

Percutaneous Treatment for FMR: A Ventricular Approach

Transpericardial LV chamber and annulus remodeling for mitral regurgitation with the iCoapsys System.

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Functional mitral regurgitation (FMR) is a left ventricular (LV) disease characterized by mitral insufficiency in the absence of structural valve abnormalities. It can present either in association with dilated (nonischemic) cardiomyopathy or ischemic (regional) wall motion abnormalities. Annular enlargement and geometric deformation of the entire valve apparatus in these settings contribute to FMR. FMR commonly provokes heart failure and increases mortality as well as morbidity rates.^{1,2} Medical therapy is of limited benefit, and currently mechanical treatment options fall only within the realm of open heart surgery,³ including annuloplasty repair or prosthetic

mitral valve replacement. These cardiac surgical techniques fail to address the primary underlying problem of LV distortion and progressive ventricular remodeling.^{4,5} There is a need for a less-invasive, but more importantly, an integrated approach, directed at both annular and ventricular reshaping. Two closely related novel therapies are currently under investigation: the surgical Coapsys and percutaneous iCoapsys devices (Myocor, Inc., Maple Grove, MN) (Figure 1).

Although the methods for delivering both devices are different, the actual implants are nearly identical. Both devices consist of an anterior and posterior epicardial pad tethered together by a subvalvular (ie, transventric-

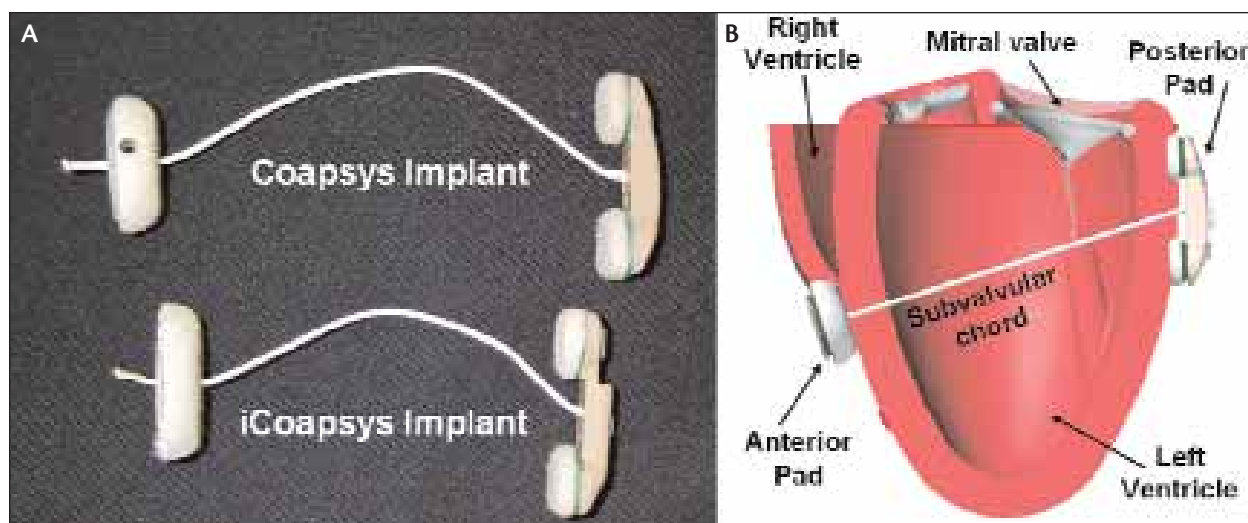


Figure 1. Photograph of the nearly identical Coapsys (surgical) and iCoapsys (percutaneous) devices (A). Diagram of the implant in position (B).

ular) chord, which passes through the LV and between the papillary muscles. After implantation, the chord length can be reduced by a sizing device under transesophageal guidance to establish an appropriate degree of septal-lateral reduction of the LV and annular dimensions. This, in turn, compresses the regurgitant orifice and reduces mitral regurgitation.

