

Optimization of Annuloplasty Rings to Address Functional Mitral Regurgitation Using the Living Heart Human Model

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Abstract: *The SIMULIA Living Heart Human Model (LHHM) is a platform to study various heart diseases and to evaluate the effectiveness of various devices. While previous studies have shown that LHHM-based simulations can be used for early-stage effectiveness assessments of devices, such as an annuloplasty ring, more thorough assessments and optimization of device function require a more rigorous framework. In this study, we focus on such a framework for Mitral Valve (MV) function:*

- 1. We established a more realistic baseline for the functioning of the MV in a healthy heart. This step involved identification and adjustments to various LHHM parameters such as the attachment locations of chordae on the MV leaflets and the lengths of the various chordae. These adjustments were carried out efficiently via the use of submodeling in conjunction with other methods in Abaqus/Explicit.*
- 2. We then introduced abnormal MV function in the LHHM. While knowledge gained in the first step can help introduce various types of abnormalities in the MV function, in the current application functional Mitral Regurgitation (MR) is simulated by introducing myocardial infarction (MI) into the new baseline model.*
- 3. A previously designed annuloplasty ring is then inserted into the diseased LHHM from Step 2 to help restore MV function. An optimization study is then carried out to modify the design and placement of the ring to further improve MV function.*

This study demonstrates that the Living Heart Human Model can be used as a platform to better understand cardiac functioning of healthy hearts, which then allows the potential to introduce disease states, and to simulate effectiveness of potential treatment options in increasingly rigorous manners. It also suggests the potential of the LHHM to successfully evaluate and predict the functioning of patient-specific cardiac medical devices.

Keywords: Mitral Valve, Myocardial Infarction, Functional Mitral Regurgitation, Annuloplasty Ring, Optimization.

1. Introduction

The mitral valve (MV) functions to regulate blood flow in one direction from the left atrium to the left ventricle (LV) and opens and closes in a precisely timed manner in a healthy heart. Functional mitral regurgitation (FMR), where there is regurgitation of the blood back into the left atrium, is a fairly common problem that is frequently caused by myocardial infarction (MI) (Glower et al., 2014). In this situation, even though the leaflets themselves are healthy, the MV leaflets do not coapt fully when they normally should because of other changes that have occurred due to the MI. A preferred surgical treatment to restore the function of the MV is to implant an annuloplasty ring, which constricts the MV annulus and thereby induces sufficient leaflet coaptation (Amini et al., 2014). However, it has been observed that regurgitation recurs in over 60% of the patients within 3-5 years after the MV repair (Flameng et al., 2003). A better understanding of various parameters that affect the MV behavior can allow for more efficient designs through optimization of the ring to better address patient needs and improve outcomes.

Computational or *in silico* modeling of various human organs has emerged as a promising tool to not only better understand their healthy behaviors, but also to understand disease states and to assess the effectiveness of various devices – the same applies to the heart as well, via the use of the SIMULIA Living Heart Human Model (LHHM). The LHHM includes all four chambers and heart valves and allows the dynamic response of the heart to be simulated by integrating electrical, structural, and fluid flow physics. In addition, the LHHM can be modified to introduce diseased states and to evaluate treatment options by introducing various types of cardiac devices into the model (LHHM User Guide, 2017).

In this study, we first make adjustments to the full LHHM (“Baseline 0”) to create an updated model (“Baseline 1”) that better corresponds to observed behavior around the mitral region. We then use a combination of submodeling and other approaches in Abaqus/Explicit to create a smaller model within which various parameters can be adjusted to match observed or targeted characteristics of the mitral valve motion. This is done first in a manual manner followed by subsequent automation with Isight. *(Note: Automation with Isight and the knowledge gained from adjustment of various parameters opens the possibility to match various diseases states of the MV. This aspect of the study will be covered in a separate forum and not discussed in this study.)* The selected parameters are then reintroduced into the global model to create a new baseline (“Baseline 2”) model into which differing levels of MI can be introduced, with each level of MI causing differing levels of regurgitation. For one of the MI levels, an annuloplasty ring is inserted into the LHHM to improve the FMR that resulted from that MI. Following this step, an optimization analysis is performed with Isight to adjust various ring characteristics to further improve the resolution of the FMR.

