

Original article

Modifications in Ventricular Fibrillation and Capture Capacity Induced by a Linear Radiofrequency Lesion

Francisco J. Chorro,^{a,b,*} Francisca Pelechano,^b Isabel Traperó,^c Xavier Ibañez-Catalá,^d Luis Such-Miquel,^e Álvaro Tormos,^d Juan Guerrero,^f Joaquín Cánoves,^a Luis Mainar,^a José Millet,^d Antonio Alberola,^g and Luis Such^g

^aServicio de Cardiología, Hospital Clínico Universitario de Valencia, INCLIVA, Valencia, Spain

^bDepartamento de Medicina, Universidad de Valencia, Estudi General, Valencia, Spain

^cDepartamento de Enfermería, Universidad de Valencia, Estudi General, Valencia, Spain

^dDepartamento de Electrónica, Universidad Politécnica de Valencia, Valencia, Spain

^eDepartamento de Fisioterapia, Universidad de Valencia, Estudi General, Valencia, Spain

^fDepartamento de Electrónica, Universidad de Valencia, Estudi General, Valencia, Spain

^gDepartamento de Fisiología, Universidad de Valencia, Estudi General, Valencia, Spain

Article history:

Received 29 April 2011

Accepted 8 September 2011

Available online 16 December 2011

Keywords:

Ablation

Electrical stimulation

Ventricular fibrillation

Radiofrequency

ABSTRACT

Introduction and objectives: An analysis was made of the effects of a radiofrequency-induced linear lesion during ventricular fibrillation and the capacity to capture myocardium through high-frequency pacing.

Methods: Using multiple epicardial electrodes, ventricular fibrillation was recorded in 22 isolated perfused rabbit hearts, analyzing the activation maps upon applying trains of stimuli at 3 different frequencies close to that of the arrhythmia: *a*) at baseline; *b*) after radio-frequency ablation to induce a lesion of the left ventricular free wall (length=10 [1] mm), and *c*) after lengthening the lesion (length=23 [2] mm).

Results: Following lesion induction, the regularity of the recorded signals decreased and significant variations in the direction of the activation fronts were observed. On lengthening the lesion, there was a slight increase in the episodes with at least 3 consecutive captures when pacing at cycles 10% longer than the arrhythmia (baseline: 0.6 [0.7]; initial lesion: 1 [1] no significant differences; lengthened lesion: 3 [2.8]; $P < .001$), while a decrease was observed in those obtained upon pacing at cycles 10% shorter than the arrhythmia.

Conclusions: The radio-frequency -induced lesion increases the heterogeneity of myocardial activation during ventricular fibrillation and modifies arrival of the activation fronts in the adjacent zones. High-frequency pacing during ventricular fibrillation produces occasional captures during at least 3 consecutive stimuli. The lengthened lesion in turn slightly increases capture capacity when using cycles slightly longer than the arrhythmia.

© 2011 Sociedad Española de Cardiología. Published by Elsevier España, S.L. All rights reserved.

Modificaciones de la fibrilación ventricular y de la capacidad de captura inducidas por una lesión lineal con radiofrecuencia

RESUMEN

Introducción y objetivos: Analizar los efectos, en la fibrilación ventricular y en la capacidad de capturar al miocardio mediante estimulación a frecuencias rápidas, de una lesión lineal producida con radiofrecuencia.

Métodos: En 22 corazones de conejo aislados y perfundidos, se utilizaron electrodos múltiples epicárdicos para registrar la fibrilación ventricular. Se analizaron los mapas de activación al aplicar trenes de estímulos a tres frecuencias distintas, cercanas a las de la arritmia, en tres situaciones: *a*) básicamente, *b*) tras producir con radiofrecuencia una lesión en la pared libre del ventrículo izquierdo (longitud, 10 ± 1 mm), y *c*) tras ampliar su extensión (longitud, 23 ± 2 mm).

Resultados: Tras la lesión, se observó una disminución de la regularidad de las señales registradas y variaciones significativas en la dirección de los frentes de activación. Con la lesión ampliada, se incrementaron ligeramente los episodios con al menos tres capturas consecutivas al estimular con ciclos un 10% más largos que los de la arritmia (basal, 0,6 ± 0,7; lesión inicial, 1 ± 1, diferencias no significativas; lesión ampliada, 3 ± 2,8; $p < 0,001$), mientras que se redujeron los obtenidos al estimular con ciclos un 10% más cortos que los de la arritmia.

Conclusiones: La lesión efectuada con radiofrecuencia aumenta la heterogeneidad de la activación miocárdica durante la fibrilación ventricular y modifica la llegada de los frentes de activación a las zonas adyacentes. La estimulación durante la fibrilación ventricular a frecuencias rápidas provoca capturas

Palabras clave:

Ablación

Estimulación eléctrica

Fibrilación ventricular

Radiofrecuencia

* Corresponding author: Servicio de Cardiología, Hospital Clínico Universitario de Valencia, Avda. Blasco Ibañez 17, 46010 Valencia, Spain.

