

Biorobotic hybrid heart as a benchtop cardiac mitral valve simulator

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Summary: In this work, we developed a high-fidelity beating heart simulator that provides accurate mitral valve pathophysiology. The benchtop platform is based on a biorobotic hybrid heart that combines preserved intracardiac tissue with soft robotic cardiac muscle providing dynamic left ventricular motion and precise anatomical features designed for testing intracardiac devices, particularly for mitral valve repair. The heart model is integrated into a mock circulatory loop, and the active myocardium drives fluid circulation producing physiological hemodynamics without an external pulsatile pump. Using biomimetic soft robotic technology, the heart can replicate both ventricular and septal wall motion, as well as intraventricular pressure-volume relationships. This enables the system to recreate the natural motion and function of the mitral valve, which allows us to demonstrate various surgical and interventional techniques. The biorobotic cardiovascular simulator allows for real-time hemodynamic data collection, direct visualization of the intracardiac procedure, and compatibility with clinical imaging modalities.

Main Text:

INTRODUCTION

Mitral regurgitation is the most prevalent form of heart valve disease globally, with an estimated 24.2 million cases worldwide.¹ Patients with moderate to severe mitral regurgitation often require therapeutic intervention, in the form of a conventional open-heart surgical approach or the less invasive transcatheter methods for mitral valve repair and replacement, which are becoming increasingly popular.² While transcatheter valve replacement has been successful for aortic valves, the optimal method for mitral valve procedures remains controversial.³ The mitral valve procedure is much more complex than that of the aortic valve due to the intricate anatomy of the mitral valve and its relationship with adjacent structures.⁴ Any disruption to the mitral apparatus, consisting of the mitral valve leaflet, mitral annulus, chordae tendineae, and papillary muscle, can lead to mitral valve dysfunction. Due to the growing complexity of disease cases, advancements in technology, and increasing pressure on surgeons to achieve higher success rates, there is a

surge in interest for surgical and percutaneous therapies for mitral valve repair and replacement.

Cardiovascular benchtop simulators have become increasingly popular in the field of cardiac surgery and interventional cardiology for research, testing, and evaluation due to their ease of use and ability to make multimodality measurements, in comparison to *in vivo* models.⁵⁻⁷ However, existing *in vitro* cardiac simulators lack the necessary biofidelity for intracardiac device testing, while *ex vivo* models have labor-intensive setup processes and limited tissue longevity.⁷ *Ex vivo* systems typically consist of passive heart tissue, including a partial or full representation of the intracardiac anatomy. Partial cardiac simulators have been developed to investigate heart valve mechanics and facilitate the development of cardiac devices. *Ex vivo* heart valves are mounted in an *in vitro* simulator and exposed to pressures and flow from a pulsatile pump to simulate the behavior of aortic and mitral valves.⁸⁻¹⁰ However, these systems test each valve in isolation and do not fully replicate their interdependence and *in vivo* anatomy and physiology. Whole heart *ex vivo* cardiac simulators utilize an external pump source, such as a pulse duplicator, connected at the apex to provide pulsatile flow and mimic physiological hemodynamics.¹¹ However, these setups produce paradoxical pressure-volume relationships due to internal fluid pressurization, which can enlarge the ventricular volume during the systolic phase. This, in turn, disrupts the motion of the mitral valve and its relationship with adjacent structures, such as the annulus, chordae tendineae, and papillary muscles. The flow pattern in many existing *ex vivo* cardiac simulators is unnatural because the flow is driven by the pump connected at the apex of the heart, instead of the native cardiac contraction, which allows for the formation of vortices and smooth redirection of flow from the inlet to the outflow tract.¹²

In the field of medical technology, there is currently no reliable benchtop mitral valve simulator that can produce relevant preclinical results and allow for rapid design iterations of cardiac devices. As a result, *in vivo* animal models are commonly used in industry to test device mechanical performance, which is both costly and time-consuming.^{13,14} A technological platform is needed to address this issue and to allow for the testing of mitral valve technologies on a bench in a realistic, beating heart environment that mimics the anatomy and biomechanics of the mitral apparatus. Such a platform would enable device manufacturers to evaluate multiple device iterations, test device function under extreme conditions, and optimize their design prior to *in vivo* or clinical testing.

Here, we present a biorobotic cardiovascular simulator that serves as a versatile *in vitro* platform for mitral valve repair and replacement. Our simulator is designed to feature realistic materials, accurate anatomical details, dynamic cardiac motion, and complex procedural scenarios. It includes a high-fidelity biorobotic hybrid heart that mimics the left heart's circulation with a realistic anatomical and functional representation of the mitral valve apparatus. The biomimetic motion of the soft robotic myocardium drives the biorobotic hybrid heart, so no additional pump is required in a mock circulatory loop that recreates physiological hemodynamics. The native heart tissue valves in the endocardial scaffold demonstrate physiological motion and physiological function, thanks to the physiological pressure and volume relationships. We also demonstrate that the biorobotic cardiovascular simulator can function as an *in vitro* benchtop model for testing intracardiac mitral valve repair devices. To highlight the model's preclinical utility, we performed different interventional techniques, including surgical repair (artificial chord implantation), surgical replacement (bioprosthetic valve replacement), and minimally invasive transcatheter edge-to-edge repair procedure, in an acute mitral regurgitation model. We observed clinically relevant changes in valve motion and function, as well as hemodynamics. Overall, our biorobotic cardiovascular simulator provides an advanced platform for developing and testing mitral valve interventions.

RESULTS

Architecture of biorobotic hybrid heart with intact mitral valve apparatus

The mitral valve is between the left atrium and left ventricle and ensures proper blood flow in the heart (**Figure 1A**). It consists of the mitral annulus, leaflets, chordae tendineae, and papillary muscles, and each component's precise motion is crucial for proper valve function.¹⁵ Changes to the mitral apparatus cause conditions like mitral prolapse or regurgitation.¹⁶ To study valvular biomechanics and test intracardiac devices *ex vivo*, benchtop cardiac simulators are often used.¹¹ However, the internal pressurization of the ventricular chamber using an external fluidic pump causes systolic dilation instead of contraction, which can disrupt the mitral apparatus's motion (**Figure 1B**). To overcome these limitations, we have developed a biorobotic hybrid heart that combines a chemically preserved *ex vivo* intracardiac tissue (i.e., endocardial scaffold) with a soft robotic myocardium. The endocardial scaffold is a three-dimensional structure that exhibits contractile motion driven by the surrounding soft robotic myocardium. In the actuated state, the left ventricular walls closely approach each other in a biomimetic manner, bringing the papillary muscles in proximity (**Figure 1C**).