2. Improved MV Function in the LHHM and Creating an Updated Baseline Model

2.1 LHHM “Baseline 0”

The LHHM couples the responses of electrical, structural, and fluid flow to simulate human cardiac function. Interested readers are referred to Baillargeon *et al.* (Baillargeon et al., 2015) for more details. The latest version of the LHHM includes several modeling changes and improvements:

- All 4 valves are meshed and available for analysis
- Mitral and Tricuspid Valve geometries and material properties have been updated
- Coronary arteries and veins are included
- A number of chordae tendinae have been added (total 62 strands)
- Bundle of His and Purkinje fiber network has been improved
- Various resistances and compliances adjusted to improve left ventricle PV loop

With these improvements, the global response of the model measured by various means, such as with the pressure-volume loops (“PV loops”) of the left ventricle better matches observed behavior, as seen in Figure 1 below

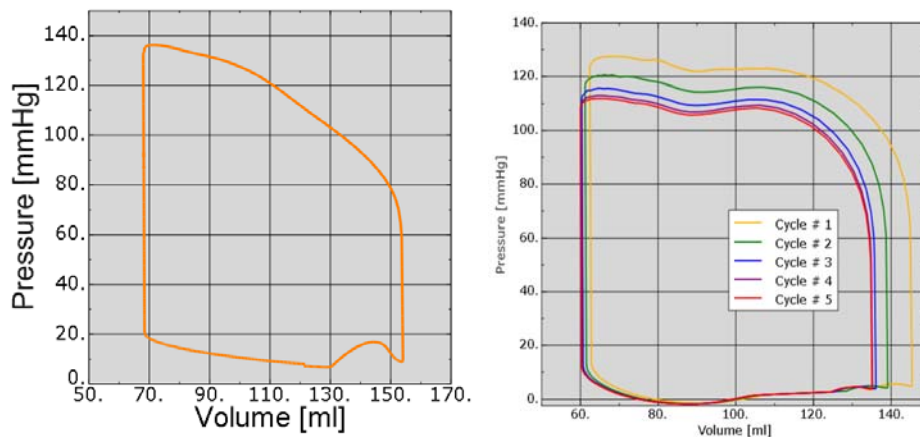


Figure 1. Comparison of the left ventricle PV loops – left showing earlier versions of LHHM and the right showing the latest improved version of the LHHM (LHHM User Guide, 2017, 2018).

Despite these global improvements, there are some local discrepancies in the MV behavior that need a closer look. For instance, there are still some gaps between the leaflets and also some unexpected deformation patterns as highlighted in Figure 2. For the purposes of clarity, we will call this model the LHHM Baseline 0 model.

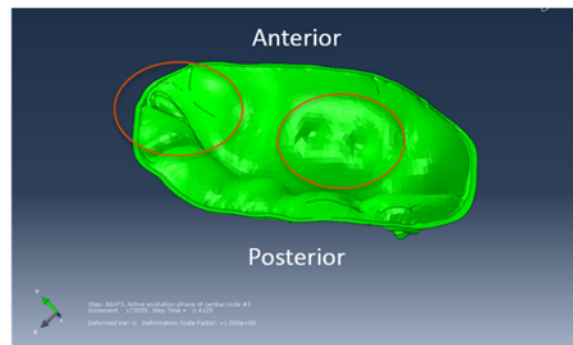


Figure 2. Local discrepancies in MV leaflet behavior in the LHHM Baseline 0.

2.2 Methodology to Improve MV Function

In the present study our focus is to improve the local behavior of the MV while still maintaining the correct global behavior. We do so with a systematic approach summarized in Figure 3:

