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Computer Based Optimization of Biventricular Pacing According to the Left Ventricular 17 Myocardial Segments

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***Abstract*— Cardiac resynchronization therapy (CRT) has shown to improve hemodynamics and clinical symptoms of congestive heart failure. The present article investigates an automated non-invasive strategy based on a computer model of the heart to optimize biventricular pacing as a CRT with respect to electrode positioning and timing delays. Accurate simulations of the electrical activities of the heart require suitable anatomical and electrophysiological models. The anatomical model used in this work, is based on segmented MR data of a patient in which a variety of tissue classes for left ventricle are considered based on AHA standard in accordance with fiber orientation. The excitation propagation is simulated with the ten Tusscher et al. electrophysiological cell model using an adaptive cellular automaton. The simulated activation times of different myocytes in the healthy and diseased heart model are compared in terms of root mean square error (E_{RMS}). The results of our investigation demonstrate that the efficacy of biventricular pacing can greatly be improved by proper electrode positioning and optimized A-V and V-V delay.**

I. INTRODUCTION

CARDIAC resynchronization therapy (CRT) with biventricular pacing (BVP) has emerged an important and indispensable treatment option in patients with moderate to advanced heart failure and left bundle branch block.

In patients with congestive heart failure, CRT leads to improved hemodynamics, better exercise capacity associated with a significantly better quality of life and less frequent hospitalization [1]. Despite its overall efficiency, 30% of CRT recipients do not appear to benefit. This may be subjected to inappropriate treatment selection or suboptimal implementation of the therapy [2-5]. Since optimization of pacing parameters such as atrio-ventricular (A-V) delay, intra-ventricular (V-V) delay and pacing lead positions in clinical way is invasive and time consuming, an automated optimization algorithm is suggested through computer simulation in this work. This optimization algorithm is an automatic, non-invasive procedure based on a computer model of the heart. The standard segments of the left ventricle recommended by American Heart Association (AHA) are used to determine different lead positions and stimuli assuming the pathologies left bundle branch block (LBBB) and infarction. The latest recommendation of the AHA suggests the use of the 17-myocardial segments model for the left ventricle. Each segment has been assigned to one of the three major coronary arteries, which is useful to model the myocardial infarction in the corresponding segment [6].

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II. METHODS

A. Computer Model

In this work, the three dimensional MRI data of a patient with left bundle branch block and minor infarction is used as anatomical model. The resolution of the data was 196 x 163 x 180 cubic voxels with 1 mm side length.

Using publications from AHA [6-7] as shown in Fig. 1, the left ventricle was subdivided into 17 segments in which myocardial infarction and ischemic areas could be placed.

An adaptive cellular automaton, which is a computer heart cell model, was used for this study. It has been applied previously to model complex arrhythmia and their therapies through electrophysiological model adoption [8-9]. The adaptive cellular automaton (ACA) utilizes pre-calculated action potentials based on ten Tusscher et al. electrophysiological cell model in order to simulate the electrical excitation propagation within the heart [10]. The ACA is composed of a finite number of nodes. Each node corresponds to a set of heart myocytes possessing the same properties in a small region of the heart. By a given time instant, the state of each node in the cellular automaton changes depending on the states of a finite number of neighboring nodes and the node's own state in the previous time steps. Different nodes may obey different criteria for state transition. The state of each node is interpreted as transmembrane voltage at a given time instant.

The criterion describing the transition include the electrophysiological parameters, type of cardiac tissue, time course of the transmembrane voltage during excitation, conduction velocity and fiber orientation in myocardium.

In addition, the fiber orientation of ventricular myocytes and the transmural heterogeneity of the myocardium have been taken into account in the model. Fig. 2 demonstrates

the transmural heterogeneity model extracted from ten Tusscher ventricular cell model.

