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Assessment of atrioventricular valve regurgitation using biomechanical cardiac modeling

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Abstract. In this work we introduce the modeling of atrioventricular valve regurgitation in a spatially reduced order biomechanical heart model. The model can be fast calibrated using non-invasive data of cardiac magnetic resonance imaging and provides an objective measure of contractile properties of the myocardium in the volume overloaded ventricle, for which the real systolic function may be masked by the significant level of the atrioventricular valve regurgitation. After demonstrating such diagnostic capabilities, we show the potential of modeling to address some clinical questions concerning possible therapeutic interventions for specific patients. The fast running of the model allows targeting specific questions of referring clinicians in a clinically acceptable time.

Keywords: cardiac modeling; reduced-order model; atrioventricular regurgitation; model-based diagnosis assistance; therapy planning

1 Introduction

Mitral or tricuspid regurgitation (MR, TR) also named mitral (tricuspid) valve insufficiency or incompetent mitral (tricuspid) valve, is a condition in which the atrioventricular (AV) valve allows backward flow (regurgitation) during systole due to anatomical or functional defects. The AV valve regurgitation (AV-R) is typically quantified by imaging techniques – echocardiography or magnetic resonance imaging (MRI) – with classification into mild (regurgitation fraction RF being below 30 %, and regurgitation volume RVol $<$ 30 ml), moderate (RF 30–40 % and RVol 30–45 ml), moderate-to-severe (RF 40–50 %, RVol 45–60 ml) and severe (RF above 50 % or RVol above 60 ml). The ventricular volume overload due to a moderate or severe AV valve insufficiency makes the assessment of the true systolic function of ventricle rather difficult. The indicators practically

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considered are the ventricular ejection fraction (EF), ventricular end-diastolic volume (EDV) indexed to body surface area (iEDV) representing the level of ventricular dilatation, the percentage of RF, the regurgitation volume RVol and the morphology of the leaking valve. Putting all these available data into a clear clinical picture is not obvious and is one of the potentials of biomechanical modeling.

Capturing the anatomy of valve leaflets coupled with a realistic 3D heart model is mathematically extremely challenging and computationally intensive [1], with a limited potential to be used at bedside. The role of such detailed models would rather be in testing new valve implants, and the intensive computations would be run in the prosthetic valve development. Our goal in this paper is to present a relatively easy approach of incorporating the AV-R into a biomechanical heart model with the capability to provide a fast quantification of the actual contractile property of the ventricle, which would allow to objectively assess the level of overload the patient's heart is facing. The abnormal contractility might play a very significant role in the mismatch between the clinical assessment of a valve insufficiency and the actual outcome of a therapeutic intervention on the valve [7] – a phenomenon not fully understood to date. We aim at providing the clinical information in a relatively short time period, typically within hours – the time scale compatible with data analysis and reporting for an MRI exam of heart disease patients – so that the added indicators could be directly taken into consideration in clinical conclusions. Secondly, once the model is set up using patient-specific data, it can be used to predict the effect of possible valve repair or other therapeutic interventions – an information of invaluable importance prior to deciding about the type of therapy.

The valve insufficiency has already been introduced in the cardiac modeling community as for instance for the pulmonary valve. In [6] a 3D mechanical heart model was constrained by external forces from processed image data to allow regurgitation flows. The model was used to estimate the constitutive properties of myocardium and a possible outcome of a complete valve repair was predicted. In our case, the global mechanical model – including the component of AV-valve insufficiency – that we are proposing allows to obtain more comprehensive predictions. Examples thereof include the investigation of the effect of a partial improvement by invasive or non-invasive techniques – as is often the case in correcting the AV valve insufficiency – or modifications of the physiological properties of the cardiovascular system by a number of interventions, pharmacological or others. We will exemplify this variety of predictions with two clinical cases and several associated treatment scenarios.

