Technology to Transform Lives:

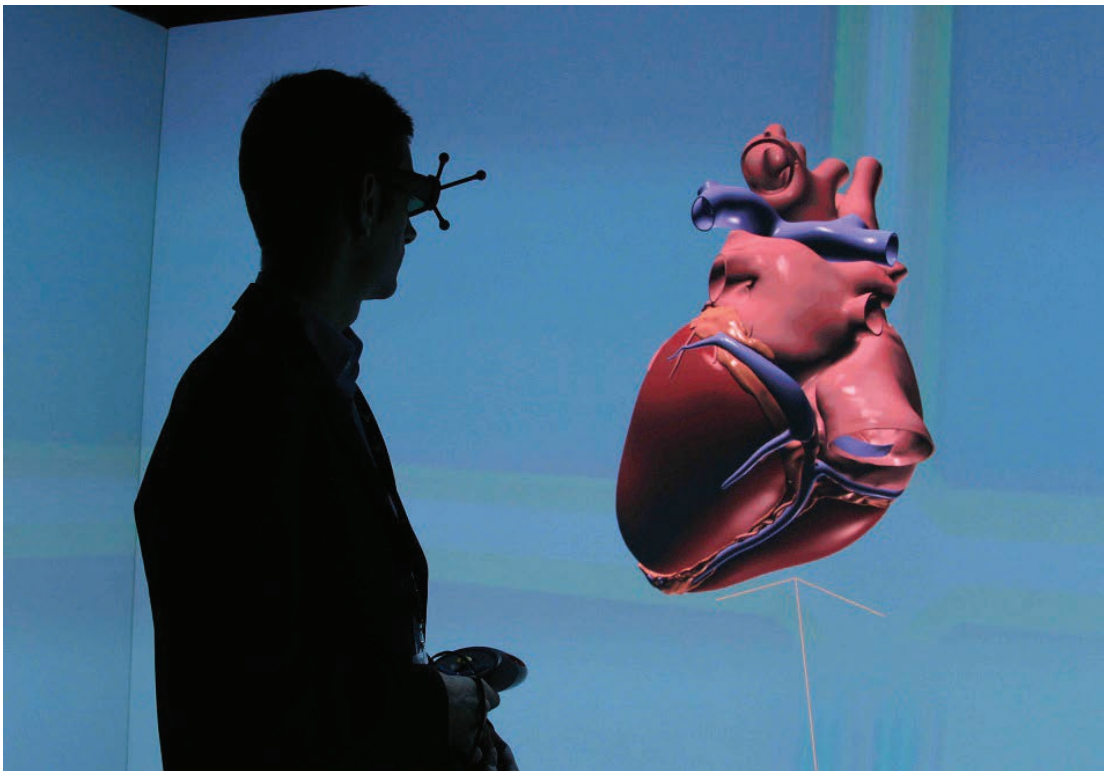
The SIMULIA Living Heart Model

Karl D'Souza
Product Manager, Virtual Human Modeling at Dassault Systèmes SIMULIA

If you or a loved one has ever received bad news at the doctor's office, you know all too well the sinking feeling of uncertainty that sets in. You know what it means to run through a hundred questions in your mind.

Do I really need this treatment? What are the risks?
If I do not go through with it, could the outcome be even worse?
How do I balance the potential risks and benefits?

Although the answers to these questions continue to be murky, technologies are being developed to help physicians better diagnose and treat a wide range of diseases. The Living Heart from Dassault Systèmes SIMULIA represents an attempt to harness the power of realistic simulation to improve cardiovascular devices and treatments, and sets the stage for many more simulation-based solutions that can transform healthcare.



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Why Model a Human Heart?

The decision to model the human heart was motivated by several reasons. Cardiovascular disease is the leading cause of death in the US and other developed countries and imposes a high socioeconomic cost. Spending on circulatory conditions (primarily heart disease and hypertension) constitutes the largest portion of US healthcare expenditure. The decline in quality of life and productivity (in addition to mental anguish of sufferers and loved ones) was also a key factor in focusing on cardiovascular disease.