SURGICAL COAPSYS DEVICE

The surgical Coapsys device has been developed to treat FMR using a simplified approach. Traditional annuloplasty requires sternotomy, cardiopulmonary bypass, and atriotomy. Although the Coapsys approach eliminates the need for cardiopulmonary bypass and atriotomy, it is nevertheless delivered using an open chest approach through a median sternotomy. The Coapsys device is implanted with specially designed surgical instruments using direct visualization of external landmarks and epicardial two-dimensional echocardiography of the internal LV structures.⁶

The Coapsys device is currently undergoing clinical

TABLE 1. THE VIVID FEASIBILITY STUDY
(VALVULAR AND VENTRICULAR IMPROVEMENT VIA iCOAPSYS DELIVERY)

Abbreviated Criteria:

Inclusion

- Age 18 to 85 years
- NYHA class II to III
- Ischemic or nonischemic FMR
- Mitral regurgitation grade 3 to 4
- LVEF $\geq 25\%$ for NYHA II
- LVEF $\geq 30\%$ for NYHA III

Exclusion

- 1° (structural) mitral valve disease
- Previous pericarditis or pericardial intervention
- Other valve lesions requiring surgery
- LVEDD > 7 cm

Study Design: Prospective, multicenter, nonrandomized, single-arm feasibility evaluation of iCoapsys in patients with FMR.

LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension.

investigation. The initial nonrandomized feasibility trial, TRACE (Treatment of FMR Without Atriotomy or Cardiopulmonary Bypass), has been completed. Thirty-four patients participated in TRACE. All patients underwent combined coronary artery bypass grafting (CABG) and Coapsys implantation for ischemic mitral regurgitation. One-year follow-up has been reported in the initial 29 participants, demonstrating durable mitral regurgitation reduction from grade 3.0 ± 0.55 to 1.1 ± 0.99 .⁷ No significant safety concerns arose. The ongoing pivotal trial, RESTORE-MV (Randomized Evaluation of a Surgical Treatment for Off-Pump Repair of the Mitral Valve) is currently randomizing patients who need CABG and

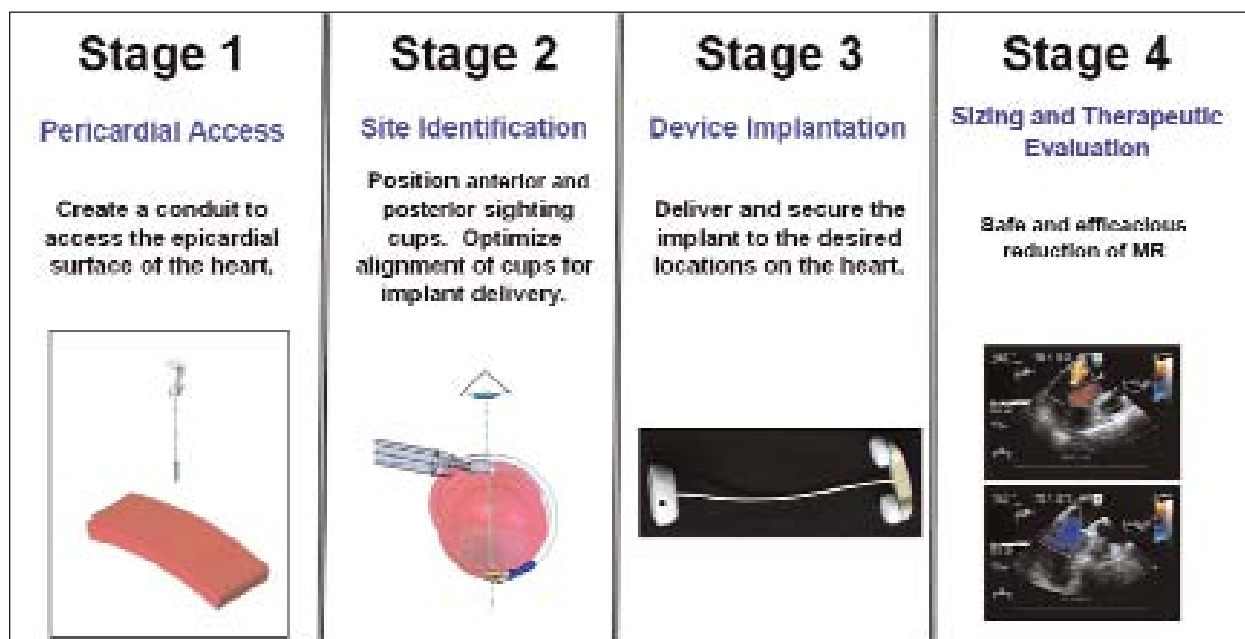


Figure 2. Procedural stages of iCoapsys implantation.