2 Methods

2.1 Clinical data

Two AV-R patients and one healthy control were analyzed in this pilot study. The data used were the non-invasively acquired magnetic resonance imaging

data (MRI), together with peripheral pressure cuff measurement. MRI data contained cine images in short axis (the stack covering whole ventricles and part of the atria) and stacks of long axis orientations (typically 5–9 slices for 2-, 3- and 4-chamber views) in order to well visualize the AV-valve defect in several orientations throughout the cycle, and phase contrast images of flow though aortic and pulmonary valves (the outflows of the ventricles).

The first patient has a moderate-to-severe MR with RF of 36 % and RVol 45 ml, see Table 1. MR was caused by an anatomical defect in the posterior valve leaflet leading to MR throughout the systole, which can be appreciated in the top line of Fig. 1. The second patient is a TR patient with dilated RV – which is connected to the systemic circulation and has outflow to the aorta (the so-called systemic RV) – and in addition has a complete atrioventricular block (i.e. the atria and ventricles beat independently with a very low ventricular rate of ∼40 bpm). The defect in the tricuspid valve is central and disappears when the RV volume falls below 200 ml (due to a decrease in size of the tricuspid valve ring), as assessed from the detailed short and long axis cine MRI stacks (see bottom line in Fig. 1).

Patient #	Age ($years$)	EDV (ml)	iEDV (ml/m^2)	EF (%)	RF (%)	RVol (ml)	type of defect
Healthy control	30	130	70	55	0	0	N/A
1	17	246	119	59	36	45	MR
2	17	308	169	55	26	43	TR

Table 1. Patients' information obtained during cardiac MRI exam.

While for the first patient mitral valve surgery might be indicated, the clinicians' main question about the second patient is whether or not to implant a pacemaker / CRT to correct the AV-block, as increasing the heart rate might lead to a reduction of TR. In the sequel we will address these clinical questions with the help of a biomechanical heart model.

2.2 Biomechanical heart model

The biomechanical model of heart function used in this work was detailed in [2]. It is a reduced-order (0D) model, in which the ventricle of concern is represented by a sphere with the inner radius R and wall thickness d adjusted according to the patient's image data. The model contains anisotropic mechanics with Holzapfel-Ogden-type hyperelastic potential in the passive component and chemically controlled model of actin-myosin interaction for the active part. The constitutive behavior is taken as transverse isotropic with respect to the fiber direction, and the fibers are assumed to be isotropically distributed in the orthoradial plane through the wall thickness. Consequently, the resulting overall behavior is different in the radial vs. orthoradial directions, as detailed in [2].

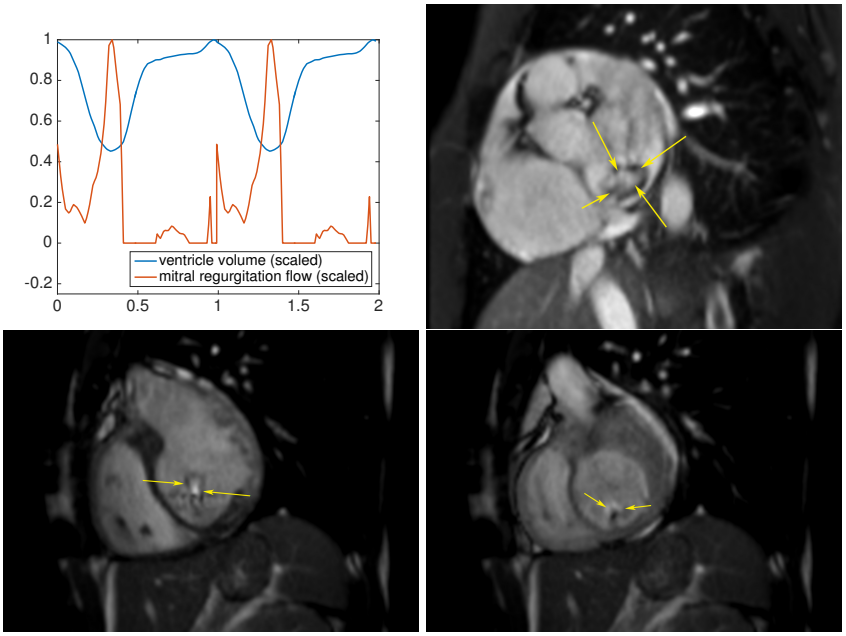

Fig. 1. Top: Mitral valve defect in Patient 1 with holosystolic regurgitant flow through the defect (the opening at end-systole is marked by arrows). Bottom: Tricuspid valve defect in Patient 2 present during early systole (left) and closing up during late systole (right).