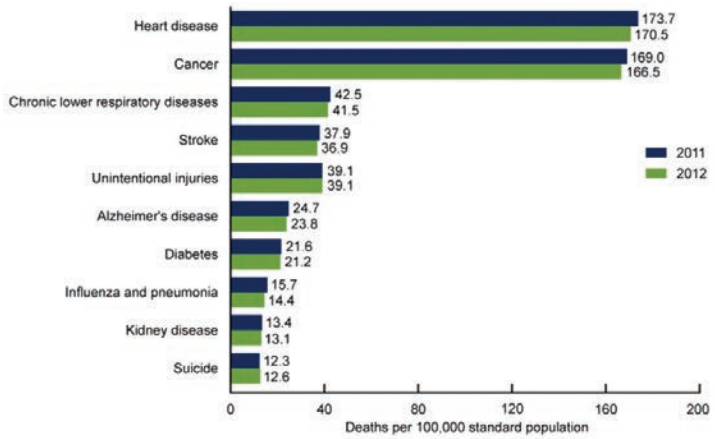

Figure 1: Age-adjusted leading causes of US deaths
Source: CDC/NCHS National Vital Statistics System, Mortality
www.cdc.gov/nchs/data/databriefs/db178.htm

While dietary and lifestyle choices can reduce the probability of heart disease, medical interventions (pharmaceuticals, devices, and surgical treatments) play a key role in managing cardiovascular problems once they occur. Just as in other industries, the efficacy of biomedical products and treatments can be greatly improved by using computer aided engineering (CAE), which has played a central role in the design, testing, and validation of products ranging from jumbo jets to razor blades, and has helped companies produce more effective, reliable, safe, and easy to use products and solutions. However, when compared with other industries, the biomedical industry has been lagging in its adoption of CAE, in part due to the lack of accurate

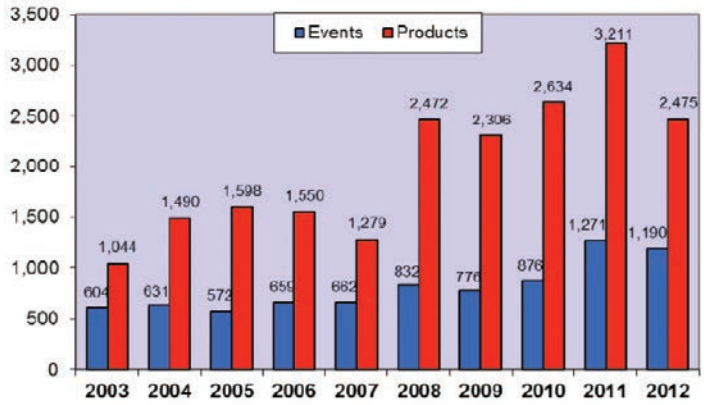

Figure 2: Number of recall events and products in the US by fiscal year
Source: FDA Medical Device Recall Report FY2003 – FY2012
www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/UCM388442.pdf

models, accepted processes, and published standards. A central problem in medical device simulation is the need to model not just the mechanical behavior of the device, but also its physical and physiological interaction with the human body. For instance, an artificial heart valve will move as the heart deforms over the cardiac cycle, and the designer must ensure its movement does not adversely affect its performance. Further, the implantation procedure may itself cause adverse physiological responses. To consider such effects, a simulation model must therefore be able to accurately represent in vivo loads and boundary conditions. However, this is not a trivial matter. It is simply not possible to instrument the human body to measure loads and responses the way one can with an automobile, and insights gained from experimenting on animals or cadavers often do not provide the accuracy required. The inability to examine the human body hosting the device often obscures the root cause of failure and is in part responsible for the regular (indeed, increasing) rate of medical device recalls of the last decade. If the aim is to enhance the predictive power of biomedical simulation, then it is imperative to create virtual models capable of realistically capturing the dynamic and adaptive nature of the human body.

Another barrier is the intense scrutiny faced by medical device manufacturers. Regulatory authorities the world over place stringent demands on device makers and device failures usually garner much negative publicity, while successes go quietly unnoticed. This has led to a culture of caution wherein device innovations often tend to be incremental improvements over existing designs, rather than the radical breakthroughs needed to combat the scourge of cardiovascular disease. Changing this approach requires the adoption of validated simulation tools and models using which all stakeholders can establish common processes and best practices to facilitate true innovation and accelerate the approval process.

