The Dynamic Cardiac Biosimulator: A Method for Training Physicians in Beating Heart Mitral Valve Repair Procedures

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GLOSSARY
ePTFE – extruded polytetrafluoroethylene

TAVR – trans-catheter aortic valve replacement

TMVR – trans-catheter mitral valve replacement

Mitra-clip™ - Mitral valve leaflet clip – Abbott, Inc

DS1000 System™ – Artificial chordae implanting device – NeoChord, Inc.

Artificial Chords – ePTFE artificial chordae tendineae

ReChord Trial – FDA-approved IDE clinical trial

2D – Two-dimensional

3D – three-dimensional

CENTRAL MESSAGE

A dynamic animal heart bio-simulator is evaluated during ePTFE artificial chordae implantation into flail mitral leaflets under echocardiographic navigation. Concomitant hemodynamic changes are displayed simultaneously.

PERSPECTIVE STATEMENT

Simulation in cardiac surgery has become important for training with new technologic devices. Many simulators are low fidelity and may not represent true anatomy or physiologic function. Herein, we describe a dynamic animal heart biosimulator that recapitulates normal valve and hemodynamic function. We tested the utility by implanting ePTFE chordae into redundant mitral leaflets under echocardiographic navigation followed by simultaneous videoscopy.

STRUCTURED ABSTRACT
Objective: Previously, cardiac surgeons and cardiologists learned to operate new clinical devices for the first time in the operating room or catheterization laboratory. We describe a biosimulator that recapitulates normal heart valve physiology with associated real-time hemodynamic performance.

Methods: To highlight the advantages of this simulation platform, trans-ventricular ePTFE artificial chordae were attached to repair flail or prolapsing mitral valve leaflets. Guidance for key repair steps was by 2-D/3-D echocardiography and simultaneous intra-cardiac videoscopy.

Results: Multiple surgeons have assessed the use of this bio-simulator during artificial chordae implantations. This simulation platform recapitulates normal and pathologic mitral valve function with associated hemodynamic changes. Clinical situations were replicated in the simulator and echocardiography was used for navigation, followed by videoscopic confirmation.

Conclusions: This beating heart biosimulator reproduces prolapsing mitral leaflet pathology. It may be the ideal platform for surgeon and cardiologist training on many trans-catheter and beating heart procedures. WC 147

INTRODUCTION

In the past, cardiac surgeons and cardiologists learned the technical aspects of new devices first in the operating room and/or catheterization laboratory. With the rapid evolution of trans-catheter aortic valve replacement (TAVR) and aortic vascular stent grafts, it became obvious that new technologic iterations would require physiologic and anatomic simulation...
training platforms that better represented clinical practice. To develop and apply beating heart
trans-catheter valve repair and replacement devices, companies generally have taught clinicians
to gain expertise using fairly low fidelity simulation platforms prior to the first clinical
applications. These systems provided the user with limited, unrealistic tactile feedback along
with minimal visual control. For this reason, new generations of simulators using biological
organs have emerged that recreate realistic anatomic and hemodynamic cardiac conditions.

Herein, we describe a dynamic heart simulator (LifeTec Group, Inc., Eindhoven, Netherlands) that presents an effective method for learning and perfecting intra-cardiac valve procedures that require Cartesian X-Y-Z plane navigation with proficiency in hand/eye coordination. This dynamic ex vivo beating heart biosimulator combines the benefits of real-time echocardiographic imaging, videoscopic vision, and hemodynamic changes during off pump mitral valve repairs using ePTFE artificial chord implantations.

