33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

A Framework for Personalization of Computational Models of the Human Atria

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***Abstract*—A framework for step-by-step personalization of a computational model of human atria is presented. Beginning with anatomical modeling based on CT or MRI data, next fiber structure is superimposed using a rule-based method. If available, late-enhancement-MRI images can be considered in order to mark fibrotic tissue. A first estimate of individual electrophysiology is gained from BSPM data solving the inverse problem of ECG. A final adjustment of electrophysiology is realized using intracardiac measurements. The framework is applied using several patient data. First clinical application will be computer assisted planning of RF-ablation for treatment of atrial flutter and atrial fibrillation.**

I. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in humans. Especially elderly people suffer from AF with a prevalence of 8% for persons above the age of 80 [1]. Sometimes AF can be treated successfully using drugs, but side effects reduce the quality of life significantly. Radiofrequency ablation (RF-ablation) is an option for curative therapy [2], [3]. Distinct lines in the atria are converted to necrotic tissue using a catheter and RF-power, thus blocking the spread of depolarization. Unfortunately, these procedures often take several hours in the so called "cath lab", which is very stressful both for the patient and the clinician. In addition the success rate for long-term prevention from AF is only about 70% [2], [3]. Very often patients have to undergo the same procedure again after 3 months and for some of them it turns out to be a complete failure.

Computational models of the heart have evolved to become an important tool for understanding several types of arrhythmias like AF [4]-[7], atrial flutter or ventricular fibrillation [8]-[11]. Also various genetic diseases leading to arrhythmias like Long-QT- or Short-QT-syndrome can be simulated successfully [12]. A solid comprehension of AF can be supported by tuning electrophysiological parameters like conduction velocity (CV) and by triggering extrasystoles from various regions in a generalized model of the human heart [7].

Consequently the next step is to adapt these computer models to the individual patient in order to guide and optimize the therapy. Only this way the gain of increased comprehension can be translated to a benefit for the patient.

The most prominent efforts in this field are the optimization of RF-ablation in case of AF [13], [14] and the optimization of cardiac resynchronization therapy [15]-[18].

In this article a framework and workflow is suggested in order to adapt a generalized model of the human atria to the individual heart of a patient. This is meant to be a first step into the direction of an individual RF-ablation planning system, which is aiming at a distinct decrease of cath lab time and a significant increase in long-term success rate.

II. Anatomical Modeling

A. Atrial Geometry

Frequently CT or MRI data are acquired for patients suffering from AF. To create a geometrical model from these data, a segmentation procedure has to be carried out. Fully automatic segmentation of the atria is not "standard" since the atrial wall is thin and image contrast is small. A first approach is based on active contours where mean shaped balloons are positioned into the two cavities and adapted according to the most important variance of the atrial geometry [19], [20]. An improved approach seeks for all four pulmonary veins of the left atrium. A large interindividual variance of the orifices of the pulmonary veins is observed. A new method has become available lately that moves into the pulmonary veins starting in the atrial cavity and seeks for the circumference and bifurcations [21].

A comprehensive geometrical model of the atria is a 3D-object that includes the thickness of the atrial wall. In most cases the epicardial surface of the atria is not clearly visible in the images. Until no better imaging data are available, the thickness of the atria has to be estimated using a rule-based procedure [22], [23]. Using an active shape model that includes labels for different areas of the atrial wall, the thickness can be adjusted according to the specific region. Thickness data can be adopted from anatomical atlases and autopsies [24], [25].

Manuscript received March 26, 2011. Research leading to these results has received funding from the European Community Seventh Framework Programme (FP7/2007-2012) under grant agreement no 224495 (euHeart project). All authors are with the Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), 76131 Karlsruhe, Germany (corresponding author phone: 0049 72160842650; fax: 0049 60842789; e-mail: Olaf.Doessel@kit.edu).

Finally an adequate mesh generator has to generate a tetrahedron or hexahedron mesh with smooth surfaces at the boundaries between different tissue classes. Fig. 1 shows the result of atrial segmentation based on clinical MRI data.