While the challenges faced by the biomedical industry are real, they are not insurmountable. Dassault Systèmes has worked for decades across many industries to help thousands of engineers imagine, develop, and deliver sustainable innovations capable of harmonizing product, nature and life. Nowhere is this more evident than within the automotive industry, where engineers can simulate and fully experience the performance of thousands of vehicle designs quickly and with low environmental impact in the virtual world, and then select the best before creating it in the real world. Using technology from Dassault Systèmes, engineers can model a full vehicle consisting of hundreds of parts and connections, multiple vehicle subsystems, complex tire-road interactions, and high fidelity dummy models, all in a single simulation. The reliability of virtual testing and the use of standardized simulation workflows have allowed manufacturers to overcome the technical, regulatory, and cultural challenges they once faced. Today, they can go directly from design to production with confidence in the performance and safety of their product. The same

Figure 3: 3DEXCITE rendering of a Ford Taurus crash simulation using Abaqus. This model was developed by The National Crash Analysis Center (NCAC) of the George Washington University under a contract with the FHWA and NHTSA of the US DOT.

success is possible in the biomedical industry if the specific challenges it faces can be overcome. We therefore decided it was time to leverage our unique technological capabilities and engineering experience to transform the biomedical industry and indeed the practice of healthcare. .

Realizing such a vision requires a cross-disciplinary team and focus on a specific area. Consequently, the Living Heart Project (LHP) was launched in 2014 to bring together academic and clinical researchers, biomedical engineers, government regulators, and medical professionals, all with expertise in cardiovascular mechanics and various aspects of the diagnosis and treatment spectrum. The main objective of the LHP is to deliver consistent and validated cardiovascular models that can be used to develop safe and effective products and treatments and thereby translate simulation technology into improved patient care. With the team in place, we set out to build the first validated human heart model.

What is the Living Heart Model?

From a functional viewpoint, the heart can be thought of as two pumps (left and right heart) with the pulmonary and systemic circulations situated between them. The flow of blood within the circulatory system is driven by muscular contractions in the heart. Thus, a complete mechanistic model of the heart must ultimately account for the fluid-structure interaction that underlies cardiac function. Cardiac contraction and relaxation are driven by a tightly coupled wave of electrical excitation that travels across the heart. Any change in the electrical behavior of the heart (e.g., pacing issues, conduction blocks) has an immediate and significant effect on cardiac output and it is therefore essential to include the electrical system in the model.

The Living Heart Model contains well-defined anatomic details including internal structures (e.g., heart valves, chordae tendineae, coronary arteries and veins) and proximal vasculature (e.g., aortic arch, pulmonary trunk, and SVC). Muscle fiber orientations, which vary across the surface and thickness of the heart, and have a strong effect on the mechanical response, are included in the model definition. The mechanical behavior of heart tissue includes both passive and active behaviors. Passive tissue response uses an anisotropic hyperelastic formulation, while active tissue response uses a time-varying elastance model to model the Frank-Starling effect, which relates stroke volume to preload and arises from the excitation-contraction coupling within cardiomyocytes. The Living Heart model benefits from SIMULIA's extensive library of nonlinear material behaviors and particular experience in modeling biological materials (e.g., flesh, bone, skin, and fat).

A closed system of fluid cavities and fluid links is used to model blood flow inside the heart chambers and through the circulation. The fluid and solid models are directly coupled within the heart while the systemic and pulmonary circuits are endowed with vascular compliances and flow resistances that can easily be modified to simulate exercise, hypertension, and other physiological states. The blood flow model is calibrated such that clinically relevant results are within their published ranges. Tissue electrical response is characterized by an action potential whose evolution is controlled by a number of biochemical

