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Patient-specific simulation of cardiac blood flow from high-resolution CT

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ABSTRACT

Cardiac hemodynamics can be computed from medical imaging data, and results could potentially aid in cardiac diagnosis and treatment optimization. However, simulations are often based on simplified geometries, ignoring features such as papillary muscles and trabeculae due to their complex shape, limitations in image acquisitions, and challenges in computational modeling. This severely hampers the use of computational fluid dynamics in clinical practice. The overall aim of this study was to develop a novel numerical framework that incorporated these geometrical features. The model included the left atrium, ventricle, ascending aorta and heart valves. The framework used image registration to obtain patient-specific wall motion, automatic remeshing to handle topological changes due to the complex trabeculae motion, and a fast interpolation routine to obtain intermediate meshes during the simulations. Velocity fields and residence time were evaluated, and they indicated that papillary muscles and trabeculae strongly interacted with the blood, which could not be observed in a simplified model. The framework resulted in a model with outstanding geometrical detail, demonstrating the feasibility as well as the importance of a framework that is capable of simulating blood flow in physiologically realistic hearts.

1 Introduction

Cardiac blood flow is normally very complex, with intricate flow patterns on both small and large scales. In the left ventricle (LV) the flow is driven by the myocardial motion and strongly interacts with valves, papillary muscles and also the protruding surfaces, trabeculae, which constitute parts of the

innermost surface in the LV. The trabeculae can be seen as both a small and a large-scale wall roughness, with complex patterns predominantly located at the free wall to the ventricular septum [1]. As the blood flow velocity close to the wall can be low, the interstitial spaces on the wall formed by the trabeculae could promote flow stagnation and increase thrombogenic risk [2].

Using phase-contrast magnetic resonance imaging (PC-MRI) it is possible to measure and quantify the cardiac blood flow in 3D and time [3–6], but while large scale features can be measured accurately, there are limitations in measuring flow close to walls and small-scale features. In addition, beat-to-beat variations cannot be obtained. An alternative to PC-MRI is echocardiography which has temporal resolution, but flow acquisition is normally limited to only one flow component in the ultrasonic beam direction. Both echocardiography and MRI are able to measure cardiac geometry and function, but limitations in resolution do not permit the extraction or quantification of trabeculae or other fine-scale geometrical details.

On the other hand, computed tomography (CT) is able to provide information about the heart and coronary arteries with geometrical details on sub-millimeter levels [7]. The drawback with CT is that it uses ionizing radiation, but recent developments in dose reduction strategies lowered the ionizing dose significantly while maintaining image quality. [8] While CT is unable to measure flow, the high-resolution geometry can be used in a numerical model to compute the flow. By using computational fluid dynamics (CFD) it is possible to compute cardiac blood flow with an arbitrary resolution that is dependent only on the available computer resources. The possibilities of cardiac CFD simulations have been shown before, but the geometries used have often been simplified and the endocardial surface has often been significantly smoothed. [9, 10] The atrium is often simplified by replacing it with a generic geometry or even removed completely [11–14], but atrial flow could have an effect on the flow patterns in the ventricle, especially during diastole.

In addition to geometrical simplifications of the LV and atrium, information about trabeculae and the motion - or even inclusion - of papillary muscles has often been neglected. These simplifications are often a result of limited spatial and temporal resolution of the available image modality, but they introduce uncertainties to the computed results. Also, from a modeling perspective it is very challenging to incorporate the highly complex geometrical structures and their motion into a computational model. Extracting of wall motion of these complicated geometries from image data is not straightforward, and changes in topology and large wall displacements make it demanding to construct computational meshes

that represent the endocardial motion.

Careful modeling is needed in order to compute the complex flow patterns and to obtain an accurate result. The importance of including trabeculae and papillary muscles was first demonstrated by Kulp *et al.* [15] who developed a framework to simulate and visualize some of the interactions between the blood flow and the trabeculae. Recently Vedula *et al.* [2] performed a study where they compared the flow field in a smoothed model and one model with trabeculations. In their study only the large-scale trabeculations were resolved in order to save computational power, and the applied wall motion was artificially added based on a simplified model. As such, some of the trabeculations were included but their motion was generic, which makes it difficult to draw conclusion on a patient-specific level.