To fabricate the biorobotic hybrid heart, we use fresh pig hearts that are preserved chemically and treated with surfactants to restore their mechanical properties for anatomical precision. We hand-dissect the native myocardial tissue from the left ventricular and interventricular septal area and replace it with a soft-robotic muscle (**Figure 1D**). The resulting model accurately replicates the functional and anatomical details of the heart, including valves, papillary muscles, and chordae tendineae, as visualized using micro-CT (**Figure 1E**).

Design, controllability, and tunability of the soft robotic myocardium

The soft robotic myocardium is designed to match the size and shape of the endocardial scaffold, using a bioinspired design that includes two layers of circumferential and helical actuators (**Figure 2A**). The circumferential actuators primarily contribute to radial contraction, while the helical actuators contribute to the twisting motion of the biorobotic heart. We previously investigated major design variables, such as architecture, material stiffness, and types of soft actuators, to assess their impact on the systolic capability of the soft robotic myocardium using finite element analysis.¹⁷ The resulting design closely mimics the biomechanics of a healthy left ventricle during systole.

Figure 2B and **Supplemental Movie S1** demonstrate the ejection of water resulting from the compression and twisting motion generated by the soft robotic myocardium when actuated. By controlling the level of actuation, the contractility of the soft robotic myocardium can be adjusted to achieve the desired ejection fraction, which is the volumetric fraction of fluid ejected from the ventricular chamber with each contraction. The relationship between input actuation pressure and ejection fraction for different initial chamber sizes of 42.4 mL and 76.5 mL is displayed in **Figure 2C**, indicating that the same two-layer design can be utilized for a range of sizes of explanted hearts without the need for re-optimizing the design of the soft robotic myocardium. Additionally, the figure shows that the soft robotic myocardium can generate up to over 80% ejection fraction, and can be tuned to a physiological range between 50% and 70%.¹⁸ The motion of the soft robotic myocardium can be controlled as desired since each actuator can be independently controlled using an electro-pneumatic control system. **Figure 2D** illustrates how activating different actuator layers can contribute to recreating twisting motion, compression motion only, or both, and shows the resulting effect on ejection fraction. The tunability of the soft-robotic myocardium to generate a range of chamber pressures, from 70 mmHg to 180 mmHg, is demonstrated in **Figure 2E**, suggesting that both the healthy and disease hemodynamics can be recreated on a bench.

A mock circulatory loop was created to simulate the left heart circulation, using a lumped parameter model that combines mechanical and hydraulic components (see Supplemental **Figure S1**). The flow loop features the soft robotic myocardium as the pump. Mechanical valves are installed at the outlet and inlet to ensure unidirectional flow and represent the aortic and mitral valves, respectively. Physical signals such as pressure and flow were measured through sensors placed throughout the circuit. Hemodynamics were controlled by adjusting the circuit's compliance, resistance, preload, and afterload levels, as well as the actuation of the soft robotic myocardium via an electro-pneumatic control system to control its contractility and heart rate. The results shown in Supplemental **Figure S2A** indicate that the biomimetic soft robotic myocardium can accurately mimic the physiological pressures of left heart circulation. Aortic and mitral flow shows that the soft robotic myocardium enables unidirectional volumetric displacement (Supplemental **Figure S2B**).

Biorobotic hybrid heart successfully replicates normal left-sided hemodynamics and physiological valve motion on a bench

Figure 2F and Supplemental **Figure S3** show the schematic diagram and photo, respectively, of the setup for the biorobotic cardiovascular simulator, which comprises a left heart mock circulatory loop and the biorobotic hybrid heart. In this setup, we rely on the native tissue valves in the endocardial scaffold of the biorobotic heart to guide the flow direction. Pressure sensors and ultrasonic flow probes measure the pressures and flows generated by the heart, which are collected in the data acquisition system, enabling real-time monitoring of hemodynamic changes. An endoscopic camera can be inserted in the biorobotic hybrid heart to visualize the motion of intracardiac structures and their interaction with devices. Moreover, the system is compatible with various clinical imaging modalities, including echocardiography, enabling a clinically relevant assessment. The biorobotic hybrid heart functions as the main pump that drives the flow in the mock circulatory loop, mimicking the pumping and distribution of blood in the systemic circulation (**Figure 3A** and Supplemental **Figure S4**). The biorobotic hybrid heart is cyclically actuated, and the soft robotic cardiac muscle generates physiological hemodynamics that represents a healthy left ventricle with systolic pressures of approximately 120 mmHg, as demonstrated in **Figure 3B**, Supplemental **Figure S5**, and Supplemental **Movie S1**. The alternating mitral and aortic flows reflect the proper functioning of both the aortic and mitral valves, which open and close due to the biomimetic motion of the soft robotic myocardium and the preserved aortomitral anatomy (**Figure 3C**). The competent valves enable pressure development in the ventricle during the systolic phase and in the aorta during the diastolic phase, resulting in physiological pressures. This indicates that the flow driven by the soft robotic muscles is well-regulated by the tissue valves in the endocardial scaffold.

We observed the contracting motion of the endocardial scaffold, which is driven by the surrounding soft robotic myocardium, using echocardiography and a video endoscope (**Figure 3D** and Supplemental **Figure S6**). When actuated, the walls of the left ventricle move towards each other, imitating a natural heart and bringing the papillary muscles close to each other. As demonstrated in **Figures 4A** and **4B**, both the aortic and mitral valves undergo physiological motion in the biorobotic hybrid heart (Supplemental **Movie S2**). During the diastolic phase, the aortic valve closes, while during the systolic phase, it opens to eject fluid. Similarly, the mitral valve opens during the diastolic phase to allow the filling of the left ventricle and tightly closes during the systolic phase. The left ventricular wall's biomimetic motion brings the papillary muscles closer, reducing the tethering force on the chordae and enabling the free edges of the mitral valve leaflet to form coaptation without any indication of mitral prolapse. Echocardiography confirms the contraction of the mitral valve annulus, which exhibits a 13.4% area reduction, as shown

in **Figure 4C**. The kinematics of valvular motion, including valve opening velocities and left ventricular wall contractility, were assessed by processing echocardiographic data (**Supplemental Figure S6**). The healthy range for MV annulus area and peak MV leaflet opening velocity, as reported in the existing literature on echocardiographic analysis, is approximately 7–12cm² and 400 ± 60 mm/s, respectively.^{19,20} Both the MV leaflet velocity and annulus area obtained from our cardiac simulator fall just outside this reported range. This alignment validates the fidelity of the biorobotic cardiovascular simulator.