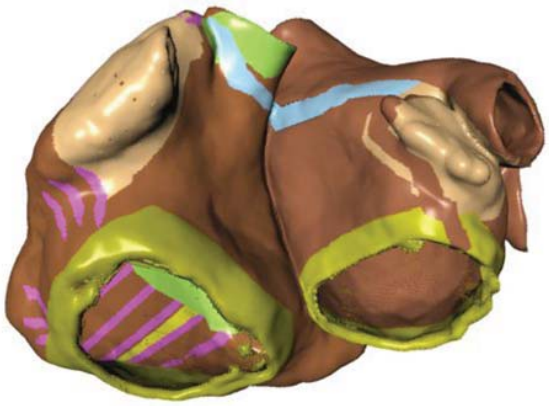

Fig. 1: Anatomy of the atria of an individual patient segmented from MRI data. Colors denote different atrial tissue classes like e.g. terminal crest, pectinate muscle, left and right atrial appendage and Bachmann bundle.

B. Atrial Fiber Direction

The spread of depolarization is significantly different in fiber direction as compared to the transverse direction. Because of this, a comprehensive model of the atria must contain the local fiber direction, which is much more complicated as compared to the ventricles. A semiautomatic algorithm has been implemented, that is able to give a good estimate of the fiber structure throughout the atria after 22 anatomical landmarks have been marked in the imaging data [26]. It is using recent detailed anatomical data [27], [28]. Fig. 2 depicts the result after inclusion of the fiber direction.

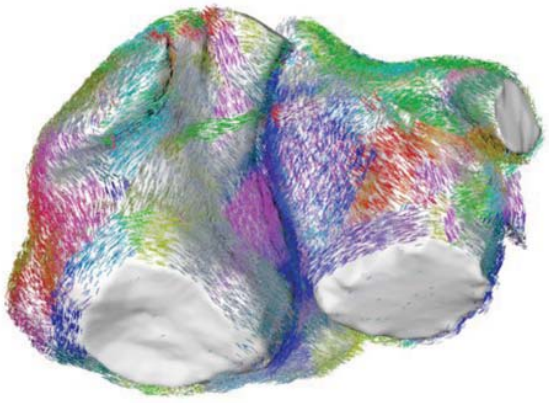

Fig. 2. Fiber direction, included into the anatomy of the atria of an individual patient.

C. Fibrotic Tissue and Late Enhancement MRI

In recent years it became possible to acquire late enhancement MRI (LE-MRI) data of the human atria [29], [30]. This way, changes in tissue properties can be visualized that originate from a delayed wash out of a contrast agent. A plausible hypothesis claims that LE-MRI depicts fibrotic tissue, which is extremely relevant for further electrophysiological modeling. In addition, scars that originate from former ablation procedures might become visible. In the framework presented here, areas that give a large signal in LE-MRI can be segmented and included into the geometrical model of the atria as an additional label [11].

III. Modeling Electrophysiology

A. Cell and Tissue Models and Remodeling

All electrophysiological models presented in this work are based on the atrial cell model of Courtemanche et al. (CRN) [31].

In a first line, a cellular automaton is parametrized using the CRN model. Cells are coupled to form small patches of atrial tissue and the action potential is calculated and stored for various heart rates and interstimulus intervals. These data are used in a cellular automaton: if a "cell" is depolarized from a neighboring cell, it will follow the predefined slope of the action potential, and it will depolarize the neighboring cells with a certain predefined CV. This way, a realistic spread of depolarization for sinus rhythm can be calculated very fast. In case of AF the cellular automaton shows some deficiencies.

In a second line, the complete electrophysiological cell model can be used for all "cells" at any time instant using the monodomain or even the bidomain scheme [32], [33]. This will deliver more realistic results with larger numerical effort.

In addition in a third line, a phenomenological cell model was implemented: a Minimal Model (MM) [34], originally developed for ventricular cells, was adapted to the human atria. Instead of 12 ion channels that the CRN model takes into account, it only considers 3 ion channels and 4 state variables. It is possible to mimic the full CRN model in various situations with significantly reduced computational effort [35].