The circulation system is represented by a 2-stage Windkessel model (see Fig. 2). The phases of the cardiac cycle and opening / closure of valves are handled via a diode system as is described in [9]. In particular the AV-R is incorporated via a two-direction diode which is controlled by the phase of cardiac cycle. Under physiological conditions, the value of the AV valve conductance is set to a high value K_{open} when the valve is open with the resulting atrium-to-ventricle flow being given by $K_{open} \cdot (P_{at} - P_v)$, with P_{at} and P_v standing for the atrial and ventricle pressures. During the closure of the valve the conductance is set to a very low value K_{close} as a penalty for the negligible flow $K_{close} \cdot (P_v - P_{at})$. By increasing the coefficient K_{close} the AV-R can be introduced and tuned to the observed level of RF.

The complete heart-circulation model – i.e. the 0D cavity with the connected Windkessel model – is calibrated sequentially. The order for calibrating each component is given by the available data so that the calibrated part of a given module is carried further into a more complete model. First, the geometry is adjusted according to the data (reference volume and wall thickness of the ventricle [5]). Taking the advantage of having the measured flows leaving the ventricles at hand, the parameters of Windkessel model (representing the circulation, we

recall Fig. 2) are tuned by directly imposing the measured flow at the inlet and using the peak and minimal arterial pressure taken by cuff measurement. The passive parameters are adjusted according to the clinically predicted atrial pressure. Finally, the active contractility is calibrated in order to obtain the peak aortic flow velocity as in the data. The main mechanical parameters of the model are summarized in Table 2.

Concerning the calibration of the AV valve insufficiency, we kept the coefficient K_{close} constant for Patient 1, while for Patient 2 we made K_{close} linearly dependent on the volume of ventricle V_v with no regurgitation for the ventricular volume below the limit observed in the image data ($V_v^{competent} = 200$ ml). In detail,

$$K_{close} = \begin{cases} \alpha K_{close}^{incompetent\ valve} + (1-\alpha) K_{close}^{competent} & \text{when } \ V_v > V_v^{competent} \\ K_{close}^{competent} & \text{when } \ V_v \leq V_v^{competent}, \end{cases}$$

with linear interpolation factor $\alpha = \frac{V_v - V_v^{competent}}{V_v^{EDV} - V_v^{competent}}$.

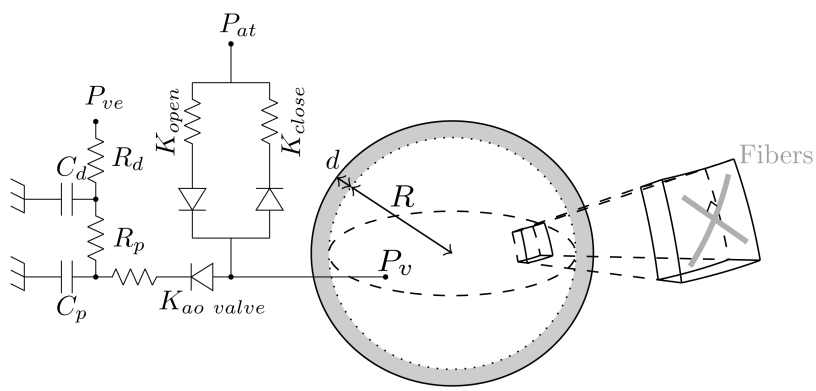

Fig. 2. Schematics of the model including the dual-direction diode for the AV-valve.