TECHNIQUE

While the bio-simulator can be used to evaluate any type of intra-cardiac device, procedure, and/or other types of structural heart disease, our goal was to train surgeons to perform off-pump trans-ventricular mitral valve repairs on prolapsed or flail mitral valve leaflets. The ex vivo heart simulator was an optimal tool for pre-clinical training because of the combined benefits of bi-modal intra-cardiac visualization, pathologic and hemodynamic replication, operative rehearsal, and post-procedure skill assessment. The DS1000™ System (NeoChord, Inc., St. Louis Park, MN) is a commercially available device that is intended to treat patients having mitral valve regurgitation resulting from prolapsed or flail mitral valve leaflets that are secondary to ruptured or elongated native chordae tendineae. This technology was used as the control technology to assess the pre-clinical teaching potential using this bio-simulator. (8)
The Dynamic Cardiac Bio-simulator

The bio-simulator is comprised of a pulsatile dynamic fluid system that is attached to an explanted porcine heart (Figures 1 and 2). The left ventricle is pressurized cyclically to clinical levels by a pulse duplicator system, attached through a sealed apical cannula. Saline is used as a working fluid to allow intra-cardiac videoscopic visualization. Figure 3 shows the DS1000™ System being inserted into the left ventricle near the apex. The trans-esophageal echo probe is placed on the posterior left atrium. Figure 4 shows the surgeon and anesthesiologist working together to navigate the device to deploy ePTFE chordae into the flail mitral leaflet. Cardiac chamber pressures are monitored constantly and can be regulated by adjusting pre- and after-load modules to the desired in vivo clinical levels. As an example, in the presence of a flail mitral valve leaflet, left atrial pressures rise while systemic blood pressure falls. By restoring normal leaflet coaptation, repairing the leak, these pressures revert to normal levels (Figure 5).

Imaging

With the simulator, the working mitral valve is visualized simultaneously using a trans-esophageal echocardiographic probe placed directly on the left atrial posterior wall (Figures 2 and 3) and an intra-cardiac 2-D endoscope that is passed into the left atrium (Figure 6). Throughout the procedure, a skilled echocardiographer manipulates the echo probe to render ideal two-dimensional, multi-plane images, displaying two orthogonal 2-D planes (long axis and mitral commissure) simultaneously (Figure 7). Additionally, three-dimensional surgeon’s en face views are displayed. All main procedure steps can be performed under echo guidance alone and include: 1) Device insertion and passage through left ventricular cavity, subvalvular apparatus, and mitral annular plane (2-D multi-plane mode). 2) Positioning the device in reference to the prolapsing segment (3-D zoom mode with surgeon’s en face view). 3) Leaflet
capture, device application, artificial chord attachment, and evaluation of the anatomical (3D zoom mode with en-face view) and functional aspects of the repair (2D color Doppler mode only possible using heparinized blood in the simulator) (Figures 7 and 8). At first the surgeon performs the procedure solely under echo guidance, as this most closely recapitulates the actual clinical scenario. Thereafter, by comparing simultaneous images between echo and intra-cardiac videoscopy, the quality of beating heart mitral valve repair can be assessed.

**Dynamic Mitral Repair – ePTFE Artificial Chordae Implantation**

Before the ex-vivo porcine heart is attached to the simulator, native chordae tendineae to the middle scallop (P₂) of the posterior leaflet are cut in the porcine heart, rendering a flail leaflet (Figure 6). After the cardiac pressurization and pulsatile flow has been achieved, echo and direct intra-cardiac video images are displayed simultaneously, demonstrating the regurgitant dysfunction.