The overall goal of this study was to develop a novel and efficient framework for modeling hemodynamics of physiologically realistic hearts with patient-specific wall motion, valves, trabeculae, and papillary muscles. A combination of high-resolution 4D CT data, image-registration and a novel way to handle changes in geometry over the cardiac cycle, made it possible to compute the flow in a detailed model of the heart. To investigate the importance of including a geometrically realistic heart in the model, a comparison with a smoothed geometry resembling models often found in literature was performed.

2 Materials and Methods

By using image registration on the 4D CT data, the cardiac motion over the entire cardiac cycle could be extracted and incorporated into the model. Before the flow solver was started, a dry-run was performed where only mesh deformation was computed, based on the extracted wall motion. Due to changes in geometry topology during the cardiac cycle, automatic remeshing was performed. In this way volumetric meshes were obtained for a number of time steps. Then the flow solver was started and using a fast cubic interpolation routine, intermediate meshes were obtained at every time step in the simulation. In this way, the complex geometrical structures and their motion could be incorporated in the model, in a fast and efficient manner. Details on each step are described in the following sections.

2.1 Image Acquisition

Image acquisition was performed using a third generation dual source CT (Siemens SOMATOM Force, Siemens Medical Solutions, Forchheim, Germany). Automated exposure control and automatic

tube potential selection was used (CARE dose 4D and CARE kV, Siemens). Acquisition parameters were as follows: detector collimation, 192x0.6 mm; gantry rotation time, 0.25 s; pitch 0.2; quality reference mAs, 276; reference kV, 100. The temporal resolution of the image acquisition was 66 ms. Retrospective image acquisition with ECG-triggered dose modulation was used. This meant that a full radiation dose was used only during heart phases that would be optimal for single phase image reconstruction. During other phases the radiation dose was lowered to 20%, which increased the noise level.

Coronary CT angiography was performed on a 76 year old male who had ST elevation during a stress test. The left ventricle was dilated and calcifications were found in the coronary arteries, but no significant stenoses were present. Proper informed consent to participate in the study was obtained from the patient.

A test bolus of 10 ml iodine contrast (iopromide, Ultravist 370 mgI ml⁻¹, Schering, Berlin, Germany), followed by 50 ml saline solution was injected to calculate the time needed for the contrast to reach the coronary arteries. Another four seconds were added to the scan start delay in order to make sure that the whole coronary artery tree would be filled with contrast once the scan started. A contrast dose of 335 mgI kg⁻¹ (maximum weight 77 kg) was used and the injection time was 11.5 s. The effective tube potential chosen by the CT system for the CCTA was 80 kV. This meant that a dual flow injection of 75 % contrast and 25 % saline solution could be used while still maintaining good opacification of the coronary arteries. A 70 ml saline chaser followed the dual flow injection.

The image reconstruction used in this case was a multiphase reconstruction including images of the whole heart at every 5 % between two R-R intervals from 0-95 % (20 phases). This could then be used to create a 4D reconstruction with a temporal resolution of 20 time frames per cardiac cycle. The reconstructed slice thickness was 0.5 mm with a 0.25 mm increment. A medium soft-tissue convolution reconstruction algorithm (Bv36) was applied as well as Advanced Modeled Iterative Reconstruction (ADMIRE, Siemens) at noise reduction level 4. In-plane image resolution was 512x512 pixels and the reconstructed resolution was 0.35x0.35x0.25 mm³. Dimensions of the papillary muscles were approximately 40x20x20 mm and interstitial spaces and trabeculae were typically on the order of 1-7 mm.

2.2 Image processing

From the 4D CT data, a map of the patient-specific wall motion was obtained, in order to prescribe the motion of the geometry in the flow model. For this purpose the heart geometry in the first time frame, representing the onset of systole, was segmented using Segment. [16] The segmentation included the pulmonary veins, atrium, mitral valve, left ventricle, aortic valve, aortic sinuses, left and right coronary artery and parts of the ascending aorta, as seen in Fig. 1. The coronary arteries were truncated after 10 mm, as coronary flow was not of interest in this study and its effect on LV flow was considered minimal.