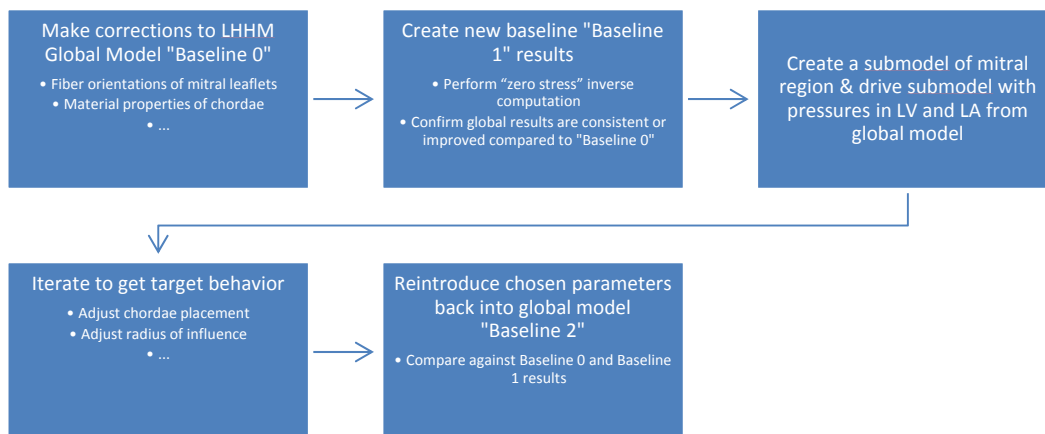


Figure 3. Methodology to adjust MV behavior to match observed characteristics.

Without getting into all the details, getting to Baseline 1 involved the following main changes:

1. Assign correct fiber orientations to the MV leaflets
2. Assign correct material properties to chordae
3. Adjust the lengths of the various chordae tendinae

A comparison of MV in the fully closed position is shown in Figure 4 for Baselines 0 and 1:

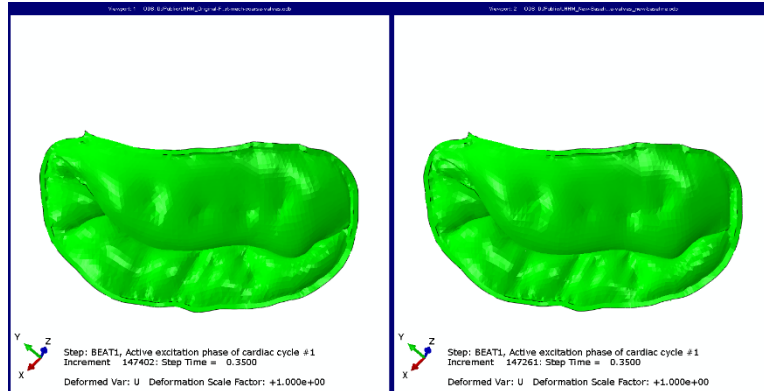


Figure 4. Methodology to adjust MV behavior to match observed characteristics.

Admittedly there is little visible difference between the two cases. However, it is important to start any subsequent adjustments that we will perform based on this more correct Baseline 1 model where all known errors have been corrected. In the next phase, we proceed with the creation and adjustments in a submodel of the MV region.

2.3 Submodeling Methodology

A submodel including MV annulus, leaflets and chordae was created based on the LHHM in Abaqus/Explicit (Figure 5). The global model was analyzed first to obtain driven variables, in this case the displacements at the nodes of MV annulus and attachment points of chordae to papillary muscles, which are then applied as boundary conditions for the submodel. The pressure difference between left ventricle and left atrium from the global model was applied on the ventricular side of the leaflets as loads.

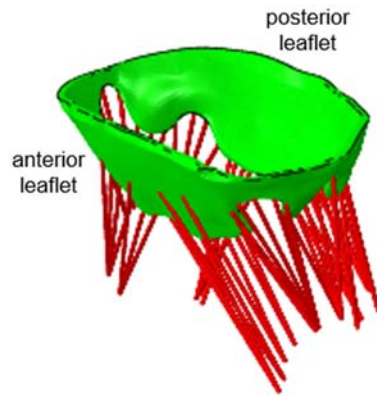


Figure 5. Submodel includes the mitral annulus, MV leaflets, and chordae created from the LHHM.

In the LHHM, the chordae are coupled to the MV via Tie constraints. They were replaced by Distributing Coupling (DCOUP) constraints in the current study to allow for the attachment locations of chordae on the leaflets to be modified. A radius of influence was specified for each DCOUP constraint to avoid unrealistic stress concentrations at the attachment points. Thermal expansion was assigned to chordae as a material property so that the lengths of the various chordae can easily be adjusted according to the difference between the predefined temperature fields and initial temperatures (Abaqus Documentation, 2017). These adjustments result in improved MV behavior as shown in Figures 6 and 7.