Once the pathology has been confirmed, a series of deep pledgeted purse string sutures are placed posterior and lateral to the cardiac apex along an orthogonal trajectory axis with the mitral annular plane. Under 2-D echocardiographic multi-plane guidance, the DS1000™ system shaft is passed into the ventricle through the purse string (Figure 3). Thereafter, the device is navigated through the ventricular cavity, past the sub-valvular apparatus, and toward the mitral valve. After the instrument tip has traversed the mitral annulus, echo guided hand-driven X-Y-Z coordinate manipulation aligns it with the flail leaflet segment. At this point, the device jaws are opened so that leaflet edge resides within the device tip (Figures 6 and 8). In addition to echocardiographic confirmation, the DS1000™ System includes a display monitor, which confirms adequate engagement. It includes fiber optic lights that trans-illuminate the leaflet tissue. When the flail or prolapsed mitral leaflet is engaged correctly, four “lighted windows” on
the display monitor become illuminated simultaneously. This indicates that the DS1000™ system tip has been oriented correctly and is closed over sufficient leaflet tissue to safely place an artificial chorda. If the closed tip is “skewed” along the leaflet surface, one or more indicator lights may not be lit, indicating less than ideal leaflet tissue engagement. Thus, simultaneous videoscopy, echocardiography, and fiber optic light confirmation are used to assess correct chorda placement along the leaflet edge.

After confirmation of mitral leaflet capture, a needle is advanced through the DS1000™ system to penetrate the mitral leaflet 3-4 mm from the free edge. As the needle is withdrawn, through the device, a loop of pre-loaded ePTFE suture is captured and is passed through the mitral leaflet. Once the needle and loop have been exteriorized, the device tip is opened, releasing the mitral leaflet, and the entire device is withdrawn, exposing the “tails” of the artificial chord. Then, both suture tails are passed through the loop creating a “hitch knot”, which is advanced to lock along the leaflet free edge.

At this point, the DS1000™ system is reloaded with a new suture cartridge, and the procedure is repeated to place at least three artificial chordae along the prolapsing leaflet segment. Once all chords have been placed, lengths are adjusted to obtain good anterior-posterior leaflet coaptation and to assess the level of residual regurgitation using 2D color echo Doppler. Thereafter, exteriorized chords are anchored through a large pericardial pledget. *The accompanying video shows the procedure under both intra-cardiac and echocardiographic visualization.

Learning, Quality, and Safety Metrics:

Although the bio-simulator was used to train most surgeons using this device in Europe, definitive metrics were not collected. (8) Nevertheless, it was clear to the trainers
that with each attempt, surgeons’ experienced iterative improvements in cardiac access, echocardiographic navigation, and accuracy of leaflet capture, PTFE chord deployment, and prolapse reduction. Lastly, the echocardiographic quality of the valve repair was assessed. Tables 1 and 2 list the learning, quality, and safety metrics that are being collected for the current US ReChord Trial.

COMMENT

Advanced training simulators should provide benefits for patients, surgeons, and device manufacturers by accelerating and flattening learning curves in a safe, reproducible, yet realistic environment. Biosimulation is likely to reduce safety and regulatory risks for companies who are introducing new devices into the market. Moreover, improved training methods such as full procedure simulations can enable skill benchmarking for specific devices and surgical procedures.

Hand-driven, low-fidelity, trans-catheter valve simulators have been successful in training clinicians during the pre-clinical phase of their learning. Mitral valve models, which have been 3-D printed from echocardiographic data, are now being used to train surgeons in minimally invasive repair techniques. \(^9\) Moreover, surgical robotic simulation has become paramount and is required for mastering the tele-manipulation based surgeon’s console, which drives the wristed instruments. Valdis, et al, demonstrated in a randomized controlled trial that operator skills improve markedly through robotic simulation. \(^10\) Robotic simulators, like the Mimic da Vinci Si Skills Simulator (MIMIC Technologies, Inc., Seattle, WA), are able to define skill progression through “report card” metrics for accuracy, speed, and ergonomic motion.
Cardiopulmonary simulators are now used in resident training and provide realistic animal hearts for vascular cannulation and off pump coronary surgery. Ex vivo simulation not only provides a natural operative environment but, at the same time, can emulate disastrous hemodynamic clinical conditions. A recent study showed that among surveyed cardiac training programs in the United States, simulation was extremely helpful in teaching cardiac surgical techniques. Currently, cardiothoracic residency programs have implemented the requirement of 20 hours of simulation training for certification by the American Board of Thoracic Surgery. Thus, the question of “Simulation in cardiothoracic training: Where do we stand?” that Trehan posed in 2014 is being answered.