[Fig. 1 about here.]

The displacement field between two arbitrary time frames was computed using a non-parametric diffeomorphic image registration algorithm [17, 18]. In order to speed up the registration process, 3 multi-resolution image pyramid levels with different number of iterations on each level were used, similar to a multi-grid approach. From the image registration the displacement field D that aligned two 3D image stacks was obtained. Using the displacement field and the perimeter of the segmentation in the first time step as a binary mask, the displacement vectors at the wall that mapped to the wall in the following time frame could be calculated. The process of computing displacement field and then extracting displacement vectors was repeated for the subsequent time steps n and $n + 1$ until the end of diastole, as schematically described in Fig. 2.

[Fig. 2 about here.]

By doing so it was sufficient to manually segment only one of the time frames, and then allowing the registration process to find the wall in all the following time frames. Thus, besides obtaining a time-resolved displacement field of the geometry, the time-consuming process of segmenting all time frames individually could also be avoided, which significantly sped up this pre-processing step. Approximately 500 000 vertices were located on the model wall (including the atrium and part of the aorta) and a one-to-one vertex correspondence between the time frames described the wall motion over the whole cardiac cycle. Segmentations obtained propagating the first frame segmentation were compared to manually thresholded geometries by an experienced user. Some time frames had a higher noise level as dose modulation was used, but no discernible effects could be seen in the image processing.

2.3 Geometry processing

A volumetric mesh model was created based on the segmented wall. Besides a baseline model where the trabeculae and papillary muscles were included, a smoothed model was also created where the ventricular surface was smoothed and the papillary muscles were removed, see Fig. 1. The smoothed model represented the convex hull of the baseline model and was very similar to geometries used in other studies [11–14], and was included in order to compare the flow fields when using the more physiologically correct model. By removing the papillary muscles and trabeculae the volume of smoothed model became slightly larger, but the applied wall motion was the same in both models. At the locations where the wall motion became undefined in the smoothed model the displacement vectors were interpolated from neighboring vertices.

The two models both consisted of two topologically different geometries; one geometry during systole when the aortic valve was open and mitral valve was closed, and one geometry during diastole when the aortic valve was closed and mitral valve was open. The mitral valve affects the LV flow patterns and it has been shown to be important to include it when modeling cardiac flow [19]. The dynamics of the valves could not be resolved with sufficient detail by the CT measurement, but the open and closed positions could be extracted. The overall shape and opening area of the mitral valve could be recreated based on the CT images, but geometrical details could not be incorporated. The aortic valve was simplified by creating three leaflets that started in the ventriculo-aortic junction and extending towards the aorta. Its shape on ventricular flow was considered to be minimal.

Similar to Chnafa *et al.* [20] the valves were assumed to be either fully opened or fully closed, and that they opened and closed instantaneously. In addition, the isovolumetric relaxation and contraction when both the aortic and mitral valve are closed at the same were not included in the model. Any deformation of the ventricle during this short time period would cause the flow solver to fail as conservation of mass would not be fulfilled. It was assumed that these parts of the cardiac cycle did not significantly affect the flow patterns.

In order to solve the flow equations a volumetric mesh was created. Due to the complex shape of the left ventricle, a general tetrahedral mesh strategy was employed with a maximum allowed side length on the order of 0.75–1 mm for the tetrahedral cells. Near the walls the side length was 0.1 mm, which gradually grew in normal direction away from the wall, and regions with high curvature or small gaps were automatically refined even further. With these automatic refinements and a near-wall mesh size

that was smaller than the CT resolution, the reconstructed geometry was considered to be adequately resolved. The total number of mesh cells was on the order of 12 million anisotropic cells which was significantly higher than mesh sizes found in other studies [2, 20]. While the meshing strategy may be not optimal in terms of number of mesh cells or type, it was simple, fully automated, and capable of handling the folding and unfolding of the complex trabeculated structures. All meshes were made in Ansys ICEM 16.0 (Ansys Inc., Canonsburg USA).