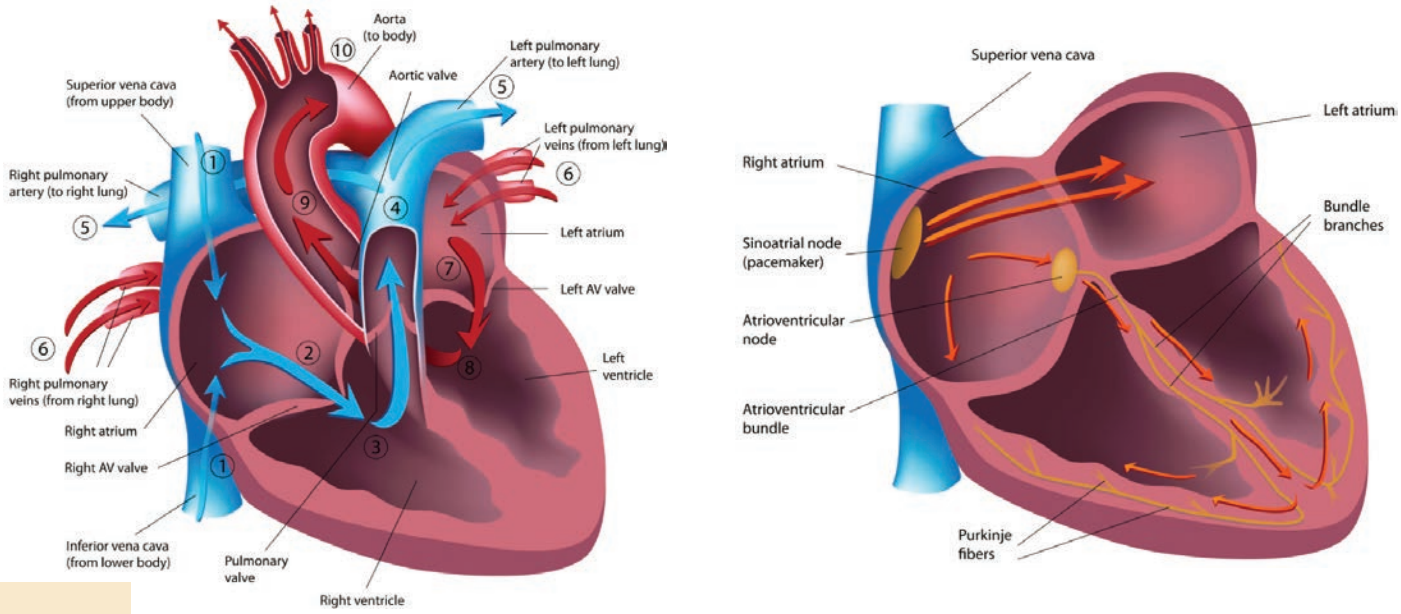

Figure 4: Internal views of the heart showing blood flow pathway (left) and electrical pathway (right)

parameters. In addition, the bundle of His and Purkinje network are modeled explicitly to generate the physiologically observed wave propagation pattern whereby the electrical signal first travels down the atrioventricular septum to the apex and then up the ventricular side walls. The SIMULIA Living Heart is thus a dynamic multiphysics model of a human heart that has been validated against a wide range of clinically relevant metrics and is now the first of its kind commercially available.

Applications of the Living Heart Model

The mitral valve controls blood flow between the left atrium (LA) and left ventricle (LV). In normal circumstances, the valve is open during ventricular diastole allowing the LV to fill. It then shuts completely during systole when blood is forced from the LV into the aorta and eventually into the systemic circuit to oxygenate the body. However, in some situations, especially after a myocardial infarction (MI, or heart attack), there may be enlargement of the LV and the mitral annulus, which may lead to incomplete closure of the mitral valve during systole. Since blood is ejected from the LV under high pressure, some of it may flow back into the LA instead of the aorta. This retrograde leakage of blood into the LA is known as mitral regurgitation and can cause weakness, fatigue, and a host of other symptoms, which, if left untreated, can be life threatening.

Collaborators in the LHP (Reference 1) used the Living Heart to assess the efficacy of a novel medical device being developed to treat this condition. The first step was to induce an MI into the model. Based on real patient post-MI data, the material properties of a region in the LV (including the posterior papillary muscle) were modified to suppress active tissue response for the entire cardiac cycle. The diseased model was then run and indeed predicted a lower cardiac ejection fraction in agreement with that observed clinically. Incomplete closure of the mitral valve during ejection was also clearly visible.

