The Future of Mitral-Valve Replacement
--Company Aims to Make Valve Replacement for Mitral Valve Regurgitation Viable Option for More Patients by Removing the Need for Cardiopulmonary Bypass--

By Robert Andrews, Medical Division Manager, Foster-Miller, Inc.
Robert Wilkins, CEO, Endovalve Inc.

Four million Americans suffer from mitral-valve regurgitation (MR),[1] a condition in which the heart's mitral valve does not close completely, allowing blood to flow backwards in the heart. Left untreated, MR is likely to cause chronic fatigue, shortness of breath, weakening of the heart, and other serious complications. These complications become more severe over time, leading to debilitation for many MR patients. Repair and replacement of the mitral valve both require open heart surgery, which involves a number of significant, sometimes fatal, risks to the patient including stroke, seizure, renal failure, blood clots and infection. Due to these risks, only about 40,000 MR patients are treated surgically each year.[2]

This unmet clinical need led Dr. Howard Hermann, a renowned interventional cardiologist at the University of Pennsylvania, and his colleagues, to invent a less risky valve replacement option for MR patients. To avoid major open-heart surgery with cardio-pulmonary bypass, Dr. Hermann and his team of researchers created the foundational design for a replacement valve to be inserted during a short, minimally invasive surgical procedure, and ultimately percutaneously via the femoral vein to reach the heart. While the idea had the potential to revolutionize MR treatment, developing and manufacturing a commercial system would prove to be difficult and costly, with significant technical challenges to be overcome.

Endovalve was founded in 2005, and has a worldwide exclusive license to develop and commercialize Dr. Hermann's less-invasive mitral-valve replacement solution. In the early, high risk, phase of product development, the company has operated as a "virtual company," leveraging the industry and regulatory expertise of third-party firms and providing significant cost-saving benefits.

The Heart of Endovalve's Technology

Sitting between the left atrium and the left ventricle of the heart, the mitral valve's role is to control blood flow to the left ventricle prohibiting regurgitation of blood back into the left atrium of the heart. With MR patients, this function is severely comprised and the mitral valve allows blood to backflow into the left atrium.

Because blood is reversing into the left atrium, a sufficient amount of blood is not being pumped throughout the body. To compensate, the left ventricle enlarges, stretching the mitral valve. This stretching, in turn, increases the leakage of the mitral valve, leading to a vicious cycle that continually debilitates MR patients.

To prevent mitral-valve leakage, cardiac surgeons can perform cardiopulmonary bypass surgery to repair the valve or replace the valve with a mechanical or bioprosthetic device.

Although these surgeries have proven success rates, many patients are either not healthy enough to undergo the surgery or opt not to have it because of the innate risks.

As an interventional cardiologist, Dr. Hermann understood that a minimally invasive surgical or percutaneously inserted valve would avoid many of the difficulties associated with the current procedures to treat MR. The treatment would remove the risks associated with cardiopulmonary bypass, and make definitive treatment available to patients not fit for surgery as well as ultimately those with only moderate leakage.

These factors led Dr. Hermann to design a mitral valve that could be inserted through a small incision directly into the heart, or via the femoral vein, to the left atrium, and anchor into position to replace the malfunctioning native valve. The valve prototype was envisioned to fold to fit through a small catheter and then unfold or open in the atrium. Here, the new valve would supplant the native valve and would function immediately.

Virtual Business to Solve a Vital Need

The complexity of designing a mitral valve for catheter insertion would prove to be a significant challenge. The valve-replacement system would need to be designed small enough to fit through the femoral vein. The valve would also need to be stable enough to anchor into position once in the mitral annulus. Because the mitral annulus is a kidney shaped-like structure, anchoring the valve in place would be very difficult.

The engineering talent needed to design such a complex product would need a wide range of expertise, not only in cardiology, but also in other disciplines such as materials science, biology and mechanical engineering. As a start-up company, internally hiring such a staff of diverse, qualified engineers and project managers would be extremely costly and reduce the risk of success.

Costs and risks deter financial investors, and as a very early stage start-up company whose only product offering had not yet demonstrated proof-of concept, the possibility of failure was still present. These issues became the catalyst for choosing a virtual business model.

The appeal of the virtual business model is the reduction in fixed costs, such as payroll and rent for office space. It also allows companies to leverage the competencies of external firms through outsourcing, and concentrate on building their internal core competencies. This model has become increasingly popular because it offers investors reduced risk of capital loss in the event of product failure. These advantages are particularly important in the medical device marketplace, a high-technology, R&D-intensive market, where the virtual company trend continues to grow.

The virtual company business model has proved to date to be an effective solution to develop the percutaneous mitral valve. As part of this model, Endovalve contracted a design engineering partner to do the early stage development of its product.