Recreating the pathological hemodynamics associated with acute mitral regurgitation in the biorobotic cardiovascular simulator

The biorobotic cardiovascular simulator can not only replicate a healthy model but also simulate pathological or abnormal conditions. Since the biorobotic hybrid heart is constructed from an *ex vivo* source, we can recreate cardiac pathology related to anatomical defects, such as heart valve leaflet perforation, chordae or papillary muscle rupture, and atrial or ventricular septal defects. In this study, acute mitral regurgitation (MR) is demonstrated in the biorobotic hybrid heart as an example, as MR is difficult to recreate in simplified models due to the complex anatomy of the mitral apparatus. The biorobotic simulator can test different interventional techniques for treating the condition of mitral regurgitation (**Supplemental Movie S3**).

As illustrated in **Figure 5A**, an acute mitral regurgitation model was induced in a biorobotic hybrid heart by cutting primary and secondary chordae in the P2 segment of the mitral valve. This caused P2 prolapse, resulting in an out-of-plane motion in that valve leaflet region, causing moderate mitral regurgitation (**Figure 5B**). To recreate a more severe form of mitral regurgitation, additional chords were cut in the A2 segments of the mitral valve, resulting in mitral leaflet flail motion without leaflet coaptation (**Figure 5C**). The changes in the hemodynamic parameters were also observed and compared, including the increased negative flow, suggesting regurgitant flow across the mitral valve (**Figure 5D**). Likewise, when the mitral valve fails to close completely, it is subjected to a lower pressure gradient or closing force during the systolic phase, as shown in **Supplemental Figure S7**. This occurs because the left ventricle experiences significantly lower pressure development due to the leaky valve as it contracts (**Figure 5E**). The left atrial pressure increases due to the incompetent mitral valve, as shown in **Figure 5F**.

Next, to display the versatility of our platform as a realistic and high-fidelity *in vitro* simulator for device testing, demonstration, and training purposes, we demonstrate the use of different interventional techniques in our biorobotic cardiovascular simulator to treat mitral regurgitation. These techniques range from surgical repair and replacement to minimally invasive transcatheter repair.

Surgical repair of mitral regurgitation and resulting hemodynamics in the Biorobotic cardiovascular simulator

To repair moderate mitral regurgitation in the biorobotic hybrid heart, a surgical repair technique using artificial chordae is demonstrated. The artificial chords, which were made of expanded polytetrafluoroethylene (ePTFE) sutures in pre-measured loops (Chord-X, CryoLife), were used to correct the mitral prolapse and produce an optimal surface of coaptation in the P2 segment (**Figure 6A**). First, the loops were fixed on the papillary muscle (**Figure 6B**), and then they were passed through the leaflet tissue in the region of prolapse, followed by tying the ends of the suture on the leaflet (**Figure 6C**). The competency of the repaired mitral valve was confirmed by performing a saline test before sealing back the left atrium (**Figure 6D**). In the biorobotic cardiovascular simulator, both qualitative and quantitative measurements were performed to evaluate the repair technique.

Using an endoscopic camera from the left atrial side, the motion of the mitral valve was inspected after the artificial chordal implant. Mitral prolapse was no longer observed after the implantation. When evaluated using 2D color Doppler echocardiography, mitral regurgitation was reduced from a severe mitral regurgitation (MR severity grade IV) after the implantation of artificial chords, demonstrating an immediate functional improvement of the defected mitral valve (Supplemental **Figure S8**). Consistent with the qualitative results, the hemodynamics data also confirmed a significant recovery in the flow and pressures. Prior to the artificial chordae implantation, there was significant retrograde mitral flow as indicated by the negative flow in **Figure 6E**. After the treatment, the coaptation of mitral valve leaflets was improved, resulting in a significant reduction in the mitral valve regurgitant fraction (MR: 0.26 ± 0.020 , Repair: 0.065 ± 0.010 ; $p < 0.01$), which is defined by retrograde flow volume divided by anterograde flow volume (**Figure 6F**). The pressures were also significantly improved after the treatment. Prior to the valve repair, the systolic ventricular pressure was underdeveloped (**Figure 6G**), and the left atrial pressure was increased due to the leakiness of the mitral valve during the systolic phase (**Figure 6H**), which also caused the drop in the transvalvular pressure gradient (Supplemental **Figure S8**). After repair, there was a significant improvement in the systolic left ventricular pressure (MR: 63 ± 1.6 mmHg, Repair: 104 ± 1.0 mmHg; $p < 0.01$), left atrial pressure (MR: 16 ± 0.24 mmHg, Repair: 9.3 ± 0.12 mmHg; $p < 0.01$) as well as mean mitral valve pressure gradient (MR: 31 ± 1.2 mmHg, Repair: 62 ± 0.10 mmHg; $p < 0.01$), as shown in **Figures 6I, 6J**, and Supplemental **Figure S9**.

Biorobotic hybrid heart as a surgical platform for replacing a malfunctioning mitral valve

To demonstrate a surgical valve replacement, we used a bioprosthetic valve made from the porcine pericardium (Trifecta™ Valve with Glide™ Technology, St. Jude Medical) in the biorobotic cardiovascular simulator. We recreated severe mitral regurgitation (MR severity grade IV) by causing chordal rupture, which resulted in flailing of both anterior and posterior leaflets. A cardiac surgeon then surgically implanted the bioprosthetic valve at the mitral annular site (**Figure 7A**). Inspection with an endoscopic camera immediately revealed proper valve motion during both diastole (open for filling) and systole (closed for ventricular pressure generation), as seen in **Figure 7B**. The replacement also improved the motion of the aortic valve. Before the mitral valve replacement, echocardiography and video endoscope showed the aortic valve did not fully open with a small effective orifice area during systole, indicating the ventricular contraction generated flow was split between forward and backward directions. However, after the bioprosthetic valve implantation, the aortic valve produced a notably larger orifice area during ejection as the forward flow improved due to the prevention of backward flow at the mitral inlet (**Figure 7C**).

Before and after the valve replacement, we performed 2D color Doppler echocardiography and found no regurgitant flow post-replacement (**Figure 7D**). Hemodynamic data supported the functional restoration of the mitral valve, with significant improvement in mitral flow after bioprosthetic valve replacement (regurgitant fraction of 0.19 ± 0.013 compared to severe mitral regurgitation model with a regurgitant fraction of 0.87 ± 0.020 ; $p < 0.01$), as depicted in **Figures 7E and 7F**. Systolic left ventricular (MR: 30 ± 0.49 mmHg, Replacement: 120 ± 0.26 mmHg; $p < 0.01$) and atrial pressures (MR: 26 ± 0.21 mmHg, Replacement: 15 ± 0.21 mmHg; $p < 0.01$) improved and returned to baseline levels after valve replacement, ensuring complete flow isolation at the mitral inlet during systole (**Figures 7G and Supplemental Figure S10**). The mitral valve pressure gradient was also close to healthy baseline levels after valve replacement, as seen in **Figure 7H** and Supplemental **Figure S10**.