The present high-fidelity biosimulator will allow clinicians to perfect skills to perform trans-catheter and/or surgical valve procedures in a more natural milieu. Leopaldi and associates developed an earlier prototype of the present biosimulator, which employed animal hearts and replicated physiologic hemodynamics. The current system allows for continual echocardiographic and videoscopic cardiac valve visualization and also is compatible with fluoroscopy. Additionally, this platform can be connected to patient-specific vascular models to replicate many trans-catheter procedures. The hemodynamic performance of this simulator has been validated to provide near normal mitral valve function that is representative of in vivo conditions. Additionally, physiologic leaflet coaptation was demonstrated without mitral insufficiency, unless there was prior chordal disruption. Although this biosimulator was used to recapitulate mitral valve dysfunction requiring valve repair, the platform can model other heart valve structural changes and can be utilized with other devices. Also, several types of fluids can be circulated in this platform, including heparinized blood. In our report, we employed a saline solution, which allowed for concurrent visualization of 2-D/3-D echocardiography with
intra-cardiac videoscopy. As there is no mitral annular dilatation associated with the heart model, we could assess technique associated with prolapsed and flail leaflet repairs, independent of other factors that can cause mitral insufficiency. Thus, this biosimulator has been ideal for reproducing clinical situations that meet the intended use for which the NeoChord DS1000 System and other chordal implantation devices have been designed. \(^{(17)}\)

The placement of ePTFE artificial chordae has been shown to be very effective in a large series of mitral valve repairs and with excellent long-term results. \(^{(18)}\) However, in these series chordal replacement was combined with an annuloplasty prosthesis in most circumstances. Recent ACC/AHA guidelines suggest that repair surgery is appropriate for asymptomatic patients with severe mitral insufficiency. \(^{(19)}\) Generally, these patients are being referred earlier, and we can assume that in many of the patients, disease progression has not yet resulted in a significantly dilated annulus. Therefore, it is reasonable to assume that by correcting the dysfunction associated with leaflet prolapse or flail, subsequent annular dilatation may be limited enough to render a stable repair. The early European experience with the DS1000™ System was presented at the Society of Thoracic Surgeons Annual Meeting (2017) and showed safety, efficacy, and excellent repairs in patients out to 2-years, especially in posterior leaflet repairs. \(^{(20)}\)

Currently, the FDA has approved the US pivotal trial (ReChord; ClinicalTrials.gov identifier: NCT02803957) as a randomized controlled design. Enrollment has been initiated in the ReChord trial, and the biosimulator platform is being used to train all trial investigators prior to their first operative cases. \(^{(21)}\) As mentioned above, learning, quality, and safety metrics are currently being collected from surgeons training for the US ReChord clinical trial. In conclusion, simulation platforms have been developed to replicate and train to various types of hemodynamic and technical clinical challenges. The custom dynamic biosimulator, described
herein, provides natural intra-cardiac mitral valve function that can be altered to emulate pathological mitral regurgitation. This platform is ideal to train surgeons to place trans-ventricular artificial chordae under echocardiographic visualization, for prolapsing or flail leaflets.

**LIMITATIONS:** The authors describe in detail this biosimulator and the use in training surgeons to replace ePTFE artificial chordae in prolapsing mitral valve leaflets under echocardiographic navigation. The paper is a descriptive one and is an attempt to bring this method of simulation to the awareness of surgeons who are training in trans-catheter methods. The limitation of this paper is the lack of metrics from multiple learners using this training method. During the ReChord trial, each investigator will be evaluated with metrics that will assess improvements in navigational accuracy, procedure times, and ideal artificial chordae placement in a successive, iterative training method. WC 2053
REFERENCES


