Noninvasive, automatic optimization strategy in cardiac resynchronization therapy

Matthias Reumann, Brigitte Osswald, Olaf Doessel***
Computational Biology Center, IBM TJ Watson Research Center, New York, USA
*Department of Cardiac Surgery, University of Heidelberg, Heidelberg, Germany
**Institute of Biomedical Engineering, Karlsruhe University (TH), Karlsruhe, Germany

ABSTRACT

Objective: Optimization of cardiac resynchronization therapy (CRT) is still unsolved. It has been shown that optimal electrode position, atrioventricular (AV) and interventricular (VV) delays improve the success of CRT and reduce the number of non-responders. However, no automatic, noninvasive optimization strategy exists to date.

Methods: Cardiac resynchronization therapy was simulated on the Visible Man and a patient data-set including fiber orientation and ventricular heterogeneity. A cellular automaton was used for fast computation of ventricular excitation. An AV block and a left bundle branch block were simulated with 100%, 80% and 60% interventricular conduction velocity. A right apical and 12 left ventricular lead positions were set. Sequential optimization and optimization with the downhill simplex algorithm (DSA) were carried out. The minimal error between isochrones of the physiologic excitation and the therapy was computed automatically and leads to an optimal lead position and timing.

Results: Up to 1512 simulations were carried out per pathology per patient. One simulation took 4 minutes on an Apple Macintosh 2 GHz PowerPC G5. For each electrode pair an optimal pacemaker delay was found. The DSA reduced the number of simulations by an order of magnitude and the AV-delay and VV- delay were determined with a much higher resolution. The findings are well comparable with clinical studies.

Conclusion: The presented computer model of CRT automatically evaluates an optimal lead position and AV-delay and VV-delay, which can be used to noninvasively plan an optimal therapy for an individual patient. The application of the DSA reduces the simulation time so that the strategy is suitable for pre-operative planning in clinical routine. Future work will focus on clinical evaluation of the computer models and integration of patient data for individualized therapy planning and optimization. *(Anadolu Kardiyol Derg 2007: 7 Suppl 1; 209-12)*

Key words: cardiac resynchronization therapy, automatic optimization, computer models

Introduction

An individualized optimization strategy for biventricular pacing (BiVP) as cardiac resynchronization therapy is not yet feasible in daily clinical routine (1, 2). This work presents an optimization strategy with which optimal electrode position, atrio-ventricular (AV) and interventricular (VV) delays can be computed fast and automatically to make the application suitable for clinical practice.

Methods

This work builds on optimizing BiVP by using an adaptive cellular automation to compute the activation times of a cardiac cell in a computer model of the heart based on a detailed anatomical model including fiber orientation and heterogeneity. The anatomical models were given by a heart failure patient and the Visible Man data-set (National Library of Medicine, Bethesda, USA). The pathologies simulated were an AV block and a left bundle branch block (LBBB). For each, the left ventricular conduction velocity was reduced by 0%, 20% and 40%. The root mean square error E_{RMS} of the activation times during sinus rhythm versus pathology/therapy was used as optimization parameter (3). Overall 12 different left ventricular electrode positions (Fig. 2) were investigated, which cover more electrode positions tested in clinical trials yet (4). Four were placed in the anterior coronary sinus branches, four were put in the posterior coronary sinus branches and four were placed on the left ventricular free wall to evaluate the electrode position independently of the coronary sinus branches. The right ventricular lead was placed in the apex. The AV and VV delays were determined by the Downhill Simplex Algorithm (DSA) (5). The DSA is moving the triangle to the minimum of the parameter space (Fig. 1). A termination criterion $c_{termination}$ is defined to stop the iteration:

$$\frac{max\left(E_{RMS}\right) - min\left(E_{RMS}\right)}{max\left(E_{RMS}\right) + min\left(E_{RMS}\right)} < c_{termination}$$

with $c_{termination}$=0.0005, min(ERMS) being the lowest value of the three simplex points and max(ERMS) being the highest value after an iteration step.

The results were compared with sequentially searching the 2 dimensional parameter space given by AV and VV delays. The timing was set according to literature (6) by sampling the AV delay between 60 - 220 ms/260 ms (Visible Man/patient) with increments of 20 ms. For each AV delay, the VV delay was set to -30 - 50 ms/70 ms (Visible Man/patient) with 10 ms increments.

Address for Correspondence: Matthias Reumann, PhD, Computational Biology Center, IBM TJ Watson Research Center, 1101 Kitchawan Road, Route 136 Yorktown Heights, NY 10598 USA Phone: +49-177-6727731 Fax: +1 - 914 945-4217 E-mail: mreumann@ieee.org

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A negative VV delay in this work means that the right ventricular electrode is pacing before the left ventricular electrode.

Results

Up to 1512 simulations were carried out per pathology per patient. One simulation took 4 minutes on an Apple Macintosh 2 GHz PowerPC G5. Tables 1 and 2 summarize the results and Figure 2 gives an example of the optimal electrode positions in the patient data-set. The optimal electrode positions are in accordance with clinical practice. The optimal timing delays are within the range described in clinical studies. The DSA reduced the number of simulations to 15 - 25% of the simulations needed for the sequential search.