Patients undergoing an ablation procedure are very unlikely to show physiological action potentials. An atrial computer model aiming at being similar to a patient's heart must take into account the most important remodeling processes [36]. In this project the cellular automaton, the CRN model and the Minimal Model have been adapted to remodeled atria [37].

Fig. 3 shows an example of a simulation of sinus rhythm using the anatomy of an individual patient's heart.

B. BSPM Measurements and Inverse Problem.

Information about the electrophysiological properties of the patient's heart can be gained non-invasively via Body Surface

Potential Mapping (BSPM). In this work an 80 channel system (Biosemi, Amsterdam) was employed. All electrodes are localized with a magnetic localizer (Polhemus).

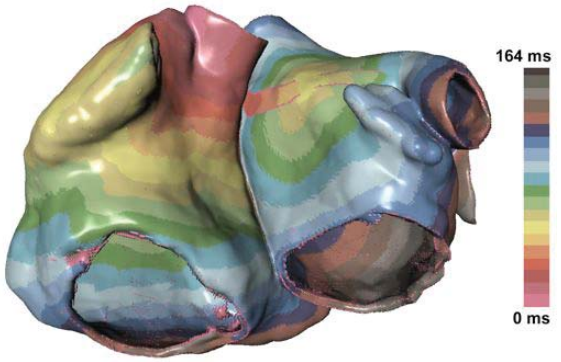

Fig. 3. Simulation of sinus rhythm, using the anatomy of an individual patient's atria including fiber distribution. Activation times are depicted color-coded.

The first idea to derive electrophysiological data from BSPM is to solve the inverse problem. The additional effort is a thorax scan of the patient (CT or MRI), a segmentation procedure for the most important organs [38] and the calculation of the lead field matrix using e.g. FEM. Activation time imaging delivered promising results about the localization of the sinus node and the origin of extrasystoles [39], [40]. But unfortunately, the inverse problem of ECG is extremely ill-posed for atrial sources and details are smeared out.

Another promising approach is the successive forward calculation of various hypotheses about the spread of depolarization and the CV with a subsequent comparison of the simulated and the measured BSPMs [41]. This way quite accurate data about the interatrial conduction path and the global CV can be gained.

Fig. 4 shows a comparison of a measured and a simulated BSPM temporal integral map after adjusting the interatrial conduction path and the CV to the individual patient.

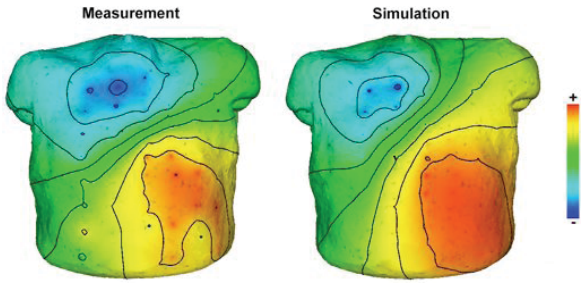

Fig. 4. Comparison of a measured and a simulated BSPM integral map of the P-wave, after adjusting the interatrial conduction path and the CV to the individual patient.

C. Intracardiac Measurements and Extraction of Electrophysiological Properties

Before any RF-ablation procedure in human atria can be started, a thorough investigation of the intracardiac electric signals using multi-electrode catheters must be carried out. These data can be employed to further adapt the computational model to the patient concerning electrophysiology.

In this framework, a method is applied that allows for the detection of the local direction of a wavefront and the CV of a single heart beat using the data of a circular multi-electrode catheter [42]. These data can directly be incorporated into all three atrial models (cellular automaton, Minimal Model and CRN). In addition, a restitution curve can be measured by using a stimulation pulse train with accelerated frequency.

Fig. 5 shows an example of detecting the wavefront direction from sinus rhythm and various stimulation sites.

