Vanguard™ concept - the transapically implantable docking station - we have a portfolio of tissue valve technologies that spans the full range of patient ages and conditions, from "pediatric to geriatric".

I look forward to sharing details of our progress with you in the coming months.

Sincerely,

Ivan Vesely, Ph.D.
Founder and Chief Scientific Officer
ValveXchange Inc.
vesely@valveXchange.com

Recent News Releases

September, 2009. Denver - ValveXchange Inc. is pleased to announce that Michael J. Mack, M.D., has joined the VXi Medical Advisory Board. Dr. Mack is Director of Cardiovascular Research and Cardiovascular Medicine of the Heart Hospital Baylor Plano and Director of Cardiovascular Surgery for the Baylor Healthcare System. He is considered to be the most noted authority on the emerging field of transcatheter valves. [Read More.](#)

June, 2009. Denver - ValveXchange Inc. announces that Walter Randolph "Randy" Chitwood, Jr., M.D., FACS, FRCS has joined the VXi Medical Advisory Board. Dr. Chitwood was the principal investigator of the FDA robotic mitral valve trials that led to approval for this use in the United States. Today, he is the world's leader in robotic mitral valve surgery. [Read More.](#)

May 15, 2009. Denver - ValveXchange Inc. is pleased to announce that it has signed an option agreement with Dr. Gerard Guiraudon to license his Universal Cardiac Introducer technology. Unlike rigid trocars, the Guiraudon Universal Cardiac Introducer (GUCI) is a flexible, collapsible system that facilitates intracardiac surgery and off-pump exchange of the VXi valve. [Read More.](#)

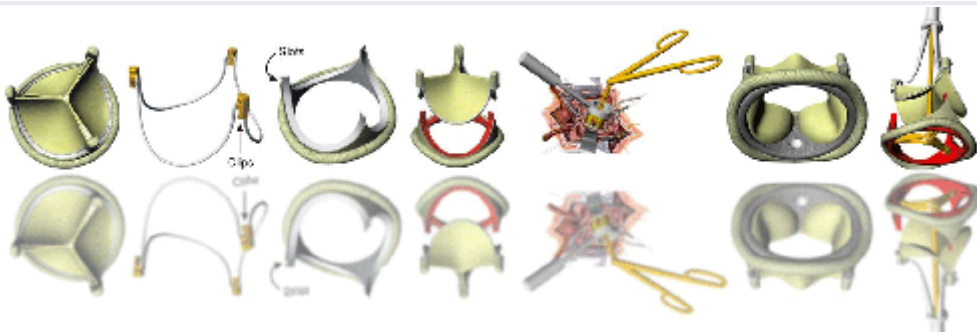
March 18, 2009. San Francisco, CA - Frost and Sullivan held their annual "Excellence in Medical Technologies & Life Sciences Awards" banquet on this date, honoring companies in the bioscience and medical device fields. ValveXchange Chairman and CEO, Larry Blankenship, was there to accept the award. [Read More.](#)

March, 2009. Denver - ValveXchange Inc. announced that Dr. Tirone E. David has joined the VXi Medical Advisory Board. Dr. David is recognized world-wide for his pioneering work in valve sparing surgery, his remarkable surgical skills and his commitment to teaching. [Read More.](#)

March 30, 2009. Denver - ValveXchange licensed its exchangeable valve technology patents from the Cleveland Clinic. The Clinic and ValveXchange have now entered into an arrangement whereby the Cleveland Clinic will in the future receive an equity position in ValveXchange, Inc. [Read More.](#)

February, 2009. Denver - ValveXchange Inc. announced that of Dr. Joseph Sabik, Chair of Cardiothoracic Surgery, The Cleveland Clinic Foundation, will serve as the Chair of the VXi Medical Advisory Board. [Read More.](#)

January 30, 2009 - Denver - ValveXchange Inc. announced that it has begun animal testing of its proprietary exchangeable valve technology, working with the College of Veterinary Medicine at the Colorado State University, Fort Collins, CO, and with Experimental Surgical Services, University of Minnesota, Minneapolis, MN. Both Institutions are well-recognized for their expertise in animal surgery. [Read More.](#)



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