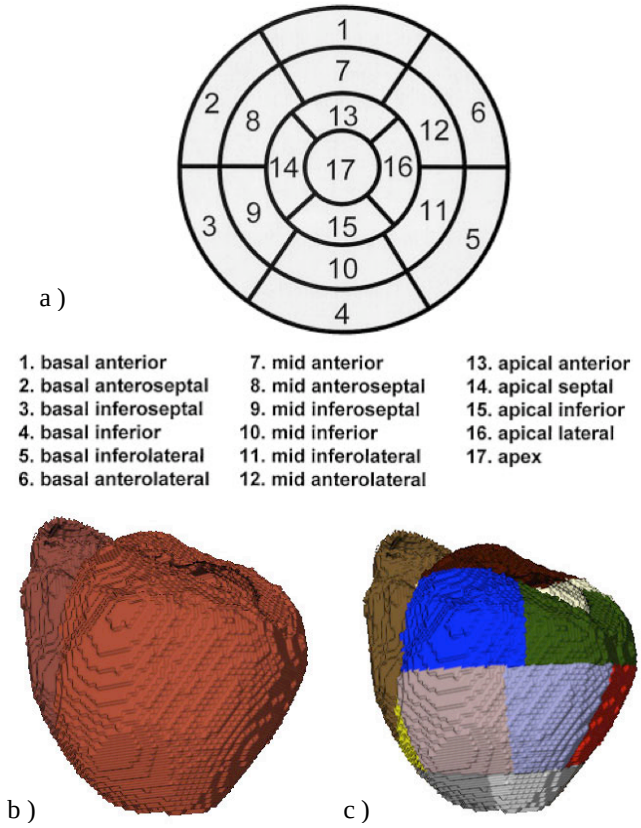

Fig. 1. a) 17 myocardial left ventricular segments [6] b) Ventricular model of the patient data, c) Segmented ventricular model based on AHA standard.

The excitation propagates in a model of bundle branches which consists of a conduction tree with atrio-ventricular (AV) node, bundle of His, left and right Tawara branches, the anterior/posterior left fascicle and the Purkinje fibers in both ventricles.

By adjusting the parameters of the cellular automaton and changing the electrical and physiological properties of a certain region in the heart model, different pathologies can be modeled. LBBB occurs when transmission of cardiac electrical excitation is delayed or fails to conduct along the main left bundle branch. Thus, the LBBB was set by blocking the left branch so that the conduction could not be propagated but the rest of the Purkinje fibers stay intact and can conduct.

Myocardial infarction, which is identified by the rapid development of irreversible myocardial necrosis, is caused by an imbalance of oxygen supply due to the blockage in a coronary artery [11-12]. Myocardial infarction consists of necrotic tissue in the center and a transition zone of ischemic tissue with gradually changing properties. This results in a change of excitation propagation ability for cardiac cells. This change is illustrated in Fig. 3 [13] as a propagation velocity factor dependent on the radius of spherical infarction zone.

In this work excitation propagation velocity and action potential amplitude of myocardial cells were set to zero in the center, while a slower conduction velocity and smaller action potential amplitude were set for the ischemic zone. The AHA classification has been utilized to set the infarction in the corresponding segment according to blockage of its coronary artery.

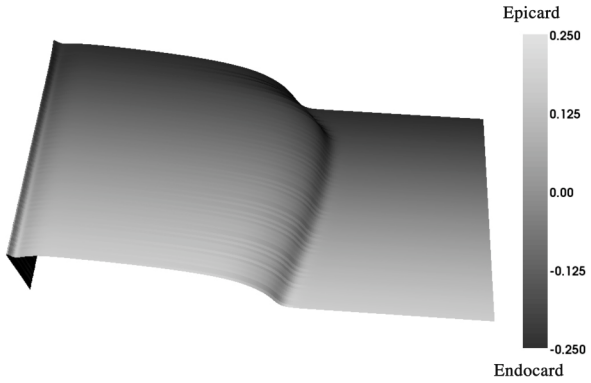

Fig. 2. The simulated action potential curves changing from endocardium to epicardium (right) [10].