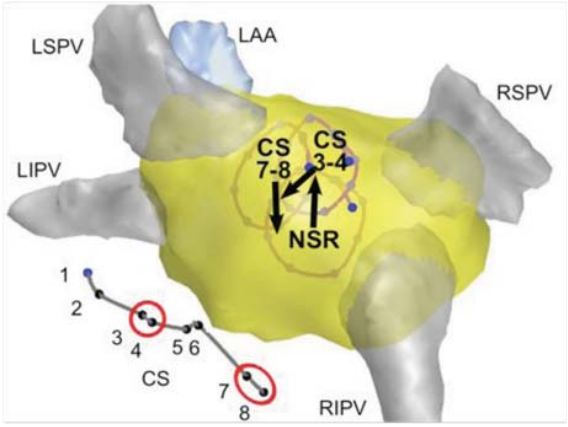

Fig. 5. Results of the detection of wavefront directions from sinus rhythm (NSR) and two stimulation sites in coronary sinus (SC 7-8 and CS 3-4).

In case that Complex Fractionated Atrial Electrograms (CFAEs, [43]) are observed, they can be classified automatically based on characteristic features and an image of the atria with an overlay of CFAE classes can be depicted [44], [45]. How precisely the information about areas with CFAEs has to be included into the electrophysiological models is not clear until now. This is a very important field of ongoing research [46]. Fig. 6 shows the result of a visualization of CFAE classes onto the anatomical model of the atria of a patient.

IV. Validation

A. Validation of Geometry

For the validation of the segmentation algorithms the standard methods of medical image processing have been

used: (a) the segmentation results have been compared to the original image data by experts and (b) a database of several manually segmented atria was created and compared to the automatically generated segmentation results using several measures of segmentation error (e.g. mean and maximum vortex to surface error [21]).

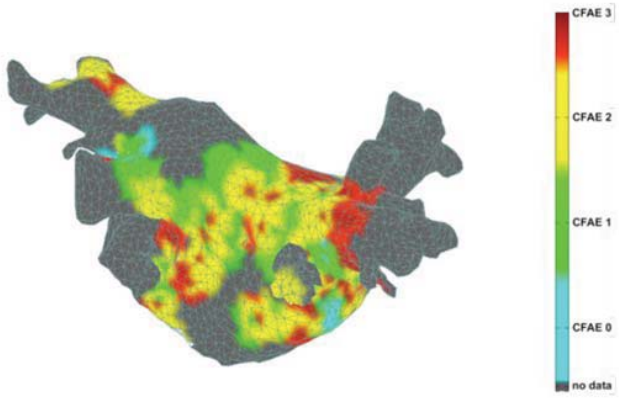

Fig 6. Visualization of CFAE classes as an overlay onto the anatomy of the atria of a patient. CFAE class 0: no irregular findings, CFAE class 1: periodic fractionated wave packages, CFAE class 2: irregular and frequent fractionated waves, CFAE class 3: continuous fractionated signals.

A systematic validation of the estimated thickness of the atrial wall and the estimated fiber direction is not possible until today. The thorough inspection by clinical experts is the only option to "validate" the results.

B. Validation of Electrophysiology

A validation of the individualized electrophysiology is also a difficult task. Today we only see one option: First the electrophysiological parameters are adjusted to the patient with a set of signals (sinus rhythm, flutter, fibrillation, stimuli with known origin). Next a new and independent stimulus is given to the heart. The resulting spread of depolarization is both simulated with the individual heart model and measured with a circular multi-electrode catheter and - if possible - a BSPM. The measured and simulated bioelectric signals are compared. The heart model is assumed to be equal to the patient's heart if the error is smaller than a predefined threshold.

This thorough evaluation has only been carried out with one patient until now and the results are very promising. Endocardial electrograms could be predicted with acceptable accuracy [47].

V. Discussion

A framework to adapt a computational model of the heart to an individual patient was outlined. Methods for validation have been suggested. The validation of the segmentation procedure is straight forward. Methods to validate the electrophysiological model are difficult and not reported in the literature until now. A procedure to predict measured data resulting from well-defined stimuli that have not been used for the adaptation procedure is suggested.

On the long run for the physician the clinical result is more important than the error between model and reality. The crucial question finally is: does the computer assisted planning of RF-ablation improve clinical outcome?

Acknowledgment

Research leading to these results has received funding from the European Community Seventh Framework Programme (FP7/2007-2013) under grant agreement no 224495 (euHeart project) and from Philips Research.

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