Working with a proven R&D partner also lowers risk and reduces overhead costs, increasing investment attractiveness.

Based on these qualifications, Endovalve retained the Commercial Equipment Group of Foster-Miller, a subsidiary of QinetiQ North America, as its research and development partner. The company came to the table with a wide range of medical industry experience, spanning over 50 years, and a wealth of multidisciplinary knowledge. These attributes were attractive components for the small start-up company. This type of expertise was impossible to attain in a traditional business model but accessible in a virtual business model.

Two Heads are Better than One

Employing a third-party engineering firm provides many benefits to a start-up company. A team with industry-spanning expertise, such as a third-party engineering firm, can apply the optimal technology to the product concept at a fraction of the price of a full-time engineering staff with matching capabilities.

Many engineering firms have a system of processes in place to protect IP at all levels of production. Proper IP protection must begin in the first stage of concept ideation and continue throughout the development process, including a consistent practice of checks and balances. In addition, companies can negotiate with partners to hand over all IP once the project is complete. Often, companies can also negotiate contracts with competitive exclusivity to protect the investment.

Another major benefit to partnering with a third-party engineering firm is that most firms will have a well-defined, formal process in place to facilitate regulatory compliance. Meeting regulatory standards is essential for getting a product to market as quickly as possible. Roadblocks caused by failing to meet these regulations can slow the process considerably and reduce attractiveness for additional venture capital funding.

The virtual business model can also result in efficient innovation. Inventors are sometimes hesitant to alter their original design concept. Working with an R&D partner allowed Endovalve and Dr. Hermann to distance themselves from the design process and let the engineers bring the technology to life without being married to a specific model or prototype. An unbiased partner can focus first on the function of the system without feeling tied to an intended design. In this case, the R&D partner revised the device design several times for optimum performance.

For example, Dr. Hermann's initial valve was able to fold to fit into the femoral vein and then unfold once at the native valve site. However, it was not optimized for anchoring into place, and was not able to prevent leakage around the native valve. Foster-Miller worked with the Endovalve team to alter aspects of the original design to improve the new valve's ability to function properly.

Looking to the Future

Currently, Foster-Miller and Endovalve have finalized a full-scale functional model of the new valve-replacement system to prove the feasibility of the technology. The full-scale model

performed well and establishes that the product will be able to fold and deploy. This significant achievement allows Endovalve to begin animal testing, which it has identified as the second stage of a four stage project. The third phase consists of refining the working valve design and the fourth phase will include extended animal testing, where the animal will have to survive with the valve in place for more than 120 days. Manufacturability will also be proven at this stage, while the final step comprises validation. The valve-replacement system is expected to be available on the medical market by 2014.

Due to the popularity of percutaneous cardiovascular treatments today, cardiac surgeons and cardiologists should be able to easily adapt to and perform this new procedure. The system is anticipated to do for the mitral valve what the stent did for coronary arteries: offer the benefits of traditional surgery with a less-invasive treatment. The result of this medical innovation should result in reduced recovery time and more importantly, an overall improvement in patient quality of life.

About Foster-Miller

Foster-Miller, Inc., a part of QinetiQ North America's Technology Solutions Group, is a technology and product development company with an international reputation for delivering innovative products and systems that perform under the most demanding conditions. Foster-Miller is certified Quality Systems Standard for Medical Devices ISO 13485:2003, SW-CMM Level 3 software certification from the Software Engineering Institute at Carnegie Mellon University, and Aerospace Quality Management Standard AS9100. Visit www.foster-miller.com for further information.

About QinetiQ North America

QinetiQ North America provides world-class technology and responsive solutions to U.S. government customers. More than 5,400 engineers and technologists work in partnership with customers to develop innovative technology solutions to meet the challenges of national defense, homeland security and information access. QinetiQ North America is part of QinetiQ Group plc, a leading international defense and security technology business. For more information, please visit www.QinetiQ-NA.com.

About Endovalve Inc.

Founded in 2005, Endovalve is developing a system that could provide sufferers of mitral regurgitation with a new, less invasive option for early treatment of this progressive, increasingly prevalent disease. Endovalve's mitral-valve replacement approach could provide a better, safer alternative to current treatments and a better alternative to doing nothing, as is the case with the majority of some four million Americans with significant mitral-valve insufficiency. Spun out of the University of Pennsylvania in spring 2006 with a $4-million investment from Battelle Ventures and its affiliate fund, Innovation Valley Partners, the startup company has been functioning as a virtual company, using Battelle Ventures' offices in Princeton, N.J., as its operational headquarters. For more information about Endovalve, please visit www.endovalve.com.

###

References

[1] http://www.nyp.org/news/hospital/216.html
[2] http://www.columbia.edu/cu/record/archives/vol30/vol30_iss2/page6.pdf