Before the flow simulation started, a dry-run solving only for the volumetric mesh deformation was performed. In this way intermediate meshes at every 0.01 s were obtained fully automatically. The wall motion was prescribed based on the displacement vectors obtained from the image registration process, and the tetrahedral mesh was allowed to deform based on the relation:

$$\nabla \cdot (\Gamma_{disp} \nabla \delta) = 0 \quad (1)$$

Here Γ_{disp} was the mesh stiffness which determines the degree to which regions of nodes move together and δ was the displacement relative to the previous mesh location. The mesh stiffness was computed as $\Gamma_{disp} = (\frac{L_{ref}}{d})^{C_{stiff}}$ where L_{ref} was a reference length set to 1 mm, d was the distance from the nearest boundary and the model exponent C_{stiff} was set to 10. During the dry-run, mesh quality in terms of aspect ratio and expansion factor was monitored and when the quality was considered to become unacceptable an automatic remesh was triggered to improve mesh quality. Due to the complex shape and motion of the LV, several remeshes were performed. Besides keeping mesh quality at a high level, it was in this way possible to capture the complex folding and unfolding of trabeculae at the wall and the motion of papillary muscles. Due to the remeshing procedure, both the systolic and diastolic geometry consisted of a number of different mesh topologies. In Fig. 3 examples of the volumetric mesh are shown at different times in the cardiac cycle, and the ability of the framework to handle necessary topology changes and complex geometrical structures is demonstrated.

[Fig. 3 about here.]

2.4 Numerical Model

After the image and geometrical processing were performed, the flow could be computed in the model by solving the Navier-Stokes equations. The flow simulation was performed using Ansys CFX 16.0 (Ansys Inc., Canonsburg USA). Both advection and transient schemes were second order accurate

and a convergence criteria of $1e-5$ was used. The fluid was incompressible with a density of 1060 kg m^{-3} and dynamic viscosity of $3.5e-3 \text{ Pa s}$.

The flow field was interpolated between each mesh topology using tri-linear interpolation. The boundary conditions on the wall were specified displacement from the image registration process, specified wall velocity as a result of the wall motion, and a no-slip condition. As the fluid motion was governed by the wall motion, mass flow or velocity boundary conditions on all pulmonary veins would over-constrain the model. Instead a zero relative static pressure was set at the four pulmonary veins, which resulted in approximately equal flow distribution into the atrium. The boundary conditions for the aorta and the coronary arteries were also a zero relative static pressure, which could be justified by the fact that the flow after the aortic valve was not of interest in the study and its effect on ventricular flow patterns would be minimal. This combination of zero static pressure on both the pulmonary veins (acting as inlets), and aorta and coronary arteries (acting as outlets) was possible since the mitral and aortic valves were not open at the same time. The valves were considered as walls with a no-slip condition and allowed to move together with the surrounding wall motion, but the true valve dynamics was not incorporated as it was impossible to resolve it accurately in the CT acquisition. The time step was $1e-4 \text{ s}$ and since meshes were only available at every 0.01 s , intermediate meshes at each time step were computed during run time using a fast Piecewise Cubic Hermite Interpolating Polynomial (PCHIP) interpolation FORTRAN-subroutine. In this way a new mesh for each time step was obtained and it was ensured that both velocity and acceleration of the wall were continuous and smooth. The interpolation routine has been described in more detail in an earlier work [21], and the additional computational time for obtaining intermediate meshes was less than 2% of the total computational cost. All simulations were performed at National Supercomputer Centre, Linköping, Sweden.

In Fig. 4 a flow chart describing the steps in the method is presented.

[Fig. 4 about here.]

2.5 Evaluation

Evaluation of the simulation framework was performed by visual and quantitative assessment of the flow patterns and near-wall residence time in the baseline model, as well as the smoothed model. Five cardiac cycles were first simulated and discarded, to remove any effect of initial conditions or transient effects. The results are thus based on the subsequent cardiac cycles. Flow patterns were assessed by

both velocity magnitude and vectors at a cross-sectional plane passing through the atrium, ventricle and aortic root. To identify possible regions of stagnant blood flow, a passive scalar transport equation was solved, accounting for the convective transport of a scalar ϕ . It can be seen as a virtual field, similar to a contrast agent, which was released and tracked in the flow without affecting it. The governing equation was described by a convective transport equation:

$$\frac{\partial(\phi)}{\partial t} + \nabla \cdot (\mathbf{U}\phi) = S_{\phi} \quad (2)$$

where $\mathbf{U}$ was the fluid velocity and S_{ϕ} was a source term with the value 1 s^{-1} , to increase the "age" of the transported scalar as time progresses in the simulation. The boundary conditions were $\phi = 0$ at the pulmonary veins, meaning that the value of the scalar was always zero when it entered the computational domain. The passive scalar methodology can then be used to assess both residence time and amount of mixing in the model.