have grade 2 or greater functional mitral regurgitation to either CABG with conventional annuloplasty repair or CABG with Coapsys implantation. In the initial 19 patients randomized to Coapsys, intraoperative mitral regurgitation grade was reduced from 2.7 ± 0.8 to 0.4 ± 0.7 ($P < .0001$), and epicardial-to-epicardial diastolic LV dimension was reduced from 8.5 ± 1.2 to 6.4 ± 0.8 cm ($P < .0001$).⁸

For the completed TRACE feasibility evaluation, primary adverse events (PAE) were defined as death, stroke, myocardial infarction (MI), Coapsys structural failure, and reoperation for bleeding, life-threatening arrhythmia, and heart valve repair/replacement. Survival and freedom-from-PAE rates at the end of the 1-year follow-up period were 97% and 91%, respectively. A total of three PAEs were recorded in three (9%) patients. The early PAEs (≤ 30 days postoperatively) were perioperative death due to aortic dissection caused by an intra-aortic balloon pump (not Coapsys-related) and development of ventricular arrhythmia

resulting in reoperation with graft revision. The lone late PAE (≤ 30 days postoperatively) was a case of reported stroke (neurologic impairment > 24 hours) with CT evidence, but subsequent clinical examination showed absence of neurologic sequelae. Postevent echo showed no evidence of thrombus formation on or near the subvalvular chord. During the follow-up duration, there was no evidence of Coapsys device failure, no reoperations for valve surgery, and no MI (Myocor, oral communication, March, 2000). Results of the RESTOR-MV trial (Randomized Evaluation of a Surgical Treatment for Off-Pump Repair of the Mitral Valve) are not yet available as the trial remains in the active enrollment phase.

THE iCOAPSYS DEVICE

The iCoapsys, a percutaneous transcatheter implantation system, has been developed to further reduce the invasiveness of the procedure. This device duplicates all the critical elements of the surgical (ie, Coapsys) device.

Safe delivery and accurate device positioning have now been preliminarily demonstrated in acute animal models without mitral regurgitation.⁹ As a result of the successful animal experience with the transcatheter delivery system and preliminary findings thus far obtained with the ongoing surgical Coapsys clinical investigation, the feasibility trial, VIVID (Valvular and Ventricular Improvement via iCoapsys Delivery), was developed and is now FDA approved. This multicenter phase 1 trial has just been launched and will include 15 to 30 patients with symptomatic ischemic and nonischemic FMR (Table 1).

CATHETERS AND OPERATIVE PROCEDURE

A series of specifically designed catheters have been developed for percutaneous implantation. The procedure can be divided into four stages: (1) pericardial access, (2) site identification, (3) device implantation, and (4) sizing and therapeutic evaluation (Figure 2).

Pericardial Access

A novel pericardial access system has been designed for delivery from a subxiphoid approach (Figure 3A). The pericardial access needle has a distal lancet tip and a proximally adjacent penetration stop to prevent overadvancement into the myocardium. Appropriate positioning of the pericardial entry point is preoperatively determined with coronary CTA and/or

