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YEAR FOUNDED

Spun-out of Maquet
in 2012

WHO'S BEHIND IT

Inventors are biomedical engineer Evan Anderson and cardiac surgeon Pierluca Lombardi, MD

UNMET CLINICAL NEED

Most patients with mitral regurgitation also have some degree of left ventricular dilation, which decreases the odds for long-term success after mitral valve repair or replacement

SOLUTION

A simple epicardial clip, the *Mitral Touch*, which remodels both the mitral annulus and the left ventricle

FUNDING TO DATE

A little over \$2 million since the spin-out, from private investors

ADVISORS

Michael Mack, MD (Baylor Health Care System); Vinod Thourani, MD (MedStar Heart & Vascular Institute); Isaac George, MD (New York Presbyterian/Columbia University Medical Center); Maria Sainz (Aegea Medical); Amr Salahieh (Shifamed); Husam Balkhy, MD (UChicago Medicine); Gansevoort Dunnington Jr, MD (Adventist Heart Institute)

Structural Heart

MITRE MEDICAL: A DUAL STRATEGY FOR MITRAL VALVE REPAIR

Most patients with heart failure suffer from both left ventricular dilation and mitral regurgitation. Mitre Medical has a simple epicardial clip that addresses both simultaneously.

by
MARY STUART



You might say that **Mitre Medical Corp.** has a contrarian approach to mitral valve disease. While the major companies operating in structural heart disease have recently spent \$1.7 billion to acquire companies developing transcatheter mitral valve solutions, Mitre Medical is sticking with surgeons by offering them a beating heart option in the form of an epicardial device. (*To read about acquisitions in the mitral space, see "4C Medical: Transcatheter Mitral Valve Avoids Known Issues by Design," MedTech Strategist, January 2018.*) While Mitre's product has been in the works for a while, time has lent support to its thesis of treating both mitral regurgitation (MR) and left ventricular (LV) dysfunction, surgically.

Mitre Medical's *Mitral Touch* epicardial clip entered into human studies in December 2017 and the company now has one-year follow-up data on the initial patients. But how the company got to this point is a long story.

The *Mitral Touch* project began within Guidant's cardiac surgery division under the leadership of Maria Sainz (an advisor to Mitre Medical, she's also CEO of women's health company Aegea Medical Inc.). The project moved to **Boston Scientific Corp.** upon its acquisition of Guidant. When Boston Scientific divested its cardiovascular surgery assets to the Maquet division of **Getinge**, the group continued to evolve the project, and eventually delivered successful six-month GLP studies.

However, Maquet made the strategic decision that implants did not fit into its business model. It thus granted a license to the inventors, which include biomedical engineer Evan Anderson (now the CEO of Luma Therapeutics, which he

founded) and cardiac surgeon Pierluca Lombardi, MD (now corporate medical officer for Getinge). Mitre Medical was thus founded in 2012 with the benefit of the millions of research dollars that had gone into the project.

CEO John MacMahon first encountered Mitre Medical through his connection to Stanford Biodesign in 2016, when the company had recently left the Fogarty Institute. Among many other executive positions in the medical device industry, MacMahon was CEO of Mitralign for two years, which, he says "was attempting to emulate mitral valve surgery from the catheter standpoint." **Edwards Lifesciences Corp.** eventually bought the assets of Mitralign in 2019. MacMahon says "In the course of surgical observations, I developed an appreciation for the gap between what people wish catheters could do and what surgeons actually do every day for the mitral valve." After he left Mitralign, MacMahon says that, "helping this patient still felt like unfinished business."

So when MacMahon saw what Anderson and his team had developed, he thought "Simple, surgical and beating heart. If this works, it will help a lot of real-world patients." MacMahon himself put the seed money in, assembled a team with mitral surgical and catheter backgrounds, updated the license with Maquet in December 2016, and devices were ready to be implanted in patients by December 2017.

The *Mitral Touch* is similar in form, function and delivery to a mitral annuloplasty ring—the same materials, similar shape, and surgical implantation. Unlike the rings, though, *Mitral Touch* is implanted on the outside of the heart (*see Figure*

1). The anterior arm sits above the mitral valve within the transverse sinus (the space between the mitral valve and the aorta) and the padded section sits below the valve and below the AV groove on the ventricle. "As a result you treat the left side of the heart as a structure, remodeling the ventricle with a push, and the mitral valve comes along for the ride," says MacMahon.