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Figures and Legends

**Figure 1.** Schematic diagram of the dynamic cardiac biosimulator. **Panel A.** (1) *Pulse duplicator* with a computer-controlled piston pump capable of replicating physiologic flow and ventricular pressure. (2) *Apical cannula* connecting the pulse duplicator to the left ventricle chamber. (3) *Porcine heart* (4) *Aortic cannula* connected to the ascending aorta. (5) *Compliant silicone tube* that mimics aortic compliance. (6) *Afterload module* comprised of two adjustable resistances and a compliant air tank. (7) *Service reservoir*. (8) *Centrifugal pump* used to provide fluid to the preload module. (9) *Preload module* composed of a small air tank and a silicone tube to mimic venous compliance. (10) *Adjustable Starling resistor* to ensure that atrial pressures are maintained at physiologic levels. (11) *Endoscope* with high definition camera to video the mitral valve. (12) *Atrial cannula* to convey the preload fluid to the left atrium.
Figure 2. Graphic representation of the simulator during the artificial chordae placement procedure. The echocardiographic probe placed on the posterior left atrial wall. Hemodynamic parameters are measured simultaneously with endoscopic and echo visualization.
Figure 3. (Left) The dynamic cardiac biosimulator system. Echo Probe (EP) Pulse duplicator (PD) Neochord device (D) (Right) Trans-esophageal echo probe placed on the epicardium of the left atrial wall.
Figure 4. (Left) The surgeon is navigating the device to engage the flail mitral valve leaflet with simultaneous 2-D and 3-D echo imaging as well as intra-atrial videoscopy. (Right) Echo probe manipulation and image evaluations are done simultaneously by an experienced cardiac anesthesiologist. After flail leaflet capture by the Neochord device, a ePTFE chord is placed to reduce the prolapse under hemodynamic, videoscopic, and echocardiographic monitoring.
**Figure 5.** Hemodynamic tracings showing the effect of artificial chordae implantation into a flail mitral leaflet before and after correction of mitral regurgitation (MR). **Left:** Left atrial (LAP) and aortic systemic pressures (AoP) with a prolapsing mitral valve and severe MR. **Right:** The same parameters after the mitral valve flail leaflet has been repaired with the artificial chordae. Note the decrease in LAP with concomitant rise in AoP after correction of the severe MR.
Figure 6. Left atrial endoscopic images. (Left) prolapsing mitral valve with the DS1000 System positioned to capture the prolapsing leaflet segment. (Right) The leaflet is captured and an artificial chorda is being deployed.
Figure 7. Representative 2-D echo images during the procedure. X-plane modality with long axis and bi-commisural view. (A & B) Device passage through LV cavity and mitral valve plane (C & D). Arrow - Neochord device tip. (E) Grasping of the leaflet with the open device (arrow) displayed simultaneously in 3-D and 2-D images.
Figure 8. 3-D zoom mode with en-face view of the mitral valve: A) $P_2$ prolapse with multiple ruptured chords before the procedure; B) Neochord device in the left atrium - positioning adjacent to the prolapsing segment; C) $P_2$ leaflet grasping; D) Final anatomical result after ePTFE chord implantation and length adjustment.
Table 1: Learning Metrics for Biosimulator Training*

- Number of attempts and time to cross the mitral annular plane
- Number of attempts and time to capture the leaflet for the first time
- Leaflet capture quality (by number of indicator lights activated)
- Number of attempts and time to place the first chord
- Number of attempts and time to place multiple chords
- Time to anchor chords on the left ventricle

* At least three separate animal hearts are used for training each surgeon

Table 2: Quality and Safety Metrics for Biosimulator Training

- 2-D and 3-D echocardiographic repair quality *
- Hemodynamic repair quality *
- Chord detachment
- Incorrect topographic chord implantation
- Chord tension adequacy
- Leaflet trauma or perforation
- Atrial perforation
- Ventricular trauma

*Left atrial and ventricular pressure; cardiac output
# Length of anterior and posterior leaflet coaptation; regurgitation quantitation