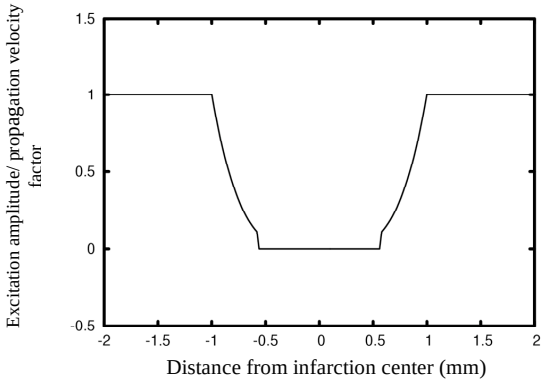

Fig. 3. The dependence of excitation amplitude and propagation velocity factor from the distance to the center of infarction [13]

B. BVP and Optimization Algorithm

Three electrodes are used to implement the biventricular pacing: one for sensing and two for stimulation. In this work, the right ventricular stimulation electrode was placed in the right ventricular apex. Various left ventricular pacing leads were inserted into the anterior and posterior branches of coronary sinus (Fig. 4). Myocardial infarction for each segment of 17 subdivisions and LBBB was implemented for the model in order to simulate the pathology. Thus, 17 pathologies with 8 electrode pacing set-ups as a therapy were carried out.

The aim of the optimization is to find the best positions for electrode set-up and proper timing delay (atrio-ventricular and intra-ventricular) for a pathological model, which leads to a depolarization sequence similar to the healthy model.

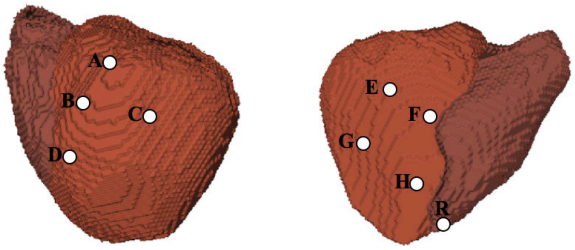

Fig. 4. The electrode positions in the ventricle model of the patient (in anterior and posterior branches of coronary sinus). Electrodes A, B, … H are referred to the left ventricular stimulation. Electrode R is referred to the right ventricular stimulation.

This optimization was implemented based on minimizing the difference of the isochrones (activation time for each myocyte in a cardiac cycle) between pathological case (with pacing) and healthy physiological case, which represents normal conditions without pathology or reduction of conduction velocity [14].

This difference was computed in terms of root mean square error (E_{RMS}):

$$E_{RMS} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(x_i - e_i\right)^2} \qquad (1)$$

Thus, the E_{RMS} delivers the deviation of the activation time of the pathology from sinus rhythm for the whole number of voxel elements N with the activation time x_i of voxel i for the sinus rhythm and the activation time e_i of voxel i for the pathology. By placing stimuli at the ventricles, the activation of the myocardium is forced to be closer to the physiological activation time. Thus, an optimization can be achieved by minimizing the E_{RMS} through adjustment of the A-V and V-V delay. So far, cardiac output is considered as the criterion for optimal pacing [15]. However, given clinical validation, the optimization of isochrones provides an alternative, automatic, non-invasive approach to CRT optimization.

For each electrode pair, the smallest resulted E_{RMS} yields the proper timing delay. Overall 8 lead positioning set-up were considered for each pathology.

An A-V delay of 60-260 ms with 20 ms increments and V-V delay of -30 ms to 70 ms with 10 ms increments were used for the estimation of optimal timing delays. Thus 986 simulations have been executed automatically according to each pathological set-up [16-17].

C. Results

A variety of infarctions in different ventricular segments was simulated to yield reference values for the optimization algorithm. Different A-V and V-V delay in conjunction with various electrode set-ups were simulated to gain the isochrones.

The calculated E_{RMS} for no-pacing cases and the best-achieved pacing results containing the minimal E_{RMS} are illustrated in Table 1. According to this table an improvement of 15% to 27% in E_{RMS} for ischemic heart with LBBB is achieved in this work. For a non-ischemic heart with LBBB the improvement is 73%, which is obvious due to the lack of the infarction. It can be noticed that the A-V delay for all optimum results is mostly between 200-240 ms. The V-V delay is mostly positive. That means the left electrode should be stimulate before the right electrode. A sample result of the optimization algorithm in terms of transmembrane voltage in the same time instant for physiology (sinus rhythm), pathology considering the LBBB and infarction in segment 5 and pacing is demonstrated in Fig. 5. It can be observed that the computed error for therapy is significantly smaller compared to the computed error from pathology.

