Biomedical modelling and simulation – towards individual models of the human cardiovascular system

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Summary Magnetic resonance imaging has developed far enough that we are able to non-invasively obtain time-resolved three-dimensional data including individual anatomy as well as velocities of the blood, the myocardium and vessel walls. Parameters such as relative pressure in the blood pool and strain in the myocardium can be extracted. A combined usage of very detailed measurements and computer simulations enables tailored tools for the clinician for enhanced diagnostics, intervention planning as well as follow-up.

Introduction

The future of computational mechanics in biomedicine deals with creating individual models of the human heart and vascular systems for enhanced diagnostics, intervention planning and follow-up. Magnetic resonance imaging has developed far enough that we are able to non-invasively obtain time-resolved three-dimensional data including individual anatomy as well as velocities of the blood, the myocardium and vessel walls. The use of these vast amounts of data is impossible without computer support. From the obtained data, new parameters such as relative pressure in the blood pool and strain in the myocardium can be extracted. Combining these parameters with anatomical information and tools for computer simulation the accuracy of diagnostics in the individual patient is greatly enhanced. Furthermore, planning of necessary interventions can be performed and optimized. The outcome of such interventions can even be simulated. As a bonus, MRI enables the possibility to perform individually tailored follow-up procedures where relevant parameters are automatically extracted.

Properties of the human heart

In order to address the future goal of non-invasively obtaining a functional model of an individual patient in order to estimate e g wall shear stress in the arteries as well as other functional, clinically relevant parameters within the human heart and the larger vessels there is a vast array of important steps that needs to be taken.

- Three-dimensional
- Non-linear
- Non-homogenous
- Anisotropic
- Time-dependent
- Active
- Individual
- Changes with age and disease

The first five items on the list (left part) is normally found in classical computational mechanics, while the last three (right part) comes from basic and/or clinical medicine. Within the field of biomedical modelling and simulation, our goal is to combine these two areas in order to handle the complexity of different biological systems. Here we use the human heart as an example; it is also the area where a lot of research is performed presently.

Geometry of the heart

In order to describe the geometry and the structure of the human heart, we need to establish detailed knowledge about a number of key parameters on an individual basis. The three-dimensional shape is obviously important and can be found using modern imaging modalities e g computerized tomography (CT), ultrasound (US) or magnetic resonance imaging (MRI). However, despite its superior resolution CT is most used for special types of diagnosis due to the radiation and US suffers from limited resolution. Therefore, MRI is the method of choice for most of these applications since it includes no radiation, can be used multiple times on one patient for follow-up etc and, as a very significant bonus, by applying a phase-contrast method, it can also be used to measure the velocity of the blood and/or the heart wall. Some important parameters of the 3D shape includes: wall thickness, curvature and a stress free reference configuration. Here wall thickness and curvature can quite easily be found from the image itself by applying some image processing method while estimating a stress-free reference configuration requires quite an effort. A reference configuration will be of great importance for further work on operation planning computer simulation programs will be developed.

Apart from the geometry of the heart, detailed knowledge about the structure of the cardiac wall is necessary. This includes the geometry and topology of the muscle fibre architecture, which as a first approximation can be descried as a double-helix with a left-handed pitch on the inner border of the heart (endocardium) and a right-handed pitch on the outer border of the heart (epicardium). Furthermore, for a detailed description of the heart, the pericardium that resembles a sack in which the heart resides needs to be taken into account. Finally, the anatomy of the coronary arteries is important, not only for feeding the muscle fibres with oxygenated blood, but also since it may have importance in the structural build-up of the heart.

Material properties

With information about the geometry we now turn to the material properties: the heart is a chemically controlled electro-mechanical pump. The pump itself is quite easy to model in terms of a pressure-volume relationship on a global level, but for a more detailed analysis we need to take into account passive as well as active properties.

The passive properties of the heart include non-linear finite elasticity and quasi-linear visco-elasticity in combination. The anisotropy of the heart is of importance since the muscle fibres can only contract along the fibre direction and since the fibres are arranged in sheets, the shear strains within the heart wall will relocate the force direction.

The heart wall is also influenced by biphasic porosity due to the transportation of blood in and out of the myocardium. The inflow/outflow through the heart wall is strongly coupled to the architecture of coronary arteries and veins.

The active properties of the heart are much more complex to model. The contractile properties of the muscle fibres are dependent on the sarcomere length and history which in turn is controlled by cellular calcium and available metabolic energy supply. Finally, the activation sequence through the entire heart has to be included. This includes detailed modelling of the motion of the wave front of an electrical wave that will travel through the heart a serve as trigger for each of the muscle cells.