Minimally invasive repair of mitral regurgitation demonstrates the utility of the biorobotic heart simulator for device testing and rehearsal of complex procedures

The MitraClip™ (Abbott Laboratories), is a minimally invasive, transcatheter edge-to-edge repair (TEER) technology that has become a popular option for patients with moderate to severe mitral valve regurgitation who are at considerable risk for open heart surgery (**Figure 8A**). To demonstrate the TEER procedure, a moderate mitral regurgitation was first induced in a biorobotic hybrid heart by introducing a P2 prolapse. The MitraClip™ was then inserted through the transeptal approach to access the left atrium (**Figure 8B**). The clip was positioned and oriented relative to the mitral valve, and then advanced past the valve and pulled back upwards to grasp the mitral leaflets. The clips were closed to hold the leaflets in a desired region of the mitral valve and detached from the delivery system, forming a double orifice that allows filling during the diastolic phase (**Figure 8C**). After the TEER procedure, the mitral valve exhibited a characteristic double-orifice morphology as observed by 3D echocardiography and showed complete closure during systole without any signs of prolapse (see **Figure 8D**).

Post-repair 2D color Doppler echocardiography shows good formation of mitral leaflet coaptation without prolapse (Supplemental **Figure S11**). The elimination of regurgitant flow after the TEER procedure was confirmed, resulting in a significant reduction from the moderate mitral regurgitation condition (MR severity grade II) prior to treatment. Hemodynamic data showed improvements in flow and pressures following the procedure. Mitral flow, which had increased in both anterograde and retrograde directions after inducing moderate regurgitation, improved after the TEER procedure (**Figure 8E**), demonstrating a significant improvement in regurgitant fraction (0.26 ± 0.016) compared to prior to treatment (MR: 0.78 ± 0.035 ; $p < 0.01$), as depicted in **Figure 8F**. Left ventricular systolic pressures also significantly improved after the procedure (**Figure 8G**), achieving physiological systolic pressures of 118 ± 0.53 mmHg compared to 89 ± 0.58 mmHg in the mitral regurgitation scenario ($p < 0.01$), as summarized in **Figure 8H**. Due to the mild degree of mitral regurgitation (MR severity grade II) for the TEER procedure compared to the previously mentioned interventional scenarios, there was less of a difference in left atrial pressures, as shown in **Figures 8I** and **8J**. The differences in the mitral valve pressure gradient were notably different after the TEER procedure ($p < 0.01$), with a mean mitral valve pressure gradient of 68 ± 0.22 mmHg compared to mitral regurgitation, which had a mean mitral valve pressure gradient of 48 ± 0.35 mmHg ($p < 0.01$), as displayed in Supplemental **Figure S12**.

DISCUSSION

Many intracardiac devices are currently being developed for mitral valve repair and replacement, ranging from surgical techniques to minimally invasive transcatheter procedures.²¹ However, there is a lack of a realistic benchtop model that can accurately mimic the anatomy, material properties, ventricular wall motion, and biomechanics of the mitral valves. This makes it challenging to test the feasibility, performance, and design of these devices, relying on costly and time-consuming animal testing. To address this issue, we have developed a high-fidelity beating heart simulator that can serve as a preclinical model for mitral valve devices. Using a biomimetic approach, we have reanimated *ex vivo* heart tissue to achieve realistic beating heart motion and can accurately simulate the functional valves in the model. Our platform allows for the testing of surgical and minimally invasive transcatheter valve repair procedures in an acute mitral regurgitation condition, and we use clinical imaging, endoscopic video imaging, and real-time hemodynamic data collection to visualize and measure the hemodynamic effects of these interventions. This approach offers a promising alternative to animal testing for device development and can reduce costs and improve preclinical testing efficiency.

Our benchtop platform utilizes a biorobotic hybrid heart that combines preserved intracardiac tissue and soft robotic cardiac muscle to recreate the dynamic ventricular motion while preserving relevant anatomical features of the mitral valve apparatus, such as the annulus, leaflets, chordae tendineae, and papillary muscles. Existing cardiovascular simulators typically use a whole *ex vivo* heart as a passive structure and supply the heart with pulsatile flow using an external fluidic pump, causing the ventricle to expand outward during the systolic phase instead of contracting inward, which affects the relationships among intracardiac structures, particularly the valves.^{8,11} Our platform overcomes this limitation with a biomimetic design that uses two layers of soft robotic actuators to replicate the fiber architecture of the native left ventricular myocardium, creating complex cardiac motion, including squeezing, twisting, and interventricular septal motion, which directs the papillary muscle position and chord tension during the systolic phase. The biomimetic soft robotic myocardium generates high intraventricular pressure during the systole, driving the motion of the mitral valve with correct pressure and volume relationships, which were previously not achievable in other *in vitro* benchtop models.^{11,22} To our knowledge, this is the first simulator to realize biomimetic septal and mitral valve motion and recreate accurate hemodynamics. Existing simulators, for example, the perfusion heart models, including Langendorff²³, normothermic *ex vivo* perfusion²⁴, and working heart setups⁷, involve the circulation of perfusate to simulate myocardial contraction. The models are complex and labor-intensive. Langendorff and working heart setups necessitate pacing for rhythm stabilization and cannot be used if the time between heart excision and perfusion exceeds 120 seconds. Arrhythmias are common, and the heart rate is primarily bradycardic. Left ventricular function in these models declines at a rate of 5-10% per hour. Normothermic *ex vivo* perfusion has been shown to improve the shelf life of hearts for transplantation with a median shelf life of up to 12 hours, but clinical trials have only looked at shorter durations, such as 4-6 hours.²⁵ In contrast, our biorobotic hybrid heart model employs controlled external robotic actuation, approximating natural physiological processes. Another advantage of our platform is controllability (heart rate, contractility, valve motion) and the ability to test across a range of parameters in a more controlled manner compared to animal or perfusion models.

