V 71

Plasma electrolyte concentrations in patients with chronic kidney disease influence cardiac pacemaking in a computational model

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Chronic kidney disease (CKD) affects more than 30 million patients in the European Union. CKD causes alterations in the extracellular plasma electrolyte concentrations, which affect cardiac electrophysiology. A total of 25% of all deaths of CKD patients are due to sudden cardiac death (SCD). Until recently, ventricular fibrillation was assumed to be the main reason. In a 2015 study, Wong et al. observed bradycardia and asystole as the predominant mechanisms of SCD in patients with CKD. This shows that the influence of electrolyte changes on the underlying mechanisms of pacemaking in the sinoatrial node (SAN) needs to be better understood. In this work, we have updated the computational model of the human SAN given by Fabbri et al. and investigated the CKD-induced change of $[Ca^{2+}]_o$ (0.6-3mM), $[K^+]_o$ (3-9mM) and $[Na^+]_o$ (120-150mM) on pacemaking. $[Ca^{2+}]_o$ had the most dominant effects on SAN function. Low $[Ca^{2+}]_o$ caused severe bradycardia in the model (down to 17 bpm) for 0.6 mM. A critical concentration range of calcium in the subspace $[Ca^{2+}]_{sub}$ was identified as the possible underlying mechanism for pacemaking. For increasing $[Ca^{2+}]_o$, the heart rate (HR) increased, resulting in 142 bpm for the highest calcium concentration. The effect of $[K^+]_o$ variation was similar to the one for $[Ca^{2+}]_o$, but caused less pronounced change. The resultant changes due to variation of $[Na^+]_o$ were relatively small. In this work, several potential mechanisms for SCD in CKD patients could be identified. The low HR for low $[Ca^{2+}]_o$ is seen as a possible link to the observed bradycardia in CKD patients. The findings in this work could lead to a better surveillance of $[Ca^{2+}]_o$ in hemodialysis patients, and therefore to a decrease in the SCD rate.

V 73

Optimal ECG lead systems to maximimze left atrial information content

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Atrial arrhythmias such as atrial flutter and atrial fibrillation are a burden for patients and a major challenge for modern healthcare systems. Identification of patients at risk to develop atrial arrhythmias at an early stage carries the potential to reduce the incidence by implementing appropriate strategies to mitigate the risks. Diagnostic methods based on the ECG are ideal risk markers due to their noninvasiveness and omnipresence. The left atrium (LA) plays a major role in the intiation and perpetuation of atrial reentry arrhythmias. However, the LA is not well represented in the P-wave derived through standard ECG leads. Here, we optimize ECG lead positions to maximize LA information content. Towards this end, we used a cohort of eight personalized computational models providing the unique opportunity to separate LA and right atrial (RA) contributions to the P-wave, which is not feasible in vivo. The location of maximum P-wave signal energy was located on the center of the chest for all subjects with marked overlap between regions of maximum LA and RA P-wave amplitude. The regions of highest ratio between LA and RA signal energy differed between patients. However, a region with LA signal energy being higher than that of the RA and providing a sufficiently large absolute P-wave amplitude was identified at the center of the back consistently across five models of the cohort. Optimized linear combinations of standard 12-lead signals yielded comparably good results. Our newly proposed electrode positions on the back as well as selected linear combinations of standard 12-lead signals improve the LA information content considerably. By using these, more relevant diagnostic information regarding the anatomical and electrophysiological properties of the LA can be derived in future.

V 74

Developing and coupling a lumped element model of the closed loop human vascular system to a model of cardiac mechanics

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Modelling the interaction of the heart and the vascular system allows to study the pumping efficiency of the heart in a controlled environment under various cardiac and vascular conditions such as arrhythmias, dyssynchronies, regions of stiffened myocardium, valvular stenoses or decreased vascular compliances.
To pose realistic hemodynamic boundary conditions to a four-chambered elastomechanical heart model, we developed a lumped element model of the closed loop human vascular system. Systemic and pulmonary circulations were each represented by a three-element Windkessel model emptying into a venous compliance. Both circulations were coupled by connecting the venous compliances to the corresponding atrium via venous resistances. Cardiac valves were represented by ideal diodes and resistances. Strong coupling between the heart and the vascular system model was accomplished by estimating the cardiac pressures that lead to continuous flows across the model interfaces. Active regulatory mechanisms were not considered. Pressures, flows and volumes throughout the circulatory system were simulated until a steady state was reached and the effects of model parameters on these hemodynamic parameters were evaluated in a sensitivity analysis.
Increasing the systemic peripheral resistance by 50% caused an 8% decrease in stroke volume (SV) and a 33% increase in mean arterial pressure. Increased venous resistance descreased the E/A wave ratio of the atrioventricular flow and led to a reduced SV by impeding passive cardiac filling. Increasing the arterial compliance decreased mean cardiac pressures, while only slightly reducing the SV. Larger arterial resistances mainly caused higher peak systolic pressures.
Furthermore, we show that embedding the heart model into surrounding elastic tissue by forcing permanent contact at the pericardial surface leads to more realistic time courses of atrial volumes and atrial pressure-volume curves composed of an A and a V loop as found in measurements.
In conclusion, this work enables simulations of diseases that involve significant cardiovascular interaction.

V 75

From clinics to the virtual beating heart – a general modeling workflow for patient-specific electromechanical heart simulations

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Generating meshes of complex structures in the human body like the heart organ is a prerequisite for computational simulations of of organ function. The quality of the conclusions derived from these simulations greatly depends on the quality and accuracy of the mesh they are based on. Volumetric computation domain can be represented by an equally-spaced voxel grid, or – in case of more sophisticated partial differential equation discretization methods (finite elements, finite volumes) – first, second or even higher order tetrahedral meshes.
Here, we present a workflow that is capable of creating high quality meshes for such simulations. The workflow contains segmentation, surface mesh generation, volume mesh generation, and patient-specific parameter fitting to produce the desired results. While segmentation itself is a more or less unique mapping from a grayscale DICOM data set to a labeled, three-dimensional voxel mesh, different approaches exist for their transformation to a surface mesh. Our process involves a two-level approach for obtaining triangular or mixed rectangular surface meshes of desired quality and resolution. Both are crucial for the next step: obtaining a volumetric tetrahedral grid with the desired degrees of freedom. In the last step, a derivative-free parameter estimation approach is used to calibrate the dynamic behavior and tailor the model patient-specifically.
All software used in the workflow is published under open source licenses and freely available. Its capability is demonstrated by means of an elastomechanical simulation of a human heart and yields measurable validation quantities in physiological ranges. We want to stress that the presented approach is generic and can easily be used for the model generation of other organs like liver, lungs or the aortic arch as well. The resulting meshes can be used for various types of simulations (electrical excitation propagation, blood flow) and use cases (clinical diagnostics, therapy planning etc.).