Cardiovascular surgeon Michael Mack, MD, an advisor to Mitre Medical, is a thought leader in the heart valve space. Mack had seen the device during its development, and, says MacMahon, he realized that the external placement would transform the procedure and empower surgeons to treat patients they presently leave untreated. Mack also found the timing ideal; the resurgence of the *Mitral Touch* was being met with clinical data

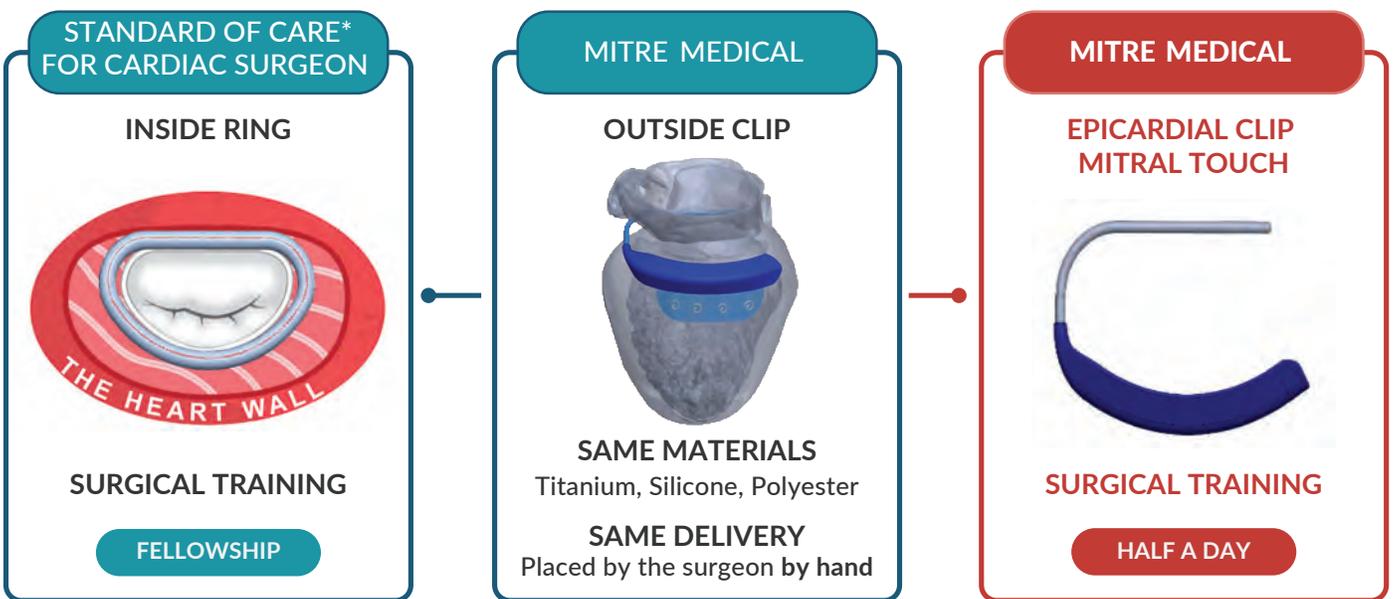
from multiple mitral valve trials. The two randomized cardiac surgery trials sponsored by the CTSNetwork demonstrated that the procedural risks for internal ring placement were not worth the long-term benefit.

The three culprit challenges were first, the atriotomy (to cut further into the heart); second, the additional hour with the patient's heart stopped while the surgeon sews the ring in place; and lastly, the ring-to-LV dilation mismatch with the result that treating the MR alone did nothing to curb the momentum of LV dilation and the subsequent return of MR at one year. In the heart failure cycle, the left ventricle grows by about 10% each year, MacMahon notes. The *Mitral Touch* overcomes all three limitations by design. "External, beating heart placement and sub-valvular support of the left ventricle is a gamechanger," said Michael Mack,

"empowering surgeons to fulfill the unmet need to treat the MR and the LV in their patients."

The need for a dual treatment strategy for both MR and the LV is reflected in recent interventional trials as well. The results of the COAPT and MITRA-FR trials demonstrated similar findings from use of **Abbott Laboratories Inc.**'s *MitraClip*, comparing the MR-only device with medical therapy. Patients whose issues were predominantly with MR had ground-breaking results for primary and all 10 secondary endpoints. But the patients with proportional MR and LV issues had neither primary nor secondary benefits. In Baylor cardiologist Paul Grayburn's meta-analysis of both trials, he proposed a new conceptual framework that distinguishes amongst the heterogeneous group of patients who have functional MR due to LV disease. (See

Figure 1
Mitral Touch Epicardial Clip Compared to Standard of Care



*Internal mitral annuloplasty ring.
Source: Mitre Medical Corp.