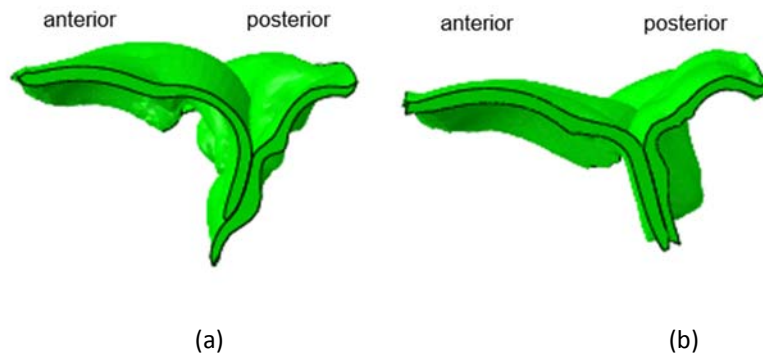


Figure 6. Comparison of MV at full closure (A2-P2 view) between Baseline 1 and the Submodel with adjusted parameters.

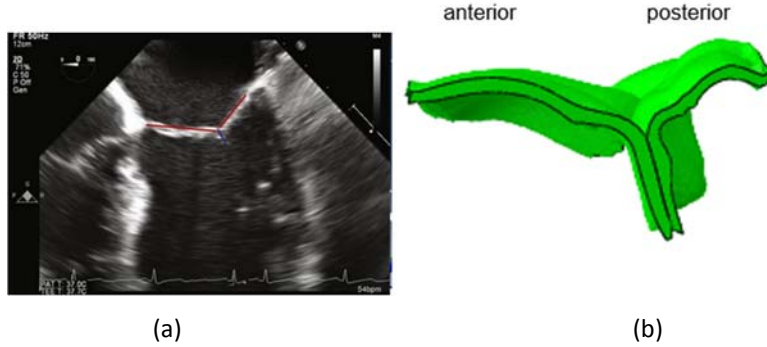


Figure 7. Comparison of MV at full closure (A2-P2 view) between imaging data (a) (Fischer and Trigo, 2015) and the submodel with adjusted parameters (b).

These parameters in the submodel are then reintroduced into the global model to create Baseline 2 that will be used in subsequent studies. (Note: This parameter adjustment process has been automated using Isight, but will not be discussed here due to space constraints).

3. LV Myocardial Infarction Model

Simulation of MI is a challenging task as both passive and active material properties of the infarcted region change immediately after the infarction and over the course of the healing, and in addition there are likely changes to the electrical behavior of the heart as well. The LHHM has the potential to take into account all of these effects, but in this study we simulate FMR caused by MI by modifying only the active material properties in the infarcted region and leave the passive material properties and electrical response unchanged.

Figure 8 shows the extent of the infarcted region of LV and the position of the infarcted region with respect to the MV for a particular MI. Chordae that are attached to the infarcted region are shown in red. The introduced MI results in an asymmetric behavior of the MV as the chordae attached to the A3 and P3 regions of leaflets are not connected to the infarcted region.

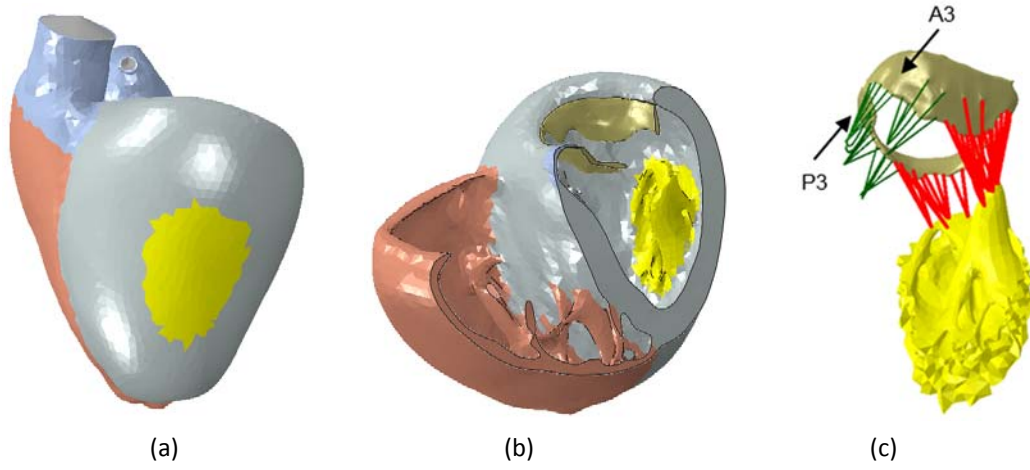


Figure 8. Extent of the infarcted region of the LV (a), transverse view of the infarcted region (b), and position with respect to the MV (c). Chordae attached to the infarcted region are shown in red.