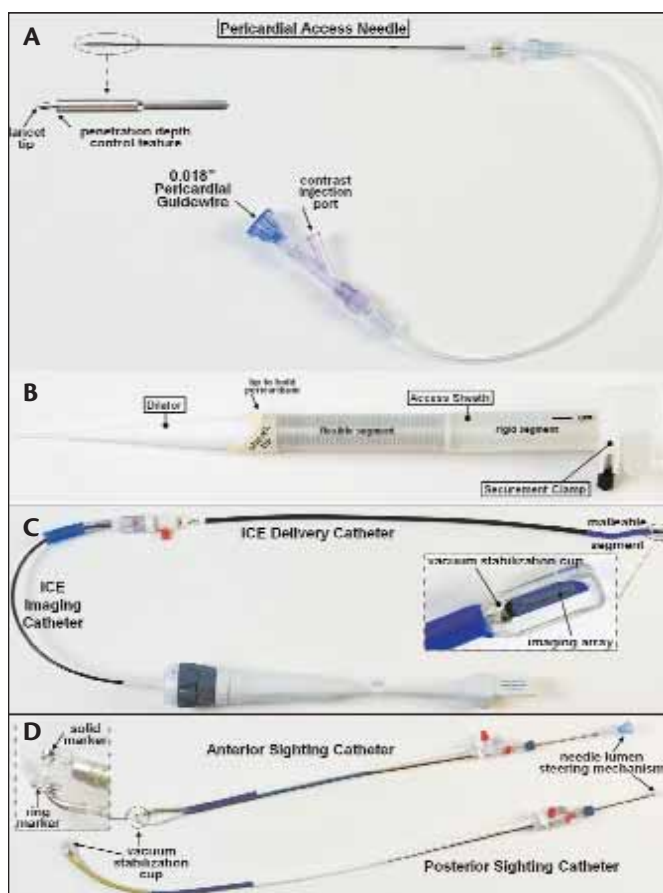


Figure 3. Pericardial access needle (A), pericardial access sheath with dilator (B), intracardiac echo (ICE) delivery catheter with imaging probe (C), and sighting catheters (D).

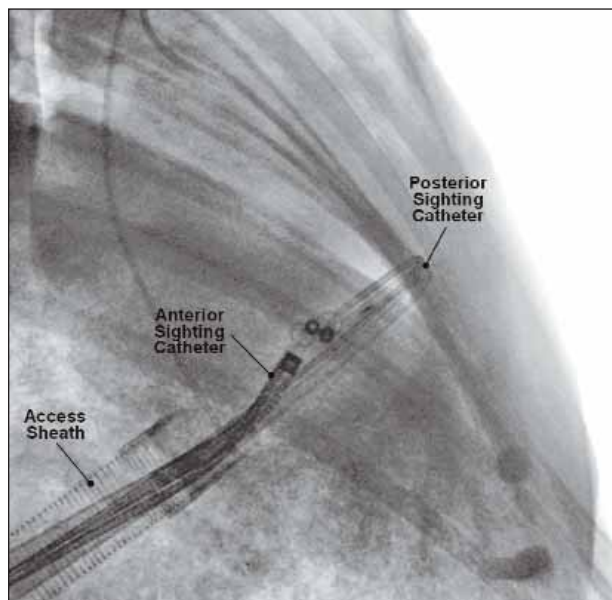


Figure 4. The “sighting view” is depicted with anterior and posterior sighting catheters superimposed. It is generally in a shallow right anterior oblique cranial angulation.

echocardiography. Intraoperative positioning is undertaken with fluoroscopic and coronary angiographic guidance. A contrast injection port on the proximal end of the needle is used to confirm pericardial space access. Guidewire exchanges are then carried out, the parietal pericardium and overlying soft tissue are predilated with peripheral angioplasty balloons, and an access sheath is ultimately placed and temporarily secured at the percutaneous entry point.

Site Identification

Specifically designed sighting catheters are used to identify the anterior and posterior implantation sites and to establish the transventricular chord. They are delivered through the pericardial access sheath and positioned under fluoroscopic and epicardial echocardiographic guidance. Initially, an ICE delivery catheter (Figure 3B) is positioned and temporarily vacuum stabilized on the anterior cardiac surface 1 to 2 cm medial to the mid-left anterior descending artery.

Echocardiographic images are then generated of the LV in cross section, extending from the papillary muscles apically to the mitral annulus at the base. The posterior sighting catheter is then delivered to the posterior LV epicardial region (Figure 3C). This posterior catheter is positioned 2 to 3 cm apical to the arteriovenous groove, and further adjustments are made with epicardial ICE guidance for precise placement midway between the papillary muscles; it is then vacuum stabi-

lized. Fluoroscopy is then performed in multiple angulated views to establish a “sighting view” whereby precise superimposition of the anterior ICE imaging transducer over the posterior catheter’s vacuum stabilization cup is achieved (Figure 4). The ICE catheter is then removed, and the anterior sighting catheter is positioned in its place (Figure 3C).

Device Implantation

A steering mechanism at the proximal end of the sighting catheter is adjusted to precisely aim the anterior and posterior epicardial cups at each other before transventricular needle delivery. The anterior needle assembly is inserted through the anterior sighting catheter’s needle lumen under fluoroscopy, 3 to 4 cm into the LV chamber. After removing the needle stylet, a snare is advanced into the LV through the needle lumen. The posterior needle is then advanced into the LV through the posterior catheter’s needle lumen. The anterior snare is used to grasp the posterior needle, which is then pulled through the anterior wall. A transventricular chord is thus established after removing the sighting catheters and exteriorizing both anterior and posterior limbs. A transventricular chord implant is delivered through the chord lumen. Anterior and posterior pads, attached to their delivery catheters, are then tracked over their respective chord limbs, positioned on the cardiac surface, and affixed to the LV epicardium.