The next step was to simulate the interaction of the device and the infarcted heart. The device under consideration was a novel annuloplasty ring with a sub-valvular component. The rationale was that the sub-valvular element would better engage the chordae and hence counterbalance the shifting of the coaptation line in patients with ischemic cardiomyopathy thereby reestablishing proper leaflet coaptation and valve function. The device was modeled as rigid and affixed to the mitral valve annulus at several distinct points representing suture locations. The heart model predicted improved leaflet coaptation upon implantation of the ring, thus providing conceptual validation to the researchers. They were also able to examine the engagement profile of the ring and the

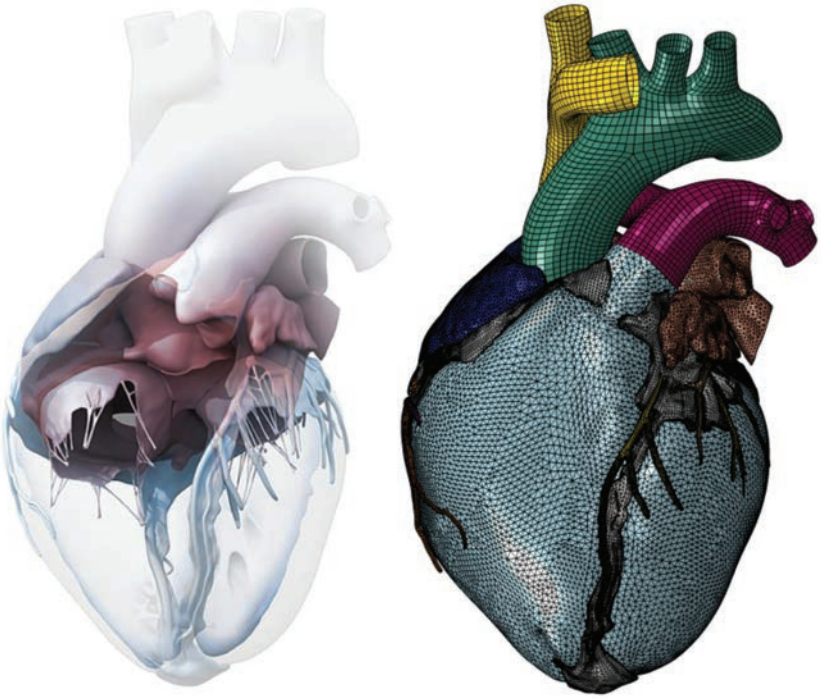

Figure 5: Interior view of geometry used to create the Living Heart Model (left) and exterior view of the SIMULIA Living Heart Model (right)