4. Annuloplasty Ring Optimization for Restoring MV Function

4.1 Introduction of Annuloplasty Ring into the LHHM with MI

A previously designed annuloplasty ring with a sub-valvular component (Baillargeon et al., 2015) was inserted into the diseased heart created in Section 3 with the goal to restore the MV function. Since the LHHM geometry in the current study is different from the one used in Baillargeon et al., 2015, initial changes to the geometry of the ring had to be made for appropriate placement on the MV annulus. Figure 9 shows the modified ring that was implanted in the LHHM and is referred to as the original ring in the rest of the current study. The ring was modeled as rigid to simplify the problem. The ring was inserted into the 70% diastolic heart and then was sutured to the mitral annulus using axial connector elements. (Note: The positioning of the sub-valvular arm relative to the chordae can have an effect on the valve functioning. In this study, the goal is to optimize the ring for a pre-selected position of the ring.)

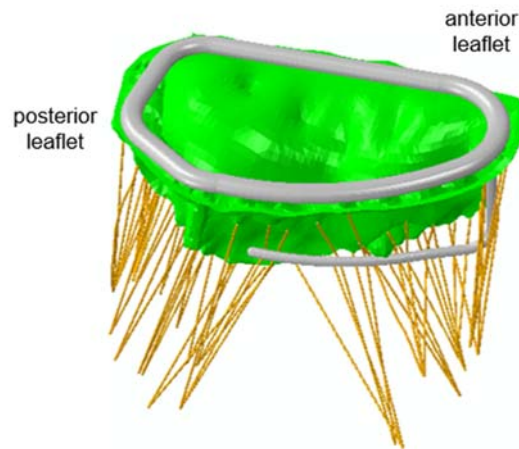


Figure 9. MV and chordae with annuloplasty ring.

Figure 10 compares the MV closure shape in the diseased heart model with MI and in the same model after the device has been inserted (The ring is not shown in Figure 10b to have a clear view of the MV shape.). It can be seen from a quick visual inspection that the installation of the annuloplasty ring with the sub-valvular arm has resulted in improved coaptation.

In order to quantify the leakage, we use the Smoothed Particle Hydrodynamics (SPH) capability and measure the number of particles passing through a threshold plane parallel to the annulus. Note that the particles from the SPH analysis do not affect the behavior of the MV and purely serve as a measure of the leakage (the objective function) through the MV at closure time that needs to be minimized during the optimization process. Figures 11a and 11b show a snapshot of the SPH particles leaking through the MV without and with the annuloplasty ring installed, respectively.

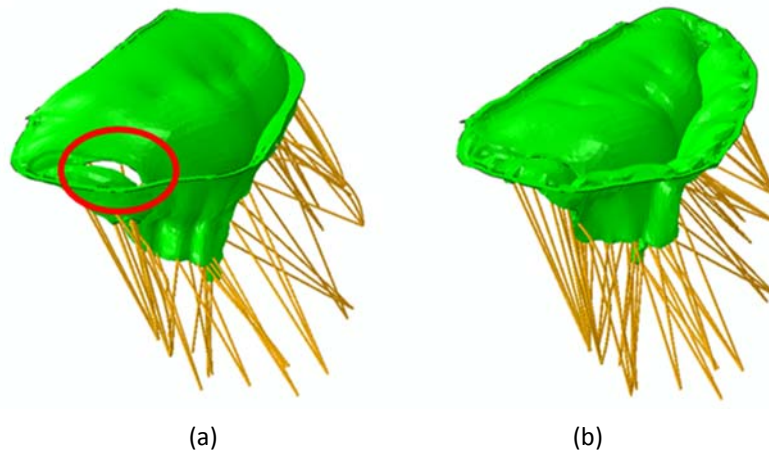


Figure 10. MV closure shape in a diseased heart with MI (a) and in the same model after the ring was installed (b).