The DSA achieves a lower ERMS value for all pathologies and both anatomical data-sets except the AV block pathology in the Visible Man data-set where it performs slightly less good. But it achieves a better temporal resolution with respect to AV and VV delay setting.

Discussion

A minimal error was found for each electrode set-up. This means that the optimization could be carried out preoperatively - to determine optimal pacing lead position with the respective AV and VV delays - and it can also be run postoperatively to find the optimal timing delays for a given electrode position. The method

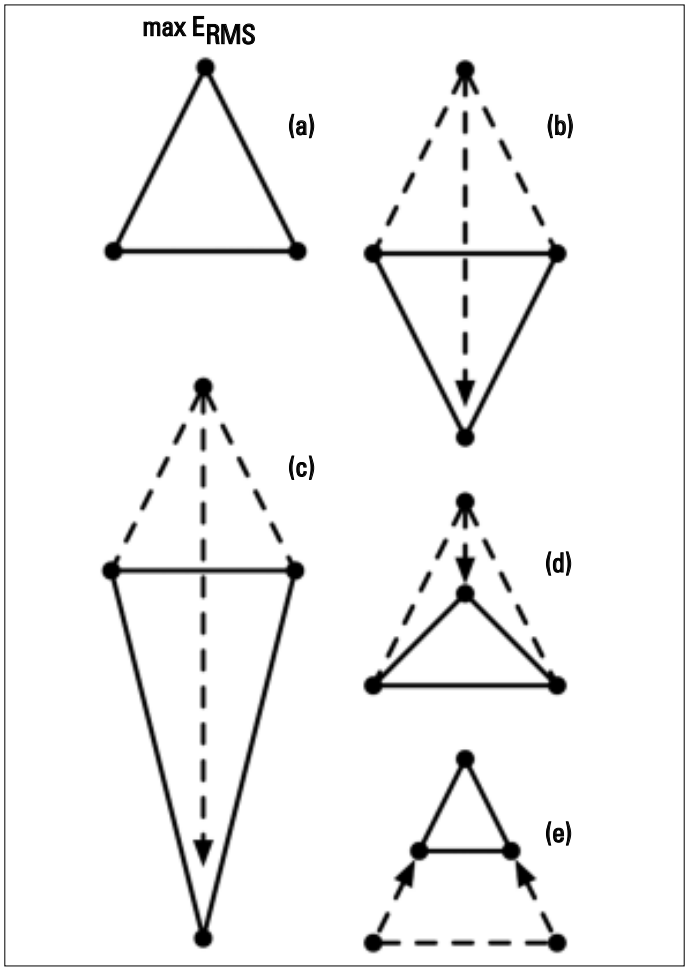

Figure 1. Possible outcomes for an iteration step of the Downhill Simplex Algorithm: (a) The initial simplex defines a triangle in two dimensions. The points define the parameters, i. e. the AV and VV delays for the three initial simulations. The resulting ERMS are sorted from lowest to highest value. The point of the highest value max(ERMS) will be reflected to find a new parameter set for the next simulation (b). If the new value is below the previous max(ERMS), the reflection is extended by factor two (c). If it is higher, the simplex will be compressed in one dimension (d). The last step in the iteration is a contraction in multiple dimension (e) before the algorithm starts the next iteration step. The points indicate the vertices, the lines the sides of the simplex. The dashed lines indicate the position of the previous simplex and the dashed arrows show the direction in which the vertices move.

AV- atrioventricular, ERMS- root mean square error of the activation times, VV- interventricular