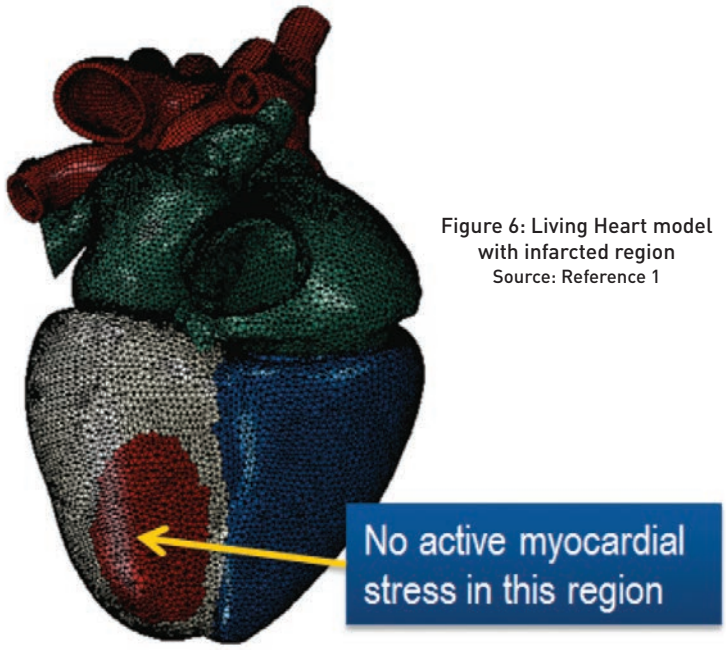

Figure 6: Living Heart model with infarcted region
Source: Reference 1

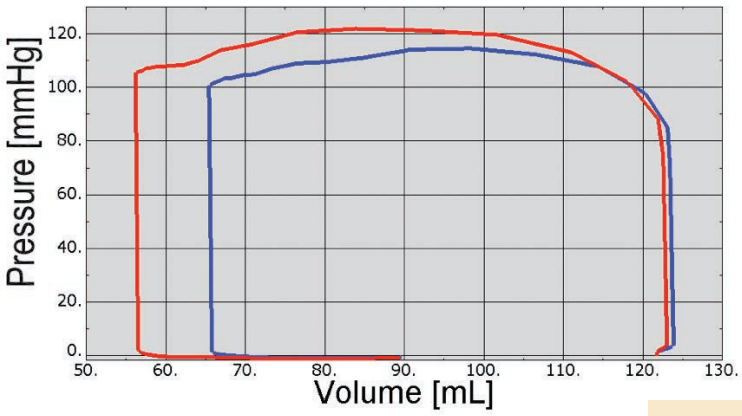

Figure 7: Pressure-Volume loops for LV showing ejection fraction drop from 55% (normal heart, red) to 45% (infarcted heart, blue)
Source: Reference 1

chordae and compare the forces generated in the chordae before and after implantation. Since the ring was able to generate chordae forces in an infarcted heart that were closer to those observed in a healthy heart, they developed greater confidence in the device. Future efforts include automating this workflow and conducting shape and/or parametric device optimizations to identify solutions customized for patient-specific heart geometries and cardiac pathologies.

Another application of the Living Heart involves the durability of pacemaker leads. Pacemakers, along with ICDs, play a key role in cardiac rhythm management and save thousands of lives. However, a significant number of pacemaker leads undergo in-service failures thereby causing distress to patients and increasing the overall cost of treatment. Many factors influence lead reliability, including lead design, composition, manufacturing process, patient characteristics, and implant route. The interdependence of these factors makes lead failure analysis a challenging task. Adding to the problem is the fact that, while some medical devices may be explanted and returned for manufacturer analysis when malfunction is suspected, leads cannot be easily removed due to local scarring and fibrosis. Even when malfunctioning leads are explanted, returned product analysis tends to be a poor predictor of failure mode and rate (Reference 2). This problem reiterates the importance of virtual models capable of accurately representing the in vivo environment.

The Living Heart is an ideal tool to help improve pacemaker lead durability. In an ongoing first-of-a-kind study, the Living Heart was used to simulate lead insertion and examine in vivo motion and stresses on the lead. The lead was first inserted through the SVC, RA, and RV, and attached to the RV apex using a tip insertion path and appropriate constraints. With the lead in position, a cardiac cycle was simulated to examine the deformation and stress on the lead using an appropriate level of damping to capture the effect of the surrounding blood. The initial data show that the dynamic response of the lead under cardiac loading conditions is in accordance with clinical observation. The model is currently being used for various sensitivity analyses, such as the dependence of lead curvature and forces on lead stiffness and location, with the ultimate goal of designing leads with higher performance and reliability.

The examples above illustrate the ease with which the Living Heart model can be modified to simulate the effects of heart disease and to introduce medical implants. More complex disease states that involve abnormal cardiac growth and remodeling of cardiac tissue (e.g., ventricular hypertrophy) can be modeled using the Abaqus user subroutine methodology. In addition, the Living Heart can be used in conjunction with other human models to inherit or supply loads and constraints. For example, some members of the LHP have long been using Abaqus to simulate the insertion, deployment, and mechanical interaction between drug-eluting stents and coronary arteries. Using anatomically accurate models of arterial sections and Abaqus material modeling and contact technology, they were able to study the effect of stent design on vascular stress distribution, which affects tissue response and thus the likelihood of restenosis. Using the Living Heart model, they can now also account for coronary artery motion induced by the pulsing heart, and thereby improve the predictive power of their analyses.