The biorobotic cardiovascular simulator offers several key features that make it an effective tool for understanding the pathology of the left side of the heart. First, it provides direct visibility of the intracardiac environment. Second, it allows for real-time measurement of hemodynamic parameters. Third, it offers precise control over cardiac motion. Fourth, it has a longer shelf-life than explanted tissue. The simulator uses optically clear fluid and endoscopic camera access to the heart chambers to provide direct visualization of the mitral valve apparatus and its interactions with devices, analogues to transesophageal echocardiography (TEE) and/or intra-cardiac echo (ICE) views. This allows users to receive instant feedback on surgical repairs or device deployment/placement and identify any issues with the device or technique. At the same time, real-time hemodynamic parameters are collected, enabling users to observe functional changes with intervention.

To demonstrate the preclinical effectiveness of our *in vitro* platform, we simulated acute mitral regurgitation (MR) through chordae rupture. We employed a variety of surgical and interventional techniques to manage the condition, including chordal repair, surgical bioprosthetic valve replacement, and transcatheter edge-to-edge repair. All procedures were performed in collaboration with clinicians from Boston Children's Hospital. We created an MR model by sequentially severing the chordae tendineae. Endoscopic cameras with an optically transparent fluid were used to visualize the pathological motion of the leaflets, which is not feasible in an animal model or operating room. After replacing the regurgitant mitral valve with the bioprosthetic valve, the regurgitant flow was eliminated owing to the complete coaptation of the implanted prosthetic valve during the systolic

phase. We also successfully demonstrated a TEER procedure. The catheter placement along with leaflet grasping and device deployment process can be rehearsed under direct visualization via endoscopic camera and echocardiography, facilitating enhanced procedural training. Changes in valve motion, competency, and hemodynamics were observed before and after each treatment. Furthermore, all relevant hemodynamic data is collected simultaneously without the need to conduct separate examinations, enabling users to obtain a comprehensive understanding of valvular biomechanics and to analyze device-tissue interactions in a holistic manner.

In addition to the interventions described in this study, there are various surgical and percutaneous methods for treating mitral valve diseases. For mitral valve surgery, options include non-resectional leaflet remodeling, leaflet resection, neochord repair, edge-to-edge repair, ring annuloplasty, and surgical valve replacement. However, treatment method selection has often been based on surgeon preference and familiarity rather than disease etiology, due to a lack of comparative studies. Transcatheter mitral valve repair has gained popularity in recent years due to its less invasive approach compared to traditional surgery.²⁶ However, it is not without complications, such as bleeding and thrombogenicity, which can result from the steep learning curve required to master the transcatheter valve repair procedure.²⁶⁻²⁸ Our biorobotic cardiovascular simulator provides a realistic beating heart environment for cardiac surgeons and interventional cardiologists to train themselves in transcatheter valve repair and replacement procedures. A complex complication associated with transcatheter mitral valve repair is left ventricular outflow tract (LVOT) obstruction, which can lead to fatal events.²⁹ This complication is often related to device protrusion into the left ventricle, aortomitral angle, anterior leaflet displacement, and excess anterior mitral leaflet with redundant chordae. Our dynamic model, which preserves aortomitral anatomy and physiology, can inform the development of devices and provide feedback on potential adverse risks, such as systolic anterior motion that could obstruct the LVOT. The demonstrated use of the dynamic model for the mitral valve procedure can also be applied to other types of intracardiac devices, such as annuloplasty rings and septal closure devices.³⁰⁻³²

The use of explanted porcine hearts as structural scaffolds for anatomical simulations in the biorobotic heart is limited to general anatomical defects, such as chordae or papillary muscle rupture, valve leaflet perforation, septal defects, etc. In the future, high-resolution multi-material 3D printing could be used to represent parts of the intracardiac tissues that are specific to a patient's geometry and relevant disease conditions. Another limitation of our study is the variability in tissue compliance resulting from the chemical treatment used for heart preservation, which varied between the two hearts used in our study. There was notable variance in the left atrial tissue compliance, which may have affected mitral flow measurement and left atrial pressures. These differences may have arisen from several sources, such as heart size differences (up to 40% chamber volume), variations in chemical treatment duration required for tissue preservation, accidental defects in the endocardial scaffold after manual dissection, and the rate of decellularization and its effect on restoring tissue modulus of the endocardial scaffold used for the biorobotic hybrid heart. The limitations could be overcome in the future by utilizing a synthetic endocardial scaffold created through advanced, high-resolution 3D-printing techniques. In its current stage, manual tissue dissection can be a limiting factor in the mass production of hybrid heart technology. However, this issue can be addressed in the future with the development of custom-designed techniques, such as automated tissue dissection. The interplay between the left and right ventricles significantly influences the motion and deformation of the septal wall, which is influenced by factors like pressure gradients. To streamline the simulation mechanics and concentrate only on left ventricular dynamics and mitral valve interventions, we opted to excise the right ventricle during tissue dissection. Although our present setup endeavors to replicate septal wall motion concerning left ventricular

dynamics in healthy hearts, enabling a focused exploration of mitral valve interventions, it does not comprehensively encompass septal interactions due to a lack of RV. Future work can involve fine-tuning septal wall motion by programming the soft robotic myocardium or integrating both right and left ventricles to explore interventricular dependencies, gaining a more comprehensive understanding of these interactions. The utilization of the soft robotic myocardium facilitates the approximation of non-contracting papillary muscles as the left ventricular wall contracts. This approximation results in the convergence of the chordae tendinae, ensuring effective valve coaptation during systole³³. In the diastolic phase, the papillary muscles retreat as the ventricular wall relaxes. Prospective research could encompass the substitution of native papillary muscles with a downsized, pneumatically driven soft robotic actuator that emulates natural contraction and relaxation. This approach would maintain appropriate tension in the chordae tendinae throughout the cardiac cycle, mimicking physiological conditions to recreate papillary muscle motion, as shown by Imbrie-Moore et al.³⁴

In conclusion, our platform combines an explanted heart with soft robotic techniques to replicate cardiac valve motion, achieve biomimetic septal and ventricular motion, recreate hemodynamics of pathological conditions, and further close the gap between the bench and operating table. By creating this hybrid system, we have developed an innovative tool that can fully enable translational cardiac research and training related to MV procedures, and potentially accelerate MV device development.

MATERIALS AND METHODS

Resource availability

Lead contact

For additional information and resource requests, please contact Professor Ellen T. Roche at etr@mit.edu.

Materials Availability

The study did not produce new unique reagents.

Data and Code Availability

The main article and Supplemental material contain all the data presented in the study. Additional information can be requested from the corresponding author.