“Proportionate and Disproportionate Functional Mitral Regurgitation: A New Conceptual Frame-work That Reconciles the Results of the MITRA-FR and COAPT Trials,” *JACC: Cardiovascular Imaging*, December 2018.)

As a mounting body of clinical evidence defines this unmet need, Mitre’s own clinical results show it is poised to fill the void, namely the company’s own six-month data from its ENRAPT-MR study of CABG patients presenting with MR, which demonstrated a 40% reduction in mitral regurgitation and a 19% reduction in the size of the left ventricle. The ENRAPT-MR study enrolled coronary artery bypass patients presenting with MR, the same patients identified in the CTSNetwork trials.

Mitre Medical will enable surgeons to serve existing coronary artery bypass patients with MR, 30% of which have moderate to severe MR, although less than 5% of them get their mitral valve treated in the same procedure. In the US, this target population represents about 48,000 patients, of which, according to findings from the CTSNetwork, only about 8,000 currently get their mitral valves treated during CABG surgery, and most of them are patients with degenerative (not functional) mitral valve disease. “Surgeons want to treat the mitral valve and the left ventricle while they’re in the OR, but the standard of care holds them back, especially for the FMR [functional MR] patient,” says MacMahon.

Because of the simplicity and ease-of-use of the *Mitral Touch*, it might close this gap. Surgeons can complete the bypass procedure first, then implant the epicardial clip. The procedure can be accomplished quickly; it took surgeons fewer than 30-minutes to implant the first two of the first five implants, says MacMahon. “From what we learned in our initial study, we expect to have even greater

MR reduction and faster implantation when we touch patients in the US later this year.”

MacMahon became aware of the gap between “what people wish catheters could do and what surgeons actually do every day for the mitral valve.”

Mitre Medical’s second target indication addresses the heart failure patients left behind by the COAPT and MITRA-FR results. The company estimates that the population of heart failure patients with proportional MR and left ventricle issues is three times the size of the MR dominant patients that match the new *MitraClip* indications. Speaking at the CRT [Cardiovascular Research Technologies] conference in 2019, Greg Stone, MD, modelled the new *MitraClip* patient population as 274,000; that gives Mitre Medical an estimated market greater than 700,000 patients who require treatment of both their MR and LV.

At the company’s first booth sponsorship at the 2019 AATS [American Association for Thoracic Surgery] Mitral Conclave, held in New York, NY in May, MacMahon says feedback highlighted the high prevalence of the dilated LV in a broad stroke of surgical patients. Cardiac surgeon and host David H. Adams, MD, also saw in the new therapy the potential to provide repair to patients who are now getting more and more replacements. He stated, “I would find cases to use it right now because when I see really

tethered leaflets, the kind of leaflets where people say, ‘Oh, we will just do a replacement now,’ I could use this technology to remodel and protect their ventricle and preserve their valve too.” Future innovations, already in development, include the ability to do minimally invasive and robotic *Mitral Touch* procedures.

At this stage of the evolution of mitral valve therapy, it’s becoming clear that the mitral toolbox now needs to include something for the left ventricle. At an earlier stage in the field, clinicians hoped that treating the MR alone would reverse the LV enlargement, but, as noted, that’s just not playing out in the clinical trials of surgical or catheter-based interventions. “That’s why LV-dedicated tools are needed,” says MacMahon.

“Surgeons know they have patients on the table with LV dilatation. They’ve told us that if they had a strategy for the left ventricle, they could grow their business into heart failure.” The *Mitral Touch* clip implant procedure presents a viable solution: simple, off-pump, and outside of the blood path (so that the chronic use of blood thinners won’t be necessary).

Mitre Medical is currently raising \$12 million in a Series B financing. To potential investors, MacMahon points out “We have one-year data; evidence of durability. The importance of the left ventricle has been validated and the clinical signature that we can treat it is documented. We have had our FDA pre-submission meeting for a fast surgical track in the US.” And he bets the company can get to US approval for \$12 million, which is a fraction of the expense faced by catheter companies. “We feel that the convergence of the data, the cardiac surgeon, and the *Mitral Touch* can raise the hopes of bypass patients with MR as well as patients left behind by the COAPT results.” 