3 Results

The CT data was acquired successfully, and the baseline LV model and the smoothed LV model were created from the data. The resulting flow rates at the pulmonary veins, mitral valve and aortic valve are presented in Fig. 5. Clinically relevant parameters could be derived from the two models, which are summarized in table 1.

[Fig. 5 about here.]

[Table 1 about here.]

The smoothed model had a slightly larger end diastolic (267 vs 255 ml) and end systolic LV volume (182 vs. 172 ml) due to the fact that the trabeculae and papillary muscles were removed. However, the stroke volumes, computed as the time integral of the ejected flow out of the LV were almost the same between the two models (82 vs. 85 ml), as well as the ejection fraction (32%), computed as the ratio of stroke volume and end diastolic volume of the LV. In addition, the ratio between early and late filling velocity through the mitral valve (E/A ratio) and the time between maximum velocity of the E wave to baseline (E deceleration time) were similar for the models. Ejection fraction was lower than considered normal for a healthy adult (55%), while the stroke volume was in the normal range (60-100 ml) [22]. While the models look geometrically different, these parameters indicate that the baseline and smoothed

models were similar from a clinical point of view. For the baseline model peak Reynolds numbers based on mean diameter for each pulmonary vein were 1035, 957, 1261 and 1326, while for the mitral and aortic flows they were 3648 and 4320, respectively. These values are in line with results presented in other studies [2, 13, 20, 23].

For both models, the cardiac blood flow field was computed. For each model one cardiac cycle took about 4 hours to simulate on 96 CPU cores. To qualitatively assess the wall-flow interaction in the baseline model, and to demonstrate the possibilities with the framework developed in this study, particle traces near the papillary muscles and the trabeculated wall were isolated and visualized, see Fig. 6.

[Fig. 6 about here.]

The traces show how the blood flow interacted and curled around the papillary muscles, and that the flow velocity in some of the interstitial spaces was low. Particles were able to travel around and even under the papillary muscles, and created a complex near-wall flow field that extended into the LV cavity.

To better understand the flow field in the two models, a cross-sectional plane through the atrium, LV and aortic sinuses was used to display velocity magnitude and vectors at five different phases during the cardiac cycle, see Fig. 7. During systole (time = 0.1 and 0.2 T) the flow field is similar between the models, with a high velocity region in the left ventricular outflow tract (LVOT) and through the aortic valve. This could be expected since both geometries were similar in that region and the LV stroke volume and ejection fraction was almost the same. The velocity in the apical region is lower in the baseline model than the smoothed model. During diastole the flow patterns appeared different between the baseline and smoothed models; the smoothed model had a high velocity flow in the mid region while the flow was more stagnant in baseline model. Instead the papillary muscles seemed to divert the flow and created a large vortex in the middle of the LV, which was not as prominent in the smoothed model. The LV filling pattern in this patient was asymmetrical, with a mitral jet directed towards the lateral side of the ventricle. Thus, a large vortex formed behind the anterior mitral leaflet, and was allowed to expand in the ventricle, while the flow on the posterior side strongly interacted with the wall.

[Fig. 7 about here.]

In addition to the velocity field, vortical structures were studied using the Q-criterion [24]. It is computed from the second invariant of the velocity gradient tensor, and allows for the detection of vortical structures. In Fig. 8 isosurfaces with the value of 300 s^{-2} are presented at five different time points

during the cardiac cycle for both models. In systole, the two models look qualitatively similar with large structures in the ventricle. During diastole more vortices are seen in the baseline model compared to the smoothed model. This is especially evident during the late filling phase ($t = 0.9T$) where a large amount of structures are present in the baseline model.