Preparation of endocardial scaffold

To obtain a porcine heart in a relaxed state, we arrested the heart during the diastolic phase by injecting saturated potassium chloride solution (0.34 g/mL) directly into the heart, or by incubating the heart in one liter of the solution for a ~ 2 to 3 hours to allow for passive diffusion. When using the submersion method, it was crucial to start the process immediately after harvesting. Once the heart was arrested, the potassium chloride solution was thoroughly washed out with DI water. The heart was then continuously treated with a two-liter of a 10% formalin solution for 18-24 hours in a gentle shaker at room temperature, followed by a dissection process to remove the myocardial tissue, as described previously.³⁵ To restore the mechanical properties and function of the chemically fixed valves, the formalin-fixed endocardial scaffold was decellularized using 10% Sodium Deoxycholate (Sigma Aldrich) and 10% Triton X-100 (Thermo Fisher Scientific) in 1× PBS (volume 2 liters) in a gentle shaker at room temperature for at least a week, as published previously.³⁶ The decellularization solution was replenished every three days, and the total decellularization period varied from heart to heart, empirically

determined visually by the texture of the valve leaflets. Finally, the chemically-treated endocardial scaffold was thoroughly washed with distilled water in a gentle shaker at room temperature, with frequent solution replenishment for at least 24 hours to ensure the removal of detergents from the tissue structure.

Fabrication of heart-specific soft robotic myocardium

To create a soft robotic myocardium that is specific to each heart's endocardial scaffold, a silicone replica of the scaffold was molded from a negative mold cast using Ecoflex 00-35 (Smooth-On) between the formalin fixation and decellularization process (see previous section). The dimensions of the actuators were measured around the silicone replica for three circumferential actuators placed in the basal, middle, and apical regions, and three helical actuators oriented at about 65 degrees from the basal plane of the endocardial scaffold, as published previously.^{17,37} Flattened McKibbens were fabricated for the circumferentially arranged actuators, while cylindrical McKibbens were used for the helically arranged actuators in the inner layer. Both types of actuators were made by assembling pre-made thermoplastic elastomer balloons with Ecoflex 00-30 (Smooth-On)-coated ¼" PET braided mesh sleeving (Techflex). To position the actuators relative to one another, they were embedded in a passive matrix layer of silicone. A thinner elastomeric matrix was used for maximizing the actuator contraction motion, therefore two thin silicone shells of approximately 1 mm thickness were prepared by coating a 3D printed mold in a standard idealized left ventricular geometry with a layer of Ecoflex 00-35 FAST. The first layer of thin silicone shell was placed onto the silicone replica of the endocardial scaffold, serving as the innermost surface contacting the scaffold. The helical actuators were then positioned and secured using an elastic net dressing (ProMed, Inc.), and the circumferential actuators were glued on top of the helical actuators at desired positions using fast-curing Ecoflex 00-35 FAST. The second silicone shell was then placed as the outermost shell. Ecoflex 00-31 (Smooth-On) was used with a syringe to fill in the gaps between the actuators and silicone shell and was cured in a 60-degree Celsius oven for about 20 minutes. The silicone replica was then removed, leaving the final assembly of a heart-specific soft robotic myocardium.

Assembly of biorobotic hybrid heart

To address the tears in the endocardial scaffold after hand dissection of the native myocardium and to prevent delamination at the tissue-silicone interface, a fixed porcine pericardium was used as an intermediate medium to seal the surface. The soft robotic myocardium was then assembled onto the pericardium-covered endocardial tissue scaffold using a custom-made tissue-silicone adhesive, which contained 1.5% (v/v) Triethoxyvinylsilane, (v/v) 3-(Triethoxysilyl) propyl isocyanate, and platinum catalyst.³⁸ To provide support to the endocardial tissue while adhering to the soft robotic myocardium, an oversized thermoformed balloon was placed inside the left ventricle through one of the pulmonary veins.

Visualization with computed tomography

A micro-computed tomography (micro-CT) was used to visualize the intracardiac structures in the endocardial scaffold of the biorobotic hybrid heart, utilizing a Skyscan 1276 X-ray microtomograph from Bruker. For imaging, aluminum and copper energy filtering were enabled, and an exposure time of 260 ms was used in the rotation mode, with a step of 0.647 degrees. The data was processed with NRecon (Bruker) software and viewed using Dataviewer (Bruker).

Biorobotic cardiovascular simulator

The left heart circulation was simulated using a mock circulatory loop consisting of hydraulic and mechanical components. We built compliance chambers in-house to represent aortic and arterial compliances and used ball valves (McMaster-Carr) to represent systemic vascular resistance. The biorobotic hybrid heart was connected to the circuit and actuated at 70 bpm using an electro-pneumatic control box, as previously described^{39,40}, to mimic the pumping function of the cardiac muscle *in vivo*. We adjusted the level of actuation, compliance, and resistance to achieve desired hemodynamics. To ensure physiological osmotic pressure for valve leaflets, we used a 0.9 % saline solution as a test fluid. We measured hemodynamic parameters using pressure sensors (PendoTECH) and ultrasonic flow probes (Transonic) connected to a T420 multichannel research console (Transonic) and recorded the data using PowerLab (AD Instruments) and LabChart software (AD Instruments). Pressure sensors were connected to 3.5 F umbilical vessel catheters (Cardinal Health), which we placed at the left ventricle, left atrium, and aorta to measure the pressure tracings. We mounted one flow probe directly onto the descending aorta above the valve to record aortic flow, and the other probe onto a ½" OD latex tubing connected to the left atrium to measure mitral flow. We used a 10 Hz low-pass digital filter in LabChart to process the pressure and flow data recordings and remove high-frequency noise. To observe valve motion, we used an endoscopic camera (Image1 HubTM, Karl Storz Endoscopy-America Inc.) to record videos at 30 fps. We had endoscopic camera access at the left atrium for viewing the mitral valve and at the aorta branch (innominate artery) for visualizing the aortic valve. To simulate physiological hemodynamics in soft robotic myocardium, we used the synthetic myocardium in combination with mechanical valves (St. Jude Medical) in place of the biorobotic hybrid heart. To ensure the flow generated by the soft robotic myocardium was unidirectional, we positioned the mechanical valves at both the inlet and outlet. We attached pressure sensors to measure aortic pressure at the outlet and left atrial pressure at the inlet of the soft robotic myocardium, and affixed flow probes to the latex tubing at both the inlet and outlet. By regulating the level, pattern, and frequency of pneumatic actuation, as well as the resistance and compliance in the circuit, we successfully attained the targeted hemodynamics. However, highly oscillatory pressure responses were observed due to the fast actuation and deactivation of the materials, such as silicone elastomer in the synthetic myocardium and latex tubing in the flow loop. We applied a 10 Hz low-pass digital filter to the time-series hemodynamics data generated by soft-robotics myocardium, effectively reducing the high-frequency noise.