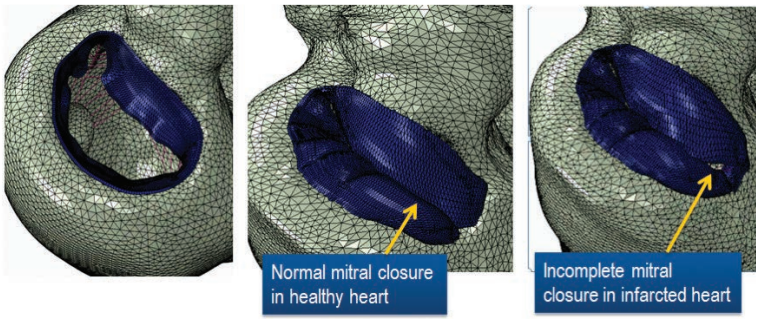

Figure 8: Close-up view of Living Heart model with LA removed to show the mitral valve open (left), closed in normal heart (middle), and incompletely closed in infarcted heart (right)
Source: Reference 1

Figure 9: Novel annuloplasty ring with sub-valvular element: Physical device (left) and finite element model (right)
Source: Reference 1

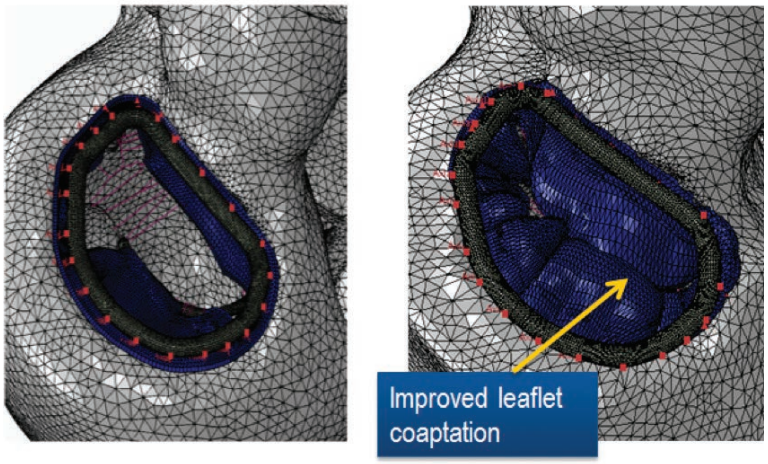

Figure 10: Annuloplasty ring in position in infarcted heart: mitral valve open (left), mitral valve closed (right)
Source: Reference 1

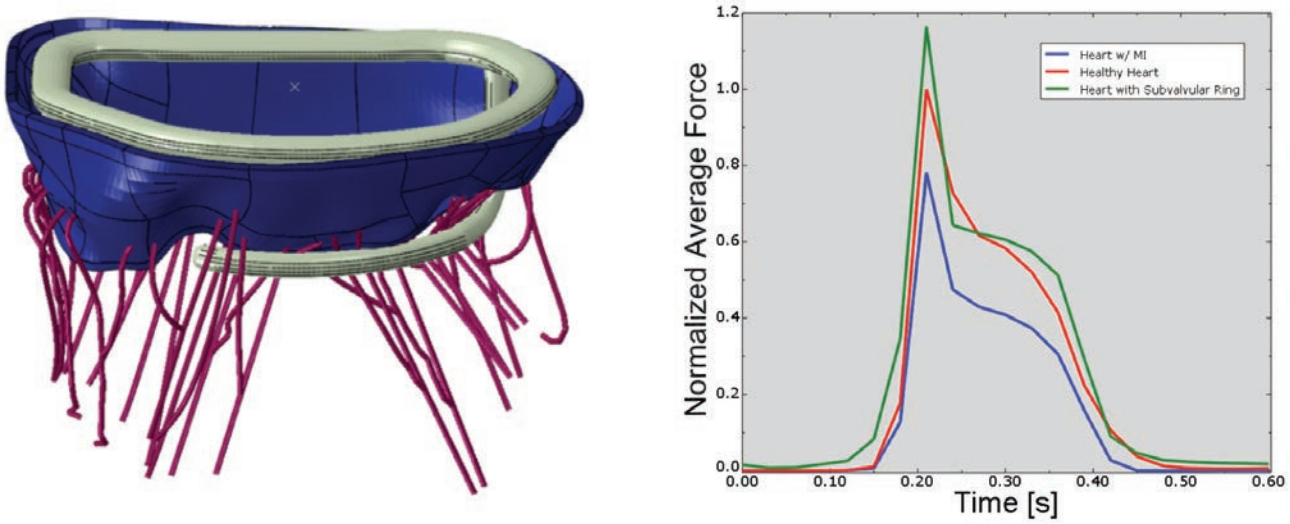

Figure 11: Sub-valvular element engaging with mitral chordae (left); restoration of chordae forces with device (right)
Source: Reference 1