Patient #	Relat. passive stiffness	Contractility (kPa)	Periph. resistance ($Pa\ s/m^3$)	Periph. capacitance (m^3/Pa)
Healthy control	1.0	60	$1.55 \cdot 10^8$	$1.1 \cdot 10^{-8}$
1	1.13	92	$1.1 \cdot 10^8$	$1.5 \cdot 10^{-8}$
2	1.0	125	10^8	$2.2 \cdot 10^{-8}$

Table 2. Main parameters of the model.

3 Results

Fig. 3 shows the level of accuracy obtained by our model representing the data in the measured key indicators. Table 1 summarizes data for the subjects in the study as obtained by a routine clinical analysis of the MR exam. Note that the ventricular size of Patient 1 is moderately increased (normal iEDV being below 100 ml/m^2) and the ventricle of Patient 2 is severely dilated. According to the standard clinical assessment of systolic function, both patients fall into normal range (EF $\geq$ 55 %). When comparing the level of ventricular contractility as estimated by the model (see Table 2), both patients have the contractility above the normal population (60–70 kPa, as exemplified by our healthy control case). The level of contractility in Patient 1 is mildly increased, and the contractility value of Patient 2 is already at moderately elevated inotropic level, even though the patient is at rest.

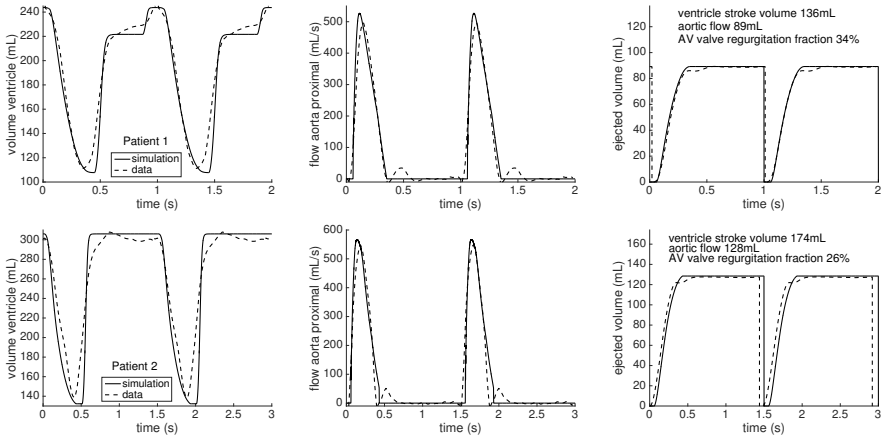

Fig. 3. Indicators of the calibrated models compared with the available data for Patient 1 (top row) and Patient 2 (bottom row).

To better appreciate the patients' heart function, we plot in Fig. 4 the cardiac output as a function of the preload. We can see that in both cases the current working point is on a rather flat part of these "Starling curves", relatively independent of the current preload. Both patients have no signs of damaged myocardium (in particular, no post-infarction scarring was present in gadolinium late-enhancement MRI), and we would therefore expect the level of contractility to be able to increase to a level of 180 kPa – in our experience the level obtained by using a moderate dose of inotropic drug in stress studies performed in clinically indicated cases [11]. The red cardiac output curve in Fig. 4 shows a prediction of such an inotropic effect. While the cardiac output of Patient 1

could significantly increase, the predicted cardiac output increase for Patient 2 is rather limited. This plot suggests that Patient 2 is more urgent to treat, as the contractile reserve of the patient's heart (which would be available to compensate for instance an acute destabilization of the patient's state) is limited, even though the level of RF is significantly less than for Patient 1.