TABLE I

The E_{RMS} results for no-pacing, best pacing set-up and the improvement percentage

Pathology	Position of infarction	No-pacing	Pacing				
		E_{RMS} (ms)	Electrode set-up	A-V delay (ms)	V-V delay (ms)	E_{RMS} (ms)	% Improvement
LBBB with infarction	Segment 1	48.68	RC	220	20	39.05	19.78
	Segment 2	47.39	RC	220	20	38.26	19.26
	Segment 3	48.32	RC	220	-10	39.03	19.22
	Segment 4	50.46	RA	220	20	40.55	19.63
	Segment 5	51.97	RF	240	-20	41.28	20.56
	Segment 6	48.94	RG	240	40	38.66	21.02
	Segment 7	59.16	RG	240	40	44.16	25.35
	Segment 8	47.37	RA	220	20	40.38	14.75
	Segment 9	54.24	RE	240	0	45.98	15.22
	Segment 10	53.24	RG	220	20	43.42	18.44
	Segment 11	53.33	RA	200	40	42.32	20.64
	Segment 12	61.15	RA	200	20	45.05	26.32
	Segment 13	61.43	RC	200	10	48.14	21.63
	Segment 14	50.78	RG	220	60	43.88	13.58
	Segment 15	49.79	RE	200	60	43.95	11.72
	Segment 16	53.62	RE	240	0	46.09	14.04
	Segment 17	50.44	RF	240	20	43.40	13.95
LBBB w/o infarction	---	37.17	RK	240	0	10.12	72.77

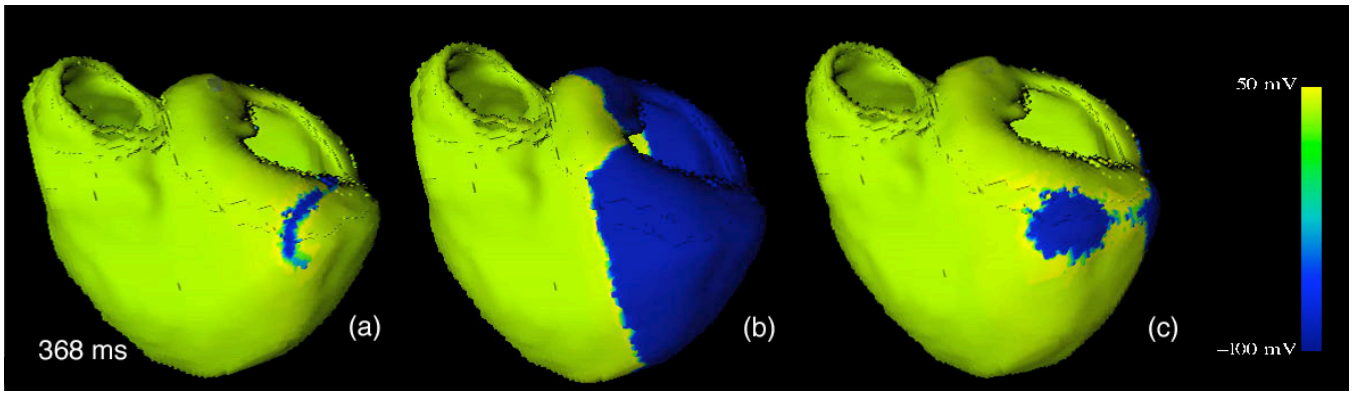

Fig. 5. Sample simulation results of transmembrane voltage in time instant of 368 ms: (a) sinus rhythm, (b) Pathology including LBBB and infarction in segment 5, (c) optimized pacing.

I. Conclusion

This work proposes a non-invasive optimization algorithm to find the best electrode positioning sites, A-V and V-V delay for a patient data set including LBBB and infarction as pathology. The AHA standard model was used to divide the left ventricle into 17 segments, which simplified the infarction positioning. Different pacing site and stimuli were applied to the simulated model with respect to the pathology of the patient model to compute the isochrone as a performance indicator.

In future the implemented work based on AHA Classification will be used in conjunction with Tissue Doppler imaging (TDI) data to identify the delayed longitudinal contraction (DLC) [18]. This way, cardiac contraction will be incorporated into the model. In addition to the clinical validation, ECG measurements will have to be carried out to measure non-invasively the heart activity by means of body surface potential map. A validation of the optimization strategy with different parameters such as blood pressure, stroke volume will have to be carried out in experimental as well as clinical studies

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