Acute mitral regurgitation model

To induce acute mitral regurgitation, the chordae in the P2 region of the mitral valve were cut, resulting in a P2 prolapse. In cases of severe mitral regurgitation, additional chordae were cut in the A2/P2 regions to create flail leaflets. The severity of mitral regurgitation was evaluated by observing the motion of the mitral valve in endoscopic videos and by analyzing the regurgitant flow jet in 2D color Doppler echocardiography. Hemodynamic data were collected for quantitative assessment.

Device testing for mitral valve repair

To treat mitral regurgitation in the biorobotic hybrid heart, a range of intracardiac devices were implanted, including surgical repair and replacement devices, as well as minimally invasive repair devices. Mitral valve repair with chordal replacement was performed by a cardiac surgeon using artificial chords made of polytetrafluoroethylene sutures and pre-measured loops called Chord-X (CryoLife). A transcatheter edge-to-edge mitral valve repair was carried out using MitraClip™ XTR (Abbott) to address moderate mitral regurgitation. This involved introducing a catheter into the left atrium via a transseptal puncture in the left atrial tissue, then positioning and orienting it above the mitral valve to

grasp the leaflets and create a double orifice before releasing the clip. For surgical replacement of a damaged mitral valve, a 23 mm Trifecta™ Valve with Glide™ Technology (St. Jude Medical) made of pericardial tissue was used. The valve was sutured around the mitral annulus in the anatomical position to allow inward flow to the left ventricle. The function of all devices was evaluated using endoscopic video, echocardiography, and hemodynamic data collected in the biorobotic cardiovascular simulator. For intervention testing, we used two hearts sourced from different pigs with distinct *ex vivo* scaffolds. One heart model was used for a surgical repair study, while the other was used first for a minimally invasive transcatheter repair procedure demonstration and then for a surgical replacement study. While we recognize that there may be inherent variations among heart specimens, we opted against making direct comparisons between the various interventional techniques highlighted here to prevent any inconsistencies.

Echocardiography

A cardiac surgeon performed 2D and 3D epicardial echocardiography on the biorobotic hybrid heart in the simulator, using an iE33 ultrasound machine (Phillips) with an x7-2 transducer probe (Philips). 2D echocardiography was used to observe the motion of the tissue valves and the left ventricular wall driven by the actuation of the soft robotic myocardium. 2D color Doppler was used to assess the severity of mitral regurgitation in both physiological and pathological models and to evaluate the device's performance. A trained surgeon evaluated the degree of mitral regurgitation based on the grading system of 2D color Doppler echocardiography.

Statistics

Hemodynamic data were collected for at least 10 consecutive cycles and the mean and standard deviation were reported, unless stated otherwise. The statistical significance (* $p < 0.01$) was determined using one-way ANOVA with Tukey correction in OriginPro 2021b (64-bit).

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Conceptualization: CP, MS, MYS, CTN, ETR
Experimental Methodology: CP, MS, MYS
Funding acquisition and Supervision: ETR
Writing – original draft: MS, CP
Writing – review & editing: MS, CP, MYS, CTN, ETR

Competing interests: ETR serves on the board of directors for Affluent Medical, as well as the board of advisors for Pumpinheart and Helios Cardio. Additionally, ETR provides consulting services for Holistick Medical and is a co-founder of Fada Medical and Spheric Bio. ETR, CP, and CTN hold a patent for "Organosynthetic dynamic heart model" U.S.

Patent Application No. 17/193,910. The other authors have declared that they do not have any competing interests.

Data and materials availability: The main article and Supplemental material contain all the data presented in the study. Additional information can be requested from the corresponding author.

Inclusion and diversity statement: We support inclusive, diverse, and equitable conduct of research.

Supplemental Materials

The Supplemental information includes Figures S1 to S12 and Movies S1 to S3.

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Figure Captions:

Figure 1. A biomimetic approach to replicating the heart for assessing mitral valve repair and replacement technologies. (A) Function and anatomy of the mitral valve, which regulates blood flow between the left atrium and ventricle in the heart. (B) Existing *ex vivo* simulators that use internal fluid pressurization to reproduce hemodynamics often produce paradoxical pressure-volume relationships. (C) Our proposed approach, using the biorobotic hybrid heart, allows for reproducing biomimetic cardiac motion, hemodynamics, and valvular motion. *P*, intraventricular pressure; *V*, intraventricular volume; PM, papillary muscle. (D) The architecture of the biorobotic hybrid heart consists of a pneumatically actuated soft robotic myocardium and a chemically-preserved endocardial scaffold. (E) A visualization of the biorobotic hybrid heart under micro-computed tomography (CT) shows the intricate internal structure of the heart model. The red-dotted line in panel D indicates the cutting plane used to obtain the slice shown in the short-axis view. LA, left atrium; LV, left ventricle; MV, mitral valve; AoV, aortic valve.

Figure 2. Design and performance of the soft robotic myocardium. (A) Design of the soft robotic myocardium, which consists of large circumferential and smaller helical pneumatic

actuators arranged in a biomimetic manner to replicate the beating motion of the heart. (B) Visual representation of the pumping ability of the soft robotic myocardium when actuated with 20 psi pressure for 300 ms. The relaxed state filled with fluid is shown on the left, and the contraction state ejecting fluid is shown on the right. Water is used for this visualization. (C) Varying input actuation pressures can produce consistent ejection fraction in soft robotic myocardium with different initial chamber volumes. $n = 2$. Shaded area = ± 1 SD. (D) Selective actuation of inner helical actuators ('Twist only'), outer circumferential actuators ('Circ only'), and both ('Twist + Circ') in the soft robotic myocardium. (E) Effect of input pressure on chamber pressure. (F) Schematic of the biorobotic cardiovascular simulator setup, which includes a soft robotics-based beating heart and a mock circulatory flow loop to simulate the left-sided hemodynamics of the heart. See also Supplemental Figures S1 and S2 and Movie S1.

Figure 3. Physiological hemodynamics and wall motion in the biorobotic cardiovascular simulator. (A) Photo of the biorobotic cardiovascular simulator setup. (B) Representative pressure waveforms. (C) Representative flow waveforms. LVP, left ventricular pressure; LAP, left atrial pressure; AoP, aortic pressure. (D) 2D Echocardiography of the biorobotic hybrid heart showing the biomimetic LV wall motion. LA, left atrium; LV, left ventricle; SRM, soft robotic myocardium; MV, mitral valve. See also Supplemental Figures S3, S4, S5, and S6 and Movie S1.