Sizing and Therapeutic Evaluation

The epicardial-to-epicardial chord distance is then shortened to achieve maximal mitral regurgitation reduction. Device sizing is carried out under transesophageal echocardiography guidance to achieve significant mitral regurgitation reduction. This is accomplished with the use of a sizing instrument advanced over the anterior limb of the transventricular chord until it comes to rest on the anterior pad surface. After releasing the epicardial pads from their delivery catheters, the anterior limb of the chord is trimmed and the access sheath is removed, completing the implant procedure (Figure 5).

CONCLUSION

In our preclinical experience, the iCoapsys system was successfully delivered and accurately positioned in all study animals. There were no cases of coronary compromise, mitral valve leaflet or subvalvular impingement identified. Additionally, there were no prolonged hemodynamic or arrhythmic complications and no excessive bleeding in these acute adult sheep implants.⁹

Moderate-to-severe mitral regurgitation occurs in <19% of patients after MI and in 15% of patients with

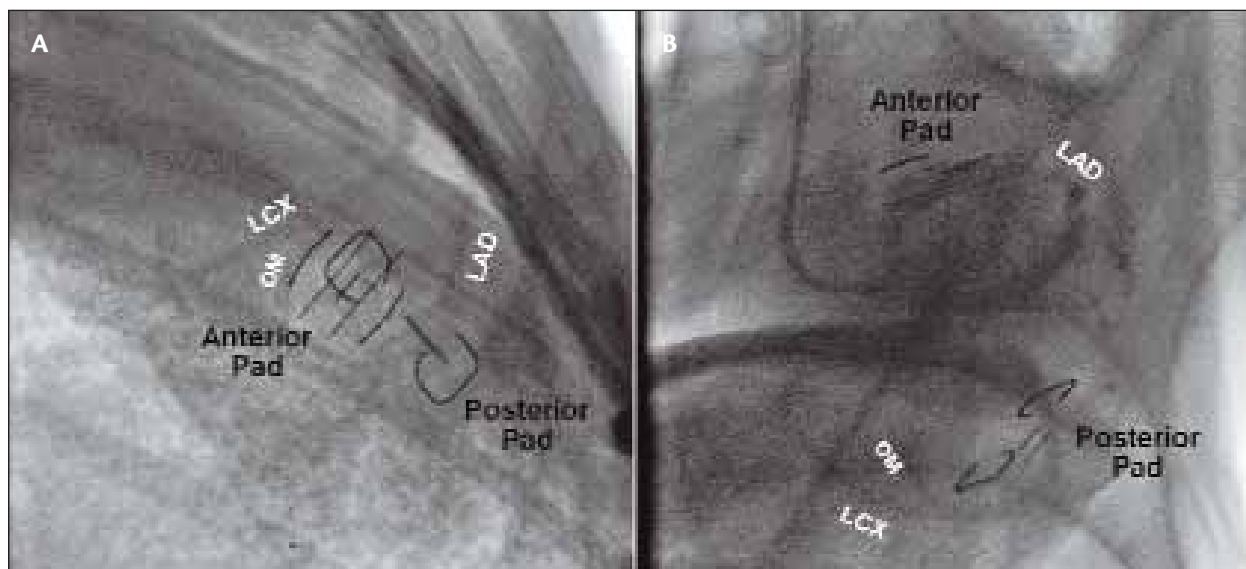


Figure 5. The completed iCoapsys implant during coronary angiography. Right anterior oblique cranial projection (A). Left anterior oblique caudal projection (B).

dilated cardiomyopathy.^{10,11} Despite its frequency, ideal surgical therapy for FMR does not exist. Traditionally, in patients with 3 to 4+ mitral regurgitation, an undersized annuloplasty ring is placed with or without coronary revascularization. Significant limitations for this conventional surgical approach include perioperative mortality rates of 6% to 12%¹²⁻¹⁴ and the recurrence of mitral regurgitation in 30% or more of patients within months of surgery.⁴ There is a clear need for less-invasive approaches, as well as a need to address the underlying LV geometric distortion in addition to treating the mitral annulus. The iCoapsys transcatheter implant, like the Coapsys device, is composed of anterior and posterior epicardial pads tethered by a load-bearing transventricular chord. Resultant conformational change of the LV at both the mitral valve annulus and the papillary muscles offers a more direct approach for the management of this LV disease while also reducing the mitral annulus. ■

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