Experimental Study of Atrial Fibrillation Cycle Length During Rapid Atrial Septal Pacing

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Abstract

Computer model-based simulations have shown that rapid stimulation at 60-100% of atrial fibrillation cycle length (AFCL) from a ring of electrodes located around the septum may induce local capture in both atria for most AF dynamics. The present study aims to investigate whether model-based results on AF septal pacing can be translated to experimental simulations. Acute experiments on swine hearts were performed in vivo. The septal ring of electrodes was experimentally implemented using a decapolar lasso catheter placed against the septal wall. Rapid septal pacing was applied in sequences of 10-sec simultaneously on four electrodes on the septal ring. The extent of local AF capture, defined as the ability of the rapid pacing sequence to take control over certain areas of the atria, was assessed via two decapolar mapping catheters in the right and left atrium. AFCL was measured on bipolar electrograms using a nonlinear filtering technique that uses short- and long-term electrogram energies for a robust CL extraction. AFCL was significantly higher in the right atrium compared to the AFCL in left atrium which indicates the existence of different AF dynamics in the two atria. Local capture was observed in both atria when pacing from four electrodes on the septum.

1. Introduction

Pacing algorithms are of interest for atrial fibrillation (AF) termination since they appear to be safe and usually well tolerated by patients [1-4]. However, clinical trials assessing rapid pacing for the treatment of AF have been inconclusive so far due to limitations of single site pacing, use of AF burden as endpoint and mixed AF populations.

Computer modelling has gained importance in the development of therapeutic strategies for atrial fibrillation [5,6]. Model-based simulations have shown capture of both atria during AF using rapid pacing from the whole septal area [7, 8]. AF septal pacing using rapid pacing at 62-70% AF cycle length (AFCL) for 10-30s, followed by a stepwise transition to slow pacing at 180% AFCL showed up to 29% of AF termination [8]. One of the advantages of this approach is that the pacing sequence is short (<30s) and can be repeated several times until termination occurs, which makes successful therapy outcome possible even if termination rate is low. Since pacing from the full septal area presents some practical limitations, pacing from a ring of stimulation electrodes around the septum has been also investigated in a previous model-based study [9]. The results indicated that the number of stimulation electrodes has a moderate effect on the septal pacing outcomes, while changes in AF dynamics lead to divergent outcomes, suggesting that different types of AF may respond differently to septal pacing.

Moving to experimental validation is an essential phase with every model-based result. In this context, the present study investigated the translation from computer modeling to experimental testing of AF rapid septal pacing algorithms.

2. Methods

2.1. Experimental protocol

All animal procedures were performed in accordance with applicable local animal welfare regulations. The analysis presented in this article is based on data collected from acute animal experiments on swine hearts performed *in vivo*. AF was induced using rapid pacing of the vagus nerve and injection of neostigmine.

The septal pacing ring of stimulation electrodes was experimentally implemented using a decapolar lasso catheter placed against the septal wall using a transseptal approach. Once AF was induced, rapid septal pacing at different pacing cycle lengths (PCL) between 50-500 ms (2-20Hz; Grass S48 Stimulator, FHC Pulsar 6b Pulse Generator) was applied in sequences of 10-sec simultaneously on the four electrodes of pacing catheter. Figure 1 illustrates the pacing electrode configuration on

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the septal wall of the left atrium. Pacing thresholds from the lasso catheter against the septal wall were 0.6-1.2V and 1.4-2.3 mA.

Two mapping catheters were placed within the right and left atrium (Marinr® CS, 10 poles) in order to assess the extent of AF capture by septal pacing.

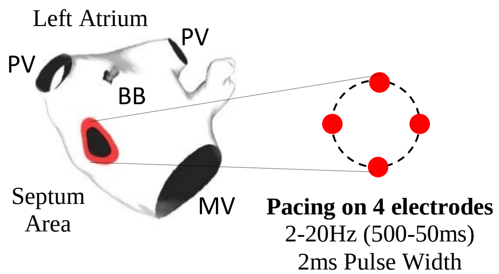


Figure 1. Electrodes configuration during septal pacing. MV : mitral valve; PV: pulmonary veins; BB: Bachmann's Bundle