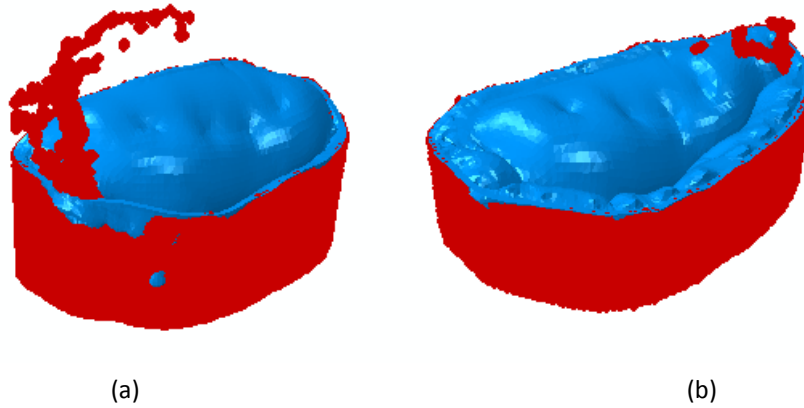


Figure 11. Leakage through MV measured using SPH in a diseased heart with MI (a) and in the same model after the ring was installed (b).

4.2 Annuloplasty Ring Optimization for Restoring MV Function

In this study we focused on geometrical changes that could be made to the sub-valvular component to improve the overall effectiveness of the ring. For this purpose, the sub-valvular component was parametrized using three parameters that are then used as the design variables during the optimization process. These parameters are the height of the arm, the length of the arm, and the radius of curvature as shown in Figure 12.

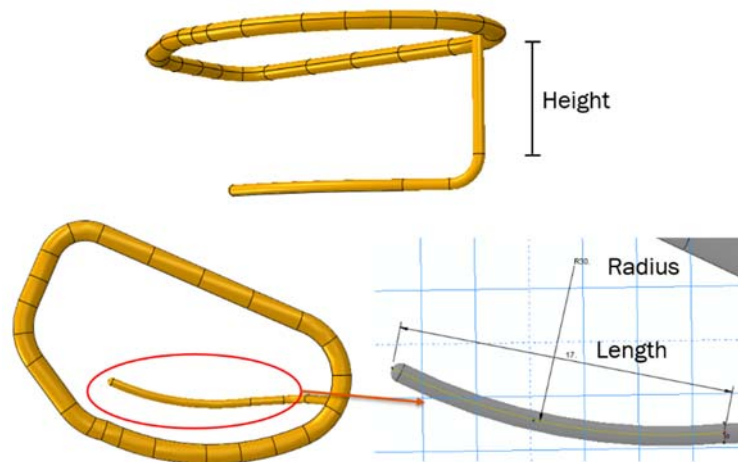


Figure 12. Three design variables of the sub-valvular arm: height, length, and radius.

A Design of experiments (DOE) analysis was firstly performed to understand the effects of the design variables on the MV responses and to estimate an optimal design. The DOE and the subsequent optimization analyses were both carried out using Isight. For the DOE, the Optimal Latin Hypercube technique was chosen to generate 40 designs that were evenly spread throughout the design space. The design variables were allowed to change within the range of $\pm 20\%$ of the original ring design values. As discussed in the previous section, the number of particles passing through a threshold plane parallel to the annulus corresponding to MV closure is used as the objective function that needs to be minimized.

Figure 13 is the main effects plot for the objective function obtained from the DOE. The height and radius have a positive main effect (leakage increases as height and radius increase) while the length has a negative main effect (leakage decreases as length increases). Among the three design variables, the strongest effect is from changing the length, which is likely due to different chordae being engaged with various lengths. This indicates the importance to identify the chordae that need to be included or excluded in the engagement with the ring to minimize MR. Based on the MI model and the ring design in the current study, the engagement of marginal chordae that attach to P3 scallop seems to affect A3-P3 coaptation segment while the basal posterior chordae are engaged to improve A2-P2 coaptation.