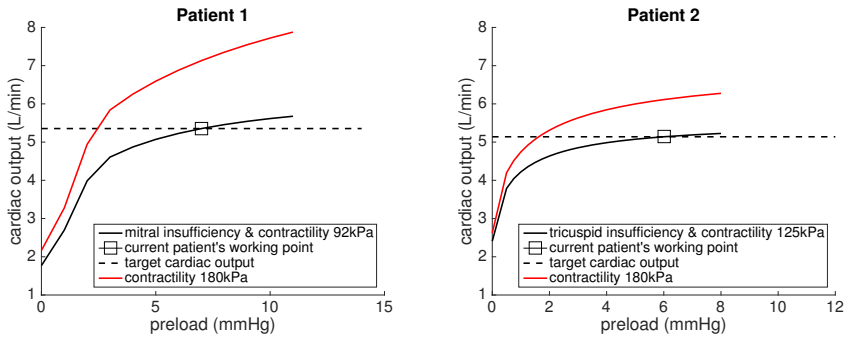

Fig. 4. Heart function presented as patient-specific cardiac output-vs-preload curves at the current physiological state (black solid line), and as predicted if the contractility was increased to a high level of 180kPa (red line).

Finally, Figs. 5 and 6 demonstrate the effect of therapies in question for the two patients. By correcting the mitral valve in Patient 1, while the inotropic level is kept at the same level, the model predicts that the heart will be working on smaller volumes (see blue curves in Fig. 5). This could be beneficial for the level of tissue stress and may induce a reverse remodeling of the dilated heart and bring the heart volumes from moderate dilatation to normal size. Alternatively, to reach the cardiac output as at baseline (5.3 l/min), the myocardial contractility could decrease by 15 % – which would have positive effects on the heart energy requests.

For Patient 2, the model predicts a significant reduction of the regurgitation fraction when increasing the heart rate from 40 bpm to the normal value of 60 bpm after implanting a pacemaker, thanks to a reduction of the ventricular volume (see blue curves in Fig. 6). Even by reducing the the contractility by 10 % represented by red curves – which would definitely be of benefit for the patient, recall Fig. 4 – RF would still be around 14 % (considered as only a trivial-to-mild level of TR).

4 Discussion and future work

A detailed visualization of the AV valve by a high number of cine slices in superior temporal resolution was key to adjust the AV-valve conductance in the

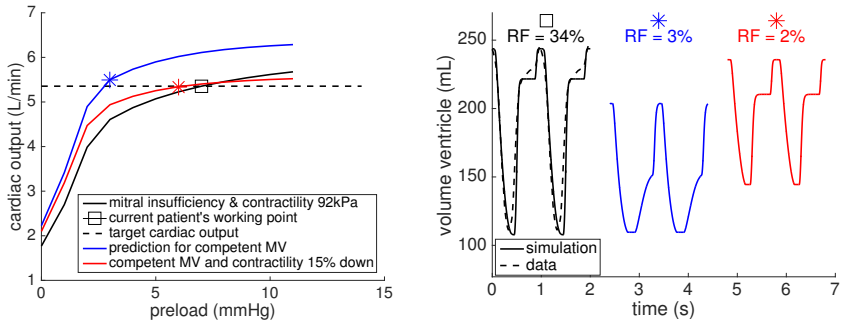

Fig. 5. Predicted effect of mitral valve repair in Patient 1: Patient's heart could work on the same level of contractility but on a lower preload (blue plot), or on a lower contractility level (red), assuming the repair would practically completely resolve the MR.

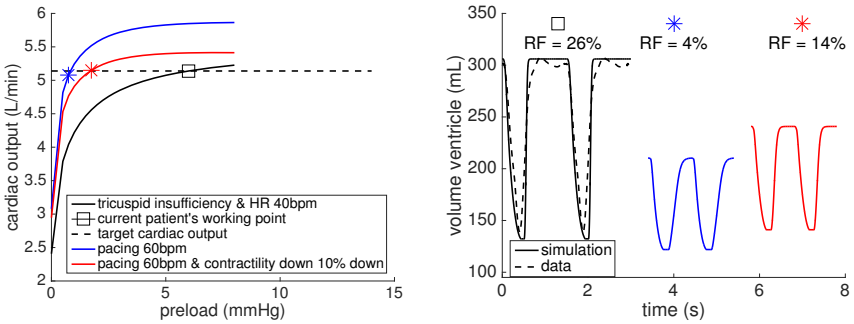

Fig. 6. Predicted effect of pacing on the tricuspid valve regurgitation fraction in Patient 2.

central-TR defect, which was closing up for the smaller ventricular volumes. Although acquiring the additional ∼20 slices in long axis orientations represents extra 10–20 minutes of scanning, this extra time is worthy for a better visual analysis and also for an increased level of model personalization in this patient.