[Fig. 8 about here.]

To quantitatively assess mixing and stagnation in the ventricle, a binary mixing approach was employed. Blood that resided in the model at time = 0 was assigned a value of 0, while blood that entered the model were assigned a value of 1. As time progresses more and more blood with the value of 1 enters the LV, and the mixing behavior can be seen in Fig. 9 at the end of diastole in different cardiac cycles. In general the blood in the ventricle mixed in less than five cardiac cycles in both models, but there were trabeculated regions in the baseline model where the flow appeared stagnant and was not mixed after 5 cardiac cycles.

[Fig. 9 about here.]

To further investigate if there were any stagnant flow regions, the residence time at the LV wall was evaluated for the baseline model after 10 heart beats, see Fig. 10. The mean near-wall residence time was on the order of 5 s, but some regions close to where the mitral valve jet interacted with the wall and had a near-wall residence time on the order of 2 s, indicating that blood was constantly flushed through those structures. On the other hand, blood in some trabeculated structures below the papillary muscles had a residence time of more than 8 s, which could indicate that the blood in that region was stagnant. The maximum residence time was 10 s (corresponding to 10 heart beats), while the minimum residence time was close to 2 s. The mean residence time on the wall was 5.18 ± 0.08 s. Qualitatively, a more homogeneous residence time was seen in the part of the heart with less trabeculations, indicating that the smooth surface does not interact as much with the flow.

[Fig. 10 about here.]

4 Discussion

In the present study, a framework for computing patient-specific hemodynamics in physiologically realistic hearts was developed and applied to a patient with a dilated left ventricle. The framework only required time-resolved CT images of the heart. After segmentation of one time frame, the model was

created by a non-parametric diffeomorphic image registration algorithm from which the complex wall motion could be extracted and prescribed in a flow solver. A dry-run where only mesh displacement was computed which resulted in a number of intermediate meshes with different topologies, and then during the simulation process a fast interpolation routine computed meshes for each time step in the flow simulation.

The model included papillary muscle motion and the folding and unfolding of left ventricular trabeculae, and the results indicated that these are important aspects to consider when computing cardiac blood flow. In addition to papillary muscles and trabeculae, the model also included the atrium, ventricle, valves, aortic root and part of the coronary arteries and ascending aorta, which has, to the authors' knowledge, never been achieved before in a computational flow model. Manual interaction was only needed to segment the heart wall in one arbitrary time frame, and to identify the open and closed heart valve positions. The subsequent steps in the framework, including wall displacement extraction, volumetric meshing, and simulation setup and computation, could be automated to a high degree.

Compared to simplified models commonly found in literature, the blood in the physiological model interacted strongly with papillary muscles and trabeculae which in turn affected the computed flow field. Specifically, the simulations showed that the complex flow patterns in the LV were affected by the blockage effect posed by the papillary muscles, which effectively reduced the amount of energetic flow that reached the apical part of the heart. The interstitial spaces in the trabeculated surface could promote stagnant blood flow, as regions of high residence time could be found in such structures. As such, the presented results suggest that over-simplified models are unable to capture details that could have important physical implications. In a recent study by Vedula et al [2], the authors argued that the effect of including trabeculae and papillary muscles allowed for a deeper penetration depth of the mitral inflow jet into the apical region. This result was not seen in the current results; here the mitral jet strongly interacted with the papillary muscles and was diverted towards the outflow tract. Clearly, mitral flow has a large impact on ventricular flow and patient-specific geometries and the imposed wall motion will affect the computed flow field.

The dynamic motion of the valves was difficult to extract from the CT data due to limitations in the temporal multiphase reconstruction of the CT images. As such, the valve dynamics is the largest limitation of this study. To capture the valve dynamics from measurements a higher temporal resolution is needed as the valves transition from fully open to fully closed on the order of 100 ms. An alternative