The best design with the smallest objective function value from the DOE was then used as the starting point in the optimization model and further optimized with the Downhill Simplex method (Isight Documentation, 2017). Three design variables were constrained to be within $\pm 20\%$ of the corresponding values from the best design of the DOE. The direct method Downhill Simplex was used to find the global minimum in the design space.

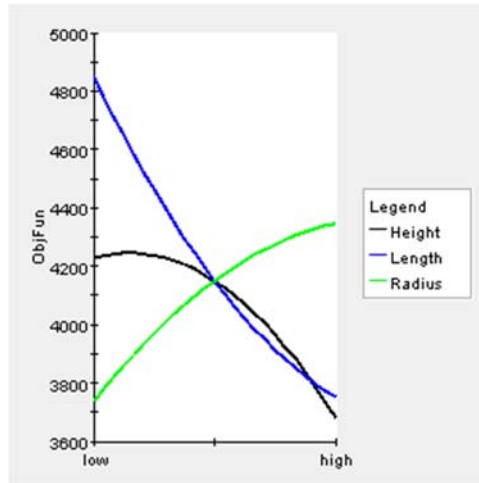
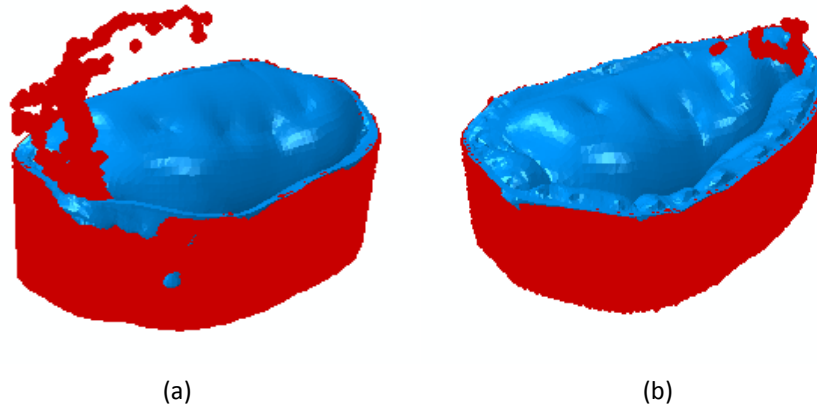
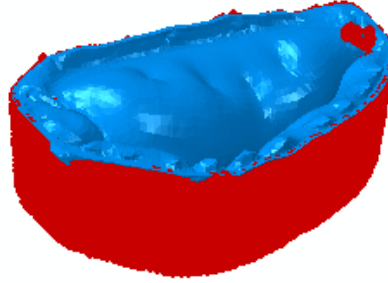


Figure 13. Main effects of design variables on the objective function.

Figure 14 shows the comparison of MR for the diseased MV and the ones corrected by different ring designs when the MV is closed. MR exhibited in the diseased state (Figure 14a) is reduced after the valve was treated with the optimum designed ring (Figure 14c). The design variables and the corresponding objective functions are listed in Table 1.





(c)

Figure 14. Comparison of MV leakage in a diseased heart (a), the same heart model with the original ring implant (b), and the optimum design (c).

Table 1. Three design variables and the corresponding objective functions of the original design, the best design in DOE, and the optimum design.

Design	Height (mm)	Length (mm)	Radius (mm)	Objective Function
Original	11	17	30	4333
DOE	12.4102	20.0515	25.539	3086
Optimum	13.7376	23.9328	23.8213	2280

5. Conclusions

This study demonstrates that the LHHM along with Abaqus/Explicit and Isight provide a powerful platform to:

1. Systematically understand the effect of various parameters on the behavior of the MV and make necessary adjustments to match observed or desired behaviors.
2. Introduce disease states such as FMR caused by MI in the left ventricle, and potentially adjust parameters once again to match desired behavioral characteristics.
3. Automate and speed up model changes and leverage optimization methods to adjust the LHHM to match targeted behaviors.

4. Introduce devices into the heart to potentially address the effects of the MI, namely FMR, and then optimize the device design to improve the resolution of the FMR.

This automated methodology provides a firm foundation upon which to simulate patient-specific MV cases in future work and potentially expand the scope to include other parts of the heart like the tricuspid valve.

6. References

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