Measurements of the AV flow by MRI are not routinely performed because of a limited reproducibility and accuracy. Our experience from the presented pilot study, however, shows that even a solely qualitative profile of the regurgitation jet (as shown for Patient 1 in Fig. 1, obtained actually from the flow image targeted on the through-aortic valve flow) would facilitate the process of setting up the model correctly, and will be included for future patients. Our study was completely non-invasive with data acquired during a routine congenital heart disease MRI exam. The obtained pressure was just a brachial cuff measurement and we tuned our model (i.e. the Winkessel resistances and capacitances R_p, R_d,

C_p and C_d, see Fig. 2) to the corresponding two measured pressure points (minimum diastolic and maximum systolic) as if these points were present directly in the proximal aorta. We are aware of the difference between the central and peripheral pressure measurements, but the error in the range of 5–10 mmHg is acceptable for our purpose (as a comparison, in the cohort of patients followed, 10–20 % error in RF does not necessarily mean any difference in a standardized therapy). We do however plan to perform a sensitivity analysis with respect to the measured peripheral pressure for a group of patients with available central aortic pressure. The uncertainty of all parameters could be studied independently for each component of the model (Winkessel, passive and active properties), and remains to be done in future.

Our model suggests that correcting the MR in Patient 1 would be beneficial, and also directly gives some complementary therapeutic guides, e.g. the effect of decreasing contractility, or volume of circulating fluid which is adjusted by intrinsic physiological mechanisms of "pressure driven diuresis / natriuresis" [4] possibly supported by antidiuretic drugs. In this work, we have not dealt with the important effect of coupling the cardiac function with venous return as in [3, 8], even though this would allow predicting using the antidiuretics, and we plan to extend our study also in this respect.

Our predictions for Patient 2 suggest a beneficial effect of pacing. We have to point out, however, that our model only captures the immediate effects and does not include possible negative effects caused by artificially fast rate. The validity of prediction of immediate effect of pacing, namely the changes of end-diastolic and stroke volume indicators, is a subject in our current clinical study in which the patients with MR conditional CRT devices are included. Instead of MRI, the echocardiography data processed into 0D signals of ventricular volumes and aortic flows could be used with the advantage of a possible validation on a much larger cohort by avoiding the contraindication of MRI in the majority of CRT patients.

Patient 2 has a congenital disease called congenitally-corrected transposition of great arteries (ccTGA), which is a very rare pathology. However, we believe that it is a group of patients who might extremely benefit from modeling. First, reduced order models – as the one used in the present work – can allow a quick assessment of the contractile properties of the remodeled systemic right ventricle – typically associated with some degree of TR – and predict the effect of possible pacing, as the AV block is commonly present in ccTGA. Secondly, the inter- and intra-ventricular delays (also common in ccTGA) may be directly treated by using a biventricular pacing (CRT) with a possibility of employing more detailed 3D models, which are able to capture the propagation of electrical activation throughout the myocardial tissue, with the aim to optimize the CRT [10]. Modeling can change the management of these patients since their early ages.

All the simulations performed in the present work rely on the assumptions of reduced order (0D) mechanical modeling [2] and therefore possess some limitations compared to 3D modeling. The 0D approach cannot rigorously capture the

inhomogenities of material parameters, such as alterations of passive myocardial stiffness and active contractility in the infarcted heart. The effective spatial averaging of these parameters may lead to errors, e.g. false negativity if trying to discover an increased level of contractility at rest. Similarly, the propagation of electrical activation – often pathological in the AV-R patients with dilated ventricles – can be taken into account only by imposing the duration of propagation of depolarization wave according to the measured QRS duration in patients' ECGs. Local branch / partial blocks therefore cannot be directly included. We expect that out of these two limitations, the former one has a larger impact, and a fully 3D approach should therefore be considered in the infarcted hearts.