Boundary conditions

With the geometry and the material properties described we finally need some boundary conditions. The most obvious boundary condition is the time dependent changes of the pressure in the cardiovascular system and the surrounding pressure. The filling pressure (preload) and the arterial pressure (afterload) are both important and requires for a successful modelling knowledge about the physiology of the heart in general and for the case of a patient specific model, also detailed measurements of pressure in that individual. More peripherally, surrounding pressures such as direct as well as indirect ventricular interaction and the pressure in the thorax and against the pericardium will influence the behaviour of the heart as well.

Furthermore, the breathing will influence the results (sometimes significantly) and there are moving structures, such as heart valves, and supporting structures, such as chordae, that needs to be considered. And, since the heart is connected to the vascular system through the aorta, there is a structural coupling there as well. Finally, the motion and pulsating air flow through the lungs will influence the heart. This motion is strongly coupled to the obtainable image quality that can be expected in the clinical setting.

At this point it is worth noting that the described complexities in modelling the human heart have so far only dealt with the normal heart. As mentioned earlier, significant changes are known to occur when aging, there are quite large differences between the males and females and, of course, the whole system changes dramatically during a disease.

Modelling and simulation

Such a project is obviously quite complex and by necessity highly interdisciplinary. Several important steps has to be solved, within several disciplines, before the goal is achieved: data acquisition, image processing, segmentation, model construction, application of an automatic mesh-generator, usage of a CFD-code for numerical flow simulations or a FE-code for bio-solid mechanics simulations, and finally, an appropriate visualization technique has to be applied. Before the last step it is normally also a step of parameter estimation, where clinically relevant parameters are estimated from the computed and/or measured information.

We have developed a new and unique technique to measure the time-resolved three-dimensional velocity field inside the human heart by using phase-contrast magnetic resonance imaging. Based on the data from phase contrast magnetic resonance imaging we have been pioneering the usage of new advanced concepts and methods for the description of blood flow patterns inside the normal human heart. One such example is using particle traces or streamlines. Recently we have been able to study and quantify the differences between normal and abnormal flow patterns. One example of quantification includes the development of an automatic technique to find and characterize vortices in the left ventricle. This technique is in many ways similar to the work we have done on automatic image segmentation (border delineation) and is inspired by the very latest development in image processing.

We are implementing a fully automatic segmentation technique (detection of the arterial wall from image information only) from which geometrical models of the artery can be developed. From the computed values we are obviously able to compute classical parameters such as pressure drop. For severe constrictions however, some turbulence model will be needed which will increase the computational effort by several orders of magnitude. Therefore, we need to include into the "chain" a numerical flow simulation code that can handle complex geometries. From advanced computer modelling we are thus able to compute numbers that cannot be measured accurately or not at all. One such parameter of particular importance is wall shear stress (WSS). WSS is of very high clinical interest since has been strongly linked as a possible cause of atherosclerosis. Combining MRI measurements, image processing and computing it is possible to estimate WSS at a very high resolution and furthermore, simple follow-up protocols can be derived on an individual basis. Furthermore, from the velocity information we have measured, combined with the border delineation we have also been able to compute the relative pressure field inside the heart. This can be done by solving a simplified fluid mechanics equation in three dimensions.

One may quantify the kinematics of the heart, and the left ventricle in particular, through estimation of strain (and strain-rate) from time-resolved three-dimensional phase-contrast magnetic resonance imaging. The technique originates from our unique method to measure four-dimensional blood flow patterns and can be used in the myocardium as well. The computed strain/strain-rate is in three dimensions a tensor with means that instead of having one value in each point (a scalar like the pressure) or three values (a vector like the velocity which includes both size and direction), strain/strain-rate is represented by nine values in each point (interpreted as size, direction and reference plane of action). From the tensor we can compute the main direction of action without anatomical reference and later correlate it to the anatomical reference.

The size if that data from today's imaging modalities are increasing rapidly and instead of one or a few images that were the standard some years go are we moving to 3D data resulting in hundreds of images – and rapidly we are also utilizing 4D data (3D time-resolved data) which means thousands of images (per patient!). Furthermore, the data is no longer anatomical only. Since we are able to measure velocities in 4D as well (simultaneously) that data is several times larger again.

Concluding remarks

From the velocities we are able to, with very high accuracy, estimate new parameters such as strain, strain-rate or pressure. Methods for automatic characterization of flow patterns and structures that can be applied to measured data from e g magnetic resonance imaging as well as data from computer simulations are of great importance for the future clinical setting to find "the vital few among the trivial many". The old saying "Messen ist Wissen" is in fact very true today in the field of biomedical modelling and simulation.