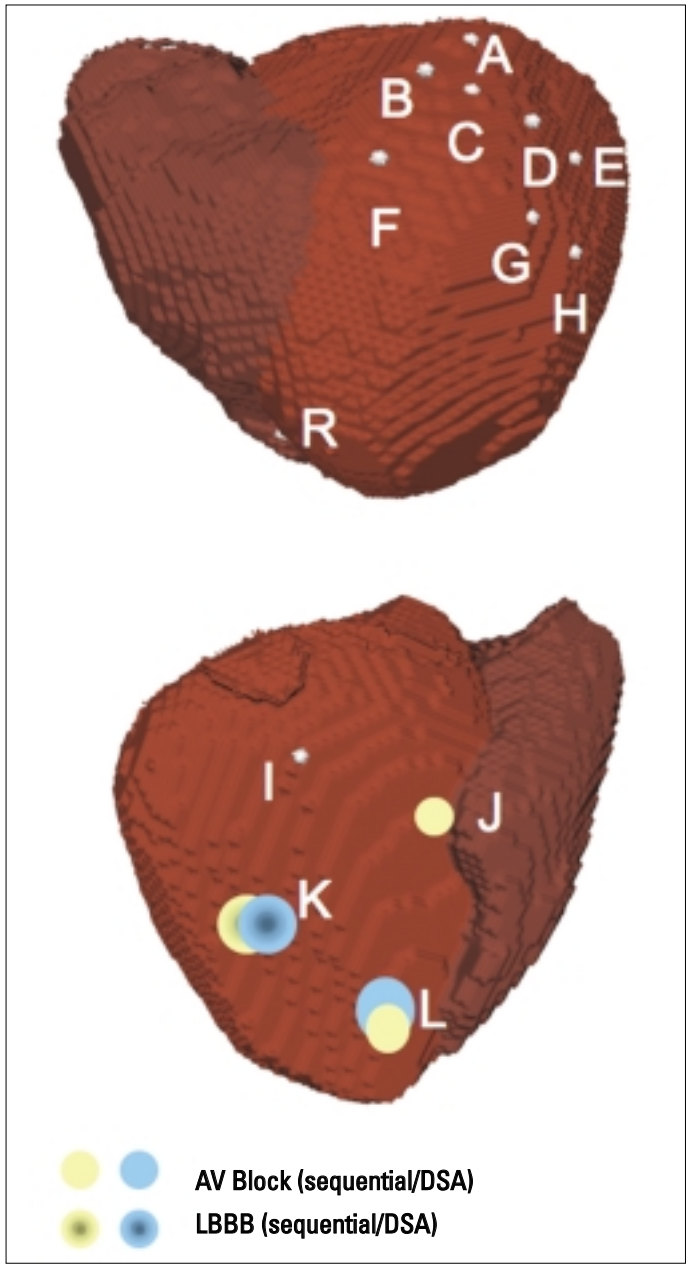

Figure 2. The figure shows the optimal left ventricular lead positions for the patient data-set.

AV- atrioventricular, DSA- Downhill Simplex Algorithm, LBBB- left bundle branch block

of optimization is independent on anatomical shape as well as pathophysiology so far. However, general trends could be observed: the lower the interventricular conduction delay, the lower the optimal AV delay. With respect to VV delay setting, a general rule cannot be determined. It has to be set independently with respect to electrode position and pathology.

Comparing with clinical studies the advantage of the presented strategy is that a multitude of electrode positions as well as AV/VV delay combinations can be investigated automatically and noninvasively, which has not been done in clinical studies yet.

Conclusion

The presented method reduces the number of simulations required drastically. While previous optimization simulations took around 5 days for one pathology and 12 pacing lead set-ups, the DSA reduces the simulation time to even less than 15 hours. Given a patient is admitted to the clinic the night before pacemaker implantation, the optimal AV and VV delays as well as electrode position could be computed automatically with a non-invasive strategy given the presented model is clinically validated. A current project of the Institute of Biomedical Engineering,

Table 1. Optimal electrode position, AV and VV delays for each pathology using both sequential search and Downhill Simplex Algorithm for the Visible Man model

Pathology	Pacing lead	AV delay, ms	VV delay, ms	E_{RMS}, ms	Number of simulations	Optimization algorithm
AV block -0%	RA	100	20	3.99	972	Sequential
AV block -20%	RL	100	10	4.59	972	Sequential
AV block -40%	RA	60	40	5.91	972	Sequential
LBBB -0%	RB	120	-10	5.28	972	Sequential
LBBB -20%	RB	100	0	6.84	972	Sequential
LBBB -40%	RK	60	30	9.50	972	Sequential
AV block -0%	RI	234	117	3.18	301	DSA
AV block -20%	RI	217	117	4.23	280	DSA
AV block -40%	RG	343	-134	5.19	256	DSA
LBBB -0%	RH	220	138	5.23	226	DSA
LBBB -20%	RE	206	13	6.77	225	DSA
LBBB -40%	RK	188	34	9.49	219	DSA

AV block- atrioventricular block, DSA- Downhill Simplex Algorithm, E*RMS*- root mean square error of the activation times,
LBBB- left bundle branch block, VV- interventricular. The percentage indicates the reduction of interventricular conduction velocity

Table 2. Optimal electrode position, AV and VV delays for each pathology using both sequential search and Downhill Simplex Algorithm for the patient model

Pathology	Pacing lead	AV delay, ms	VV delay, ms	E_{RMS}, ms	Number of simulations	Optimization algorithm
AV block -0%	RJ	260	0	3.21	1452	Sequential
AV block -20%	RL	260	-20	3.28	1452	Sequential
AV block -40%	RL	240	-30	4.63	1452	Sequential
LBBB -0%	RK	160	70	10.12	1452	Sequential
LBBB -20%	RK	160	40	13.50	1452	Sequential
LBBB -40%	RK	120	20	19.66	1452	Sequential
AV block -0%	RL	249	111	3.90	282	DSA
AV block -20%	RL	234	127	4.27	330	DSA
AV block -40%	RL	211	109	5.38	387	DSA
LBBB -0%	RK	228	11	9.89	265	DSA
LBBB -20%	RK	188	34	12.59	284	DSA
LBBB -40%	RK	109	84	18.92	212	DSA

AV block- atrioventricular block, DSA- Downhill Simplex Algorithm, ERMS - root mean square error of the activation times,
LBBB- left bundle branch block, VV- interventricular. The percentage indicates the reduction of interventricular conduction velocity

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Karlsruhe University (TH) and the Cardiology, Faculty Mannheim, and the Cardiac Surgery of the University of Heidelberg targets this issue based on this work. In future, a contraction and deformation model (7-9) will be included to compute the cardiac output.

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