The fast run of 0D simulations, however, allows investigations of a number of virtual scenarios in a very short time. Indeed, one of the objectives in carrying out this work was to allow medical doctors to directly perform such simulations and hypothetical scenarios by themselves, in parallel with reporting on patients' MRI scans. Our experience from the presented work and other projects [8] suggests that the complexity of the model is such that this aim is realistic, indeed.

5 Conclusion

This paper shows a promising pathway in employing simplified models addressing the clinical questions for a given patient to extend the capabilities of imaging techniques. Although the pathology in question is related to the valves, the consequences on the myocardium itself are what really matters. Including modeling in clinical decision making has the potential to push further the understanding of the state of patients' hearts and predicting the effect of therapeutical interventions.

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References

1. M. Astorino, J.-F. Gerbeau, O. Pantz, and O. Traoré. Fluid-structure interaction and multi-body contact: Application to aortic valves. *Comput. Methods Appl. Mech. Engrg.*, 198:3603–3612, 2009.

2. M. Caruel, R. Chabiniok, P. Moireau, Y. Lecarpentier, and D. Chapelle. Dimensional reductions of a cardiac model for effective validation and calibration. *Biomech Model Mechanobiol*, 13(4):897–914, 2014.
3. D. Chapelle, A. Felder, R. Chabiniok, A. Guellich, J.-F. Deux, and T. Damy. Patient-specific biomechanical modeling of cardiac amyloidosis – a case study. In *Proc. of FIMH 2015*, pages 295–303. Springer, 2015.
4. A.C. Guyton and J.E. Hall. *Textbook of medical physiology, 10th edition*. Saunders, 2010.
5. S. Klotz, I. Hay, M.L. Dickstein, G.-H. Yi, J. Wang, M.S. Maurer, D.A. Kass, and D. Burkhoff. Single-beat estimation of end-diastolic pressure-volume relationship: a novel method with potential for noninvasive application. *Am J Physiol Heart Circ Physiol*, 291:H403–H412, 2006.
6. T. Mansi, B. André, M. Lynch, M. Sermesant, H. Delingette, Y. Boudjemline, and N. Ayache. Virtual pulmonary valve replacement interventions with a personalised cardiac electromechanical model. In Nadia Magnenat-Thalmann, Jian J. Zhang, and David D. Feng, editors, *Recent Advances in the 3D Physiological Human*, pages 201–210. Springer, November 2009.
7. J. Ross Jr. Afterload mismatch in aortic and mitral valve disease: Implications for surgical therapy. *JACC*, 5(4):811–826, 1985.
8. B. Ruijsink, P. Moireau, K. Pushparajah, J. Wong, T. Hussain, R. Razavi, D. Chapelle, and R. Chabiniok. Biomechanical modeling of the dobutamine stress response in exercise induced failure of the Fontan circulation. *Interface focus*, 2017. Submitted.
9. J. Sainte-Marie, D. Chapelle, R. Cimrman, and M. Sorine. Modeling and estimation of the cardiac electromechanical activity. *Comput Struct*, 84:1743–1759, 2006.
10. M. Sermesant, R. Chabiniok, P. Chinchapatnam, T. Mansi, F. Billet, P. Moireau, J.M. Peyrat, K. Wong, J. Relan, K. Rhode, M. Ginks, P. Lambiase, H. Delingette, M. Sorine, C.A. Rinaldi, D. Chapelle, R. Razavi, and N. Ayache. Patient-specific electromechanical models of the heart for the prediction of pacing acute effects in CRT: A preliminary clinical validation. *Med Image Anal*, 16(1):201–215, 2012.
11. J. Wong, K. Pushparajah, A. de Vecchi, B. Ruijsink, G.F. Greil, T. Hussain, and R. Razavi. Pressure-volume loop-derived cardiac indices during dobutamine stress: a step towards understanding limitations in cardiac output in children with hypoplastic left heart syndrome. *Int J Cardiol*, 2016. In press.