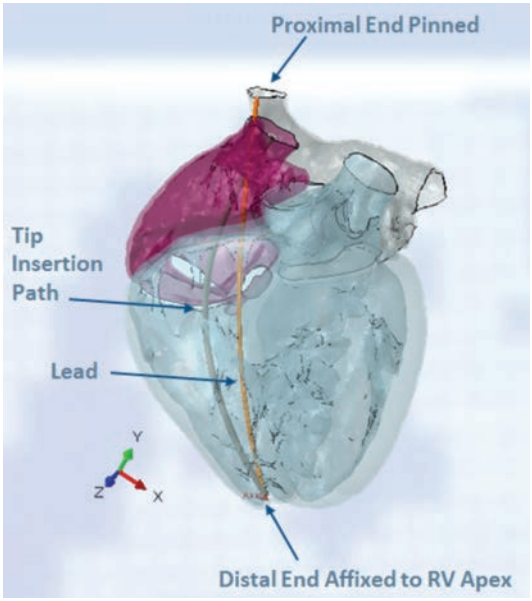

Figure 12: Living Heart model used to compute in vivo motions and forces on pacemaker lead

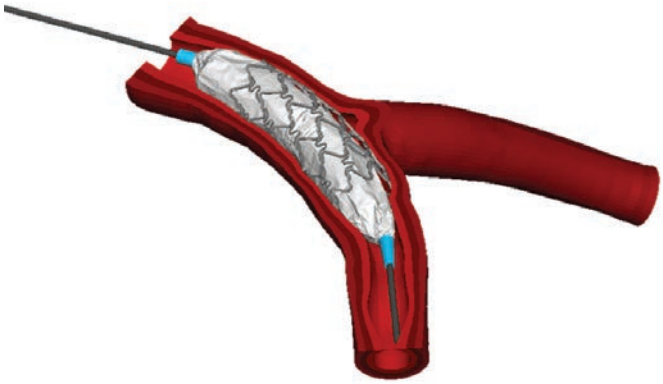

Figure 13: Insertion, deployment, and interaction of a balloon expandable stent using Abaqus
Source: Reference 3

Summary

The Living Heart relies on a conceptually unique approach of developing a single simulation model capable of reproducing a vast array of important cardiovascular applications, essential for clinical adoption and regulatory approval. Medical devices can readily be inserted into the model to examine their influence on cardiac function and examine treatment options. Using the healthy Living Heart as a baseline reference, data from modified models can be compared and interpreted. Further, by modifying its geometry, material properties, loads, and boundary conditions, the Living Heart can be used to study abnormal (diseased) cardiac function. As such, the model can truly be used in a wide range of clinically relevant applications. The Living Heart is based on proven Abaqus technology and subject to the same rigorous standards of quality as any other SIMULIA product, and therefore provides a consistent platform for innovation and collaboration.

This is only the beginning. SIMULIA and the Living Heart Project team are busy developing a product roadmap for the model. Future releases will offer enhanced usability and performance as well as extend the technical capabilities of the model to address more challenging cardiovascular diseases and device-heart interactions. We are also leveraging the 3DEXPERIENCE platform and cloud computing to bring the benefits of the technology to non (simulation) experts. Working with other brands in Dassault Systèmes, we are enabling multiscale simulations that will fundamentally improve the understanding of cardiovascular diseases and their treatments. The release of the SIMULIA Living Heart model is an important milestone in the rapidly emerging era of digital medicine in which healthcare providers and individuals will routinely use virtual human models and other computational technologies to track, manage, and improve human health and well-being.

References

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