Figure 4. Valve motion in the biorobotic cardiovascular simulator. (A) The motion of the aortic valve (AoV) during diastole and systole was captured with an endoscopic camera and echocardiography. (B) The motion of the mitral valve (MV) during diastole and systole with endoscopic videography (top) and 2D echocardiography (bottom). (C) Change in mitral valve annulus area during systole and diastole studied with echocardiography. AoV, aortic valve; MV, mitral valve. LCC, left coronary cusp; RCC, right coronary cusp; NCC, non-coronary cusp; A1, anterior segment of the anterior leaflet; A2, middle segment of the anterior leaflet; A3, posterior segment of the anterior leaflet; P1, anterior scallop of the posterior leaflet; P2, middle scallop of the posterior leaflet; P3, posterior scallop of the posterior leaflet. See also Supplemental Figure S6 and Movie S2.

Figure 5. Acute mitral regurgitation (MR) model by introducing anatomical/structural defect in the mitral valve. (A) Chordae rupture in the mitral valve induces mitral prolapse, resulting in acute mitral regurgitation. Surgical excision of primary and secondary chords in the P2 segment of the mitral valve is performed to create the MR model. (B) Pathological valve motion in an acute mitral regurgitation model with moderate mitral regurgitation by P2 prolapse. (C) Severe mitral regurgitation model, demonstrating mitral leaflet flail. The arrow denotes the prolapse in the P2 segment of the mitral valve, which causes regurgitation. PM, papillary muscle. (D) Pathological hemodynamics at various stages of acute mitral regurgitation in the biorobotic cardiovascular simulator for mitral flow. (E) The left ventricular pressure (LVP) in the acute mitral regurgitation model during diastole and systole. (F) Left atrial pressure (LAP), which compares the healthy baseline with the mitral regurgitation. See also Supplemental Figure S7 and Movie S3.

Figure 6. Simulation of a surgical repair procedure for mitral valve prolapse using artificial chord implantation under direct visualization, and characterization of resultant hemodynamics. (A) Schematic of an artificial chordae prosthesis (Chord-X) for mitral valve repair. A series of photos taken during the surgical repair procedure during (B) implantation, (C) after implantation, and (D) coaptation test with saline, showing a competent mitral valve. (E) Representative hemodynamic curves of artificial chordal repair for mitral flow, demonstrating improved backflow. (F) Summary of the hemodynamics showing mitral regurgitant fraction, indicating a significant reduction in mitral regurgitation. (G) Representative hemodynamic curves for left ventricular pressure, demonstrating improved left ventricular function. (H) Representative

hemodynamic curves for left atrial pressure, showing reduced pressure in the left atrium. (I) Summary of the hemodynamics for systolic left ventricular pressure (LVP), indicating improved left ventricular pressures post chord repair. (J) Summary for peak left atrial pressure (LAP), demonstrating reduced pressure in the left atrium after artificial chordae implantation. MR, mitral regurgitation. Data shows average $\pm$ stdev for 10 cycles, * $p < 0.01$. See also Supplemental Figures S8 and S9.

Figure 7. Simulation of a valve replacement using a prosthetic Trifecta™ Valve with Glide™ Technology (St. Jude Medical), and characterization of resultant hemodynamics.

(A) Surgical implantation of a prosthetic valve at the mitral annulus, viewed from the left atrium. (B) Motion of the prosthetic valve at the mitral valve site post-replacement, showing the valve opening during diastole and closing during systole. (C) Images from the endoscopic camera and 2D echocardiography, showing the (left) narrow opening of the aortic valve during systole prior to treatment in the severe mitral regurgitation (MR) condition, and (right) larger opening of the aortic valve after replacement with the prosthetic valve. (D) 2D color Doppler images of prosthetic valve replacement, showing a competent valve at the mitral annulus. (E) Representative hemodynamic waveforms of prosthetic valve replacement for mitral flow, demonstrating improved backflow. (F) Summary of the hemodynamics for mitral regurgitant fraction, indicating a significant reduction in MR after replacement with the prosthetic valve. (G) Representative hemodynamic waveforms for left ventricular pressure (LVP), demonstrating improved left ventricular function post valve replacement. (H) Summary of mean mitral valve pressure gradient during systolic phase, indicating improved valve function. MR, mitral regurgitation. Data shows average $\pm$ stdev for 10 cycles, * $p < 0.01$. See also Supplemental Figure S10 and Movie S3.

Figure 8. Demonstration of transcatheter edge-to-edge repair (TEER) procedure with direct visualization, and characterization of resultant hemodynamics. (A) MitraClip™ device used for the TEER procedure. Schematics adapted from Abbott Laboratories

(www.cardiovascular.abbott). (B) Biorobotic hybrid heart used for the TEER procedure, showing the MitraClip™ being inserted through the transseptal region. (C) Endoscopic images of the TEER procedure in the biorobotic hybrid heart, showing the (left) insertion, (middle) positioning and grasping, and (right) deployment of the MitraClip™ device. Schematics adapted from Abbott Laboratories (www.cardiovascular.abbott). (D) Double-orifice mitral valve (MV) after TEER repair, showing the successful repair of the valve (top). The repaired MV is functional and competent, exhibiting complete closure during systole as seen via 3D echocardiography (bottom). (E) Hemodynamic assessment of TEER repair. Representative hemodynamic waveforms of the TEER repair for mitral flow, indicating improved mitral valve function after the procedure. (F) Summary of the hemodynamics of the TEER repair, showing reduced mitral regurgitant fraction. (G) Hemodynamic curves of the TEER repair for left ventricular pressure (LVP), indicating improved LVP after the procedure. (H) Summary of the hemodynamics of the TEER repair for LVP, demonstrating successful repair of the valve. (I) The hemodynamic waveforms depicting left atrial pressure (LAP) indicate an improvement in LAP following the TEER repair procedure. (J) A summary of the hemodynamics related to the TEER repair procedure demonstrates an improvement in left atrial pressure (LAP). Data shows average $\pm$ stdev for 10 cycles, * $p < 0.01$. LA, left atrium; LAP, left atrial pressure; MV, mitral valve; MR, mitral regurgitation. See also Supplemental Figures S11 and S12 and Movie S3.

Supplemental video titles

Supplemental Movie S1: Performance of the soft robotic myocardium to eject fluid and recreation of biohybrid LV wall motion on a bench.

929 **Supplemental Movie S2:** Simulating healthy aortic and mitral valve motion in the biorobotic
930 hybrid heart.
931 **Supplemental Movie S3:** Assessment of mitral valve pathological and repaired models using
932 endoscopic camera and echocardiography in the biorobotic hybrid heart.
933