would be to model the position of the valves as dependent on the incoming flow, either using a 2-way fluid structure interaction simulation or an immersed boundary technique [14,20], but information about valve composition and the open and closed position would still be needed. The flow in the LV was recently investigated by Chnafa *et al* [20] who performed a large-eddy simulation and characterized the complex flow patterns as neither laminar or fully turbulent, in line with a recent PC-MRI study by Zajac *et al.* [25] Flow modeling to account of this type of transitional flow was not performed in this study, but the high spatial and temporal resolution in these simulations could probably account for any eventual flow instability. The framework requires CT images in order to create geometries that include trabeculae and their motion, as the spatial image resolution is one order of magnitude better than other imaging modalities. As such, the method described here is limited to patients that require a clinical time-resolved CT acquisition. While simulations on anatomically accurate geometries are more physiologically relevant than simplified models, the manual segmentation of images and the computational cost of computing the flow are the major obstacles from translating computational results into clinical practice.

A recent study by Vedula *et al.* [14] suggested that the hemodynamics in the left atrium does not significantly affect the flow patterns in the left ventricle, as the vortices generated by the flow from the pulmonary veins quickly dissipates. However, only one normal heart was studied and it is unclear whether the conclusion holds for a larger population. Conversely, Dahl *et al.* [26] found that in order to obtain a physiologically correct LV filling flow pattern, subject-specific atrial and venous anatomies should be included. In this study the atrium and parts of the pulmonary veins were included, but the assumption made on equal static pressure in the pulmonary veins may affect the flow patterns in particular in the atrium [20,26].

From a clinical perspective, the framework developed here opens up for the possibility to artificially add pathologies such as myocardial infarction or hypertrophy to the model. The wall motion can be turned off or tuned, the size of LV can be changed, and the valves can allow for regurgitant flow. The patient-specific effects on the cardiac blood flow from these pathological conditions could be interesting to study from a physiological point of view.

In conclusion, the novel framework developed in this study enables the inclusion of geometrical features on a scale that has never been achieved before. In addition, the feasibility, as well as importance, of including the motion of papillary muscles and trabeculae in computational models of cardiac

hemodynamics was demonstrated.

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List of Figures

1	Top row: The two models used in the study: a baseline model including papillary muscles and trabeculae, and a smoothed model without any geometrical details or papillary muscles in the left ventricle. Bottom row: systolic and diastolic geometries for the baseline model, highlighting the open and closed valves (AV, MV) and the papillary muscles (PM).	19
2	Schematic figure representing the registration process and computation of displacement vectors. The image registration was applied sequentially to the time frames and the displacement field $D(n, n + 1)$ that aligned time frame n with $n + 1$ was obtained. Using the perimeter of the segmentation in the first time frame as a binary mask, displacement vectors at the wall could be computed. The process was then repeated using the displaced wall as a new binary mask. For visualization purposes the images are shown in 2D, but the image registration and displacement vectors were in 3D.	20
3	Examples of the volumetric mesh in the LV. The motion of the papillary muscles (PM, highlighted in red) and the folding and unfolding of trabeculae at the LV wall created several different geometrical topologies during the cardiac cycle. By monitoring mesh quality the framework was able to handle these topological changes by automatically trigger a remesh. (T = duration of cardiac cycle.)	21
4	Flow chart describing all steps in the method. From the acquired images a geometry was segmented at one time frame and image registration was used to obtain the wall motion. The segmented geometry was meshed and the wall motion was then applied and the deformation was computed. If the mesh quality became too low, a automatic remesh was triggered. In this was meshes were obtained every 0.01 s. Then, the flow solver was started and using PCHIP interpolation in time intermediate meshes were obtained for each time step in the flow simulation.	22
5	Resulting flow rates at the pulmonary veins, mitral valve and aortic valve for the baseline model.	23
6	Visualization of particle traces near the papillary muscles and trabeculated structures. A: anterior papillary muscle, B: posterior papillary muscle, C: geometrical structure below the anterior papillary muscle.	24
7	Cross-section through the two models, showing velocity magnitude and in-plane velocity vectors. Upper row is baseline model, while lower is the smoothed model. Left part of the figure show the flow field during systole (0.1 and 0.2T, T = duration of cardiac cycle) while the right part shows the flow field during diastole (0.5, 0.7 and 0.9T). Notice the different color range between systole and diastole.	25
8	Vortical structures identified by the Q-criterion at $Q = 300 \text{ s}^{-2}$ for the two models at five time points.	26
9	Visualization of mixing of blood using the residence time variable. At time = 0 the residence time is 0 everywhere, and then during the first heart beat (time period T) blood with value 1 is injected from the pulmonary veins. Mixing is shown at different cardiac cycles at the end of diastole. Arrow indicate region with no mixing and stagnant flow. Upper row: baseline model, lower row: smoothed model.	27
10	Illustration of the residence time at the LV of the baseline model after 10 simulated cardiac cycles. Highlighted areas show that some of the trabeculae have elevated residence time compared to the surrounding LV wall. Minimum, maximum and mean $\pm$ std of the residence time at the wall are indicated in lower right panel.	28