2.2. Assessment of AF capture during rapid pacing

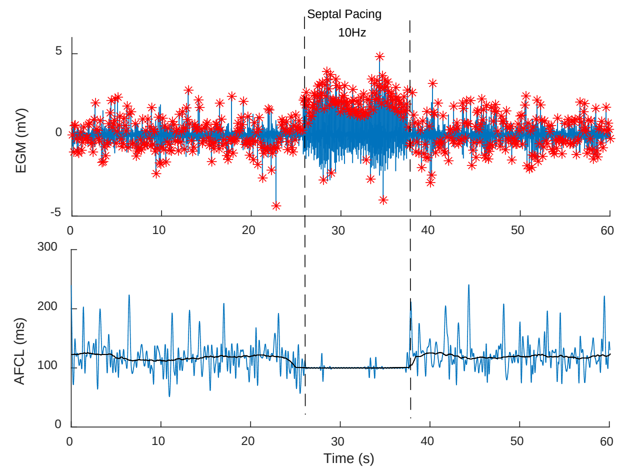
The extent of local AF capture, defined as the ability of the rapid pacing sequence to take control over certain areas of the atria, was assessed using the two catheters placed within the right and left atrium. One dipole neighbourhood was considered captured if the local CL was within ±5% of the PCL. AFCL was measured on bipolar electrograms using a nonlinear filtering technique that uses short- and long-term electrogram energies for robust AFCL extraction [10,11]. Sliding short- and long-term signal energies were measured for each sample in the EGM. A coefficient signal was then created as the ratio between the corresponding short- and long-term energies. Filtering was carried out by multiplying the coefficient signal with the EGM. Since atrial activations have relatively higher amplitude than that of the noise and other EGM activities, the coefficient signal values are close to one when atrial activation takes place, while insignificant otherwise.

2.3. Statistical analysis

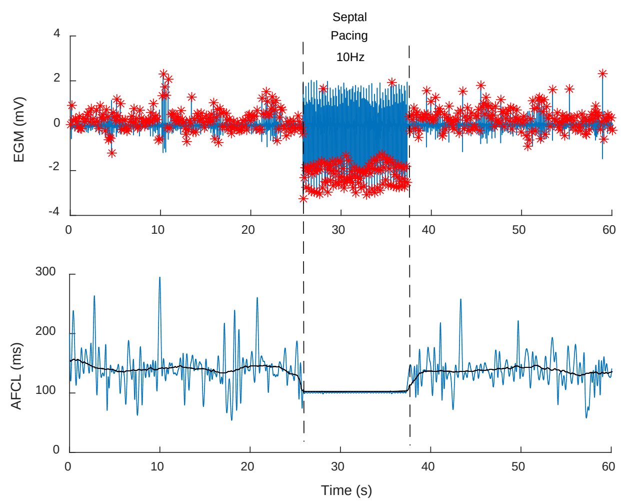
All values were expressed as a mean ± standard deviation. The statistical comparison between the data sets was performed using the two-sample *t*-test. Results were considered to be statistically significant at $p<0.05$.

3. Results

Figure 1 shows an example for a pacing sequence of 10-sec at a pacing rate of 10Hz (PCL = 100 ms). For each panel, the top plot shows 60-sec EGM signal acquired from the catheter placed within the left atrium (**A**) or within the right atrium (**B**); the bottom plot shows the instantaneous atrial CL estimated from the electrogram represented in the upper plot (average CL over a 500-ms sliding window is illustrated by solid black line). It can be observed that during pacing the local CL is very close to the PCL, which is indicative of a local capture of AF by the pacing sequence.



(A)



(B)

Figure 2. Example of rapid septal pacing. Continuous EGM signals acquired from the catheter in left atrium (A) and the catheter in right atrium (B) are illustrated together with detected atrial activations (red star). The instantaneous CL (blue) and an average CL (evaluated on a 500-ms sliding window) are indicated for each EGM.

Note that, local capture of AF was observed on all five dipoles of the mapping catheter placed in the right atrium and on only three dipoles (of five) of the left catheter.

It is worth noting that the local AFCL evaluated during AF (before septal pacing) on EGMs acquired separately from each dipole of the two mapping catheters was significantly higher in the right atrium compared to the AFCL in left atrium (130±12 ms vs 111±8 ms, $p<0.01$), which indicates the existence of different AF dynamics in the two atria.

4. Conclusion

The present experimental study entails the following findings: (*i*) local capture could be observed in both atria when pacing from the septum; (*ii*) AF dynamics significantly impacted the septal pacing outcomes. In fact, these findings show that AF septal pacing induces similar AF capture mechanisms in experimental settings and in computer simulations.

Different septal outcomes were obtained for the two atria which could be explained by the fact that the pacing cycle length was fixed (100 ms) and not adapted to the local AFCL. Moreover, the presence of different AF dynamics due to heterogeneities in vagal activation or in repolarization has been shown to affect the septal pacing outcomes in model-based simulations [7, 9]. All these results suggest that that different types of AF dynamics may respond differently to therapeutic pacing and the optimal pacing sequence has to be determined individually for each type of AF.

Additionally, it is noteworthy that pacing from only four electrodes located on the decapolar catheter was sufficient for a local capture of AF in experimental settings. This is in line with previous model-based results [9] which have indicated that pacing from a ring with 3-4 stimulation electrodes around the septum would be sufficient to induce AF capture for most AF dynamics.

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