Fig. 1: Top row: The two models used in the study: a baseline model including papillary muscles and trabeculae, and a smoothed model without any geometrical details or papillary muscles in the left ventricle. Bottom row: systolic and diastolic geometries for the baseline model, highlighting the open and closed valves (AV, MV) and the papillary muscles (PM).

Sequential image registration in time to obtain displacement field $D(n,n+1)$

Fig. 2: Schematic figure representing the registration process and computation of displacement vectors. The image registration was applied sequentially to the time frames and the displacement field $D(n,n+1)$ that aligned time frame n with $n+1$ was obtained. Using the perimeter of the segmentation in the first time frame as a binary mask, displacement vectors at the wall could be computed. The process was then repeated using the displaced wall as a new binary mask. For visualization purposes the images are shown in 2D, but the image registration and displacement vectors were in 3D.

Fig. 3: Examples of the volumetric mesh in the LV. The motion of the papillary muscles (PM, highlighted in red) and the folding and unfolding of trabeculae at the LV wall created several different geometrical topologies during the cardiac cycle. By monitoring mesh quality the framework was able to handle these topological changes by automatically trigger a remesh. (T = duration of cardiac cycle.)

Fig. 4: Flow chart describing all steps in the method. From the acquired images a geometry was segmented at one time frame and image registration was used to obtain the wall motion. The segmented geometry was meshed and the wall motion was then applied and the deformation was computed. If the mesh quality became too low, a automatic remesh was triggered. In this was meshes were obtained every 0.01 s. Then, the flow solver was started and using PCHIP interpolation in time intermediate meshes were obtained for each time step in the flow simulation.

Fig. 5: Resulting flow rates at the pulmonary veins, mitral valve and aortic valve for the baseline model.

Fig. 6: Visualization of particle traces near the papillary muscles and trabeculated structures. A: anterior papillary muscle, B: posterior papillary muscle, C: geometrical structure below the anterior papillary muscle.

Fig. 7: Cross-section through the two models, showing velocity magnitude and in-plane velocity vectors. Upper row is baseline model, while lower is the smoothed model. Left part of the figure show the flow field during systole (0.1 and 0.2T, T = duration of cardiac cycle) while the right part shows the flow field during diastole (0.5, 0.7 and 0.9T). Notice the different color range between systole and diastole.

Fig. 8: Vortical structures identified by the Q-criterion at $Q = 300 \text{ s}^{-2}$ for the two models at five time points.

Fig. 9: Visualization of mixing of blood using the residence time variable. At time = 0 the residence time is 0 everywhere, and then during the first heart beat (time period T) blood with value 1 is injected from the pulmonary veins. Mixing is shown at different cardiac cycles at the end of diastole. Arrow indicate region with no mixing and stagnant flow. Upper row: baseline model, lower row: smoothed model.

Fig. 10: Illustration of the residence time at the LV of the baseline model after 10 simulated cardiac cycles. Highlighted areas show that some of the trabeculae have elevated residence time compared to the surrounding LV wall. Minimum, maximum and mean $\pm$ std of the residence time at the wall are indicated in lower right panel.

List of Tables

1	Derived LV parameters from the simulations	30
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Table 1: Derived LV parameters from the simulations

	Baseline	Smoothed
End diastolic LV volume	255 ml	267 ml
End systolic LV volume	172 ml	182 ml
Stroke volume	82 ml	85 ml
Ejection fraction	32 %	32 %
E/A ratio	0.82	0.83
E deceleration time	170 ms	167 ms