E-mail address: Francisco.J.Chorro@uv.es (F.J. Chorro).

ocasionales durante al menos tres estímulos consecutivos. La lesión ampliada incrementa ligeramente la capacidad de captura al utilizar ciclos ligeramente más largos que los de la fibrilación ventricular.
© 2011 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L. Todos los derechos reservados.

Abbreviations

LV: left ventricle
RF: radiofrequency
RI: regularity index
VF: ventricular fibrillation

INTRODUCTION

Although there is still controversy over the basic mechanisms responsible for ventricular fibrillation (VF), the amount of information available has increased.^{1–7} In parallel with studies on the mechanisms that initiate or maintain arrhythmias, other studies have investigated the various factors that lead to their onset and perpetuation.^{8–14} These studies have used pacing, shocks, or radiofrequency (RF) ablation; the latter is applied to control the factors that lead to onset^{15–18} and is increasingly studied because very little information is available on its modifying effects on the substrate.^{19–21}

The effects of pacing at frequencies close to those of the arrhythmia^{22–25} have been investigated, since it has been demonstrated that these procedures have the capacity to modify atrial fibrillation activation patterns.^{26,27} Pacing has been used during fibrillation to attempt to capture a large area of the myocardium in order to interrupt these processes or facilitate their control using other measures.^{23–25,28} However, the capacity to alter activation patterns is limited to small areas. It is unknown whether modifying the arrival of the activation wavefronts at the site to which electrical pulses are applied also modifies the capacity to achieve myocardial capture and thus to terminate the arrhythmia. The induction of RF lesions is one of the procedures for modifying the substrate and activation patterns during VF, although their effects on the capacity to capture the myocardium using overpacing have not been studied.

The present study analyzed these aspects in an experimental model using isolated Langendorff-perfused rabbit hearts. High-resolution mapping procedures were used to record VF during high-frequency pacing at baseline and after inducing linear RF lesions. This study had the following aims: *a*) to analyze changes in ventricular activation during VF following the induction of a linear RF lesion in the left ventricular (LV) free wall and after increasing its length, and *b*) to study the capacity to capture myocardium during VF by high-frequency pacing at baseline and after lesion induction in a region close to the application site.

METHODS

Experimental Preparation

We followed the guidelines of the American Physiological Society on laboratory animal research. New Zealand white rabbits were used ($n=22$). After anesthesia with ketamine (25 mg/kg, IM) and administration of heparin, the hearts were removed and immersed in cold Tyrode. Within 3 min, they were connected via the aorta to a Langendorff system and perfused with oxygenated Tyrode solution at 60 mmHg and 37 (0.5) °C. Mapping records were

acquired using 2 multiple electrodes (121 and 115 stainless steel unipolar electrodes, 0.125-mm diameter; interelectrode distance, 1 mm) placed on the LV free wall. We used a mapping system (MAPTECH, Waalre, Netherlands) at a sampling frequency of 1 kHz per channel. The reference electrode was an Ag/AgCl 4×6-mm plate placed on the aorta. Ventricular pacing was performed with bipolar electrodes (0.2-mm diameter; interelectrode distance, 1 mm) placed at the center of each multiple electrode. To achieve ventricular capture during VF, biphasic stimuli were applied for 2 ms at an amplitude 6 times the diastolic threshold.

Experimental Protocol

Thirty minutes after placing the electrodes, VF was induced by stimulation at increasing frequencies, maintaining coronary perfusion during the arrhythmia. After 5 min, a train of stimuli was applied for 15 s at 3 different cycles (10% shorter than, equal to, or 10% longer than the mean cycle during VF) with 15-s pauses between them. This phase lasted 15 min. Stimulation was applied to the LV anterior wall in half of the experiments and to the posterolateral wall in the other half. After applying the trains of stimuli (10 in each cycle), a linear vertical RF lesion was induced in the middle region of the anterolateral LV wall (Fig. 1). This involved successive applications of RF (10 W for 20 s) using a needle electrode that was inserted perpendicular to the epicardium, ensuring that the portion inserted was slightly longer than the mean thickness of the wall.^{20,29} At this stage, lesion length was 10 (1) mm with a maximum width of 3.9 (0.2) mm. After 10 min of stabilization, the protocol was repeated; upon completion, lesion length was increased (mean length, 23 [2] mm; maximum width, 4.1 [0.3] mm) (Figs. 2 and 3) and the stimulation protocol repeated after 10 min. The time from VF induction until the completion of the protocol was 70 min and the total duration of each experiment was always less than 2 h beyond the moment of removal of the heart.

Parameters Analyzed

Myocardial Activation During Ventricular Fibrillation

Local activation times in each electrode were identified by determining the maximum negative slope of the unipolar electrograms; when 2 or more deflections appeared, the steepest slope was selected. Histograms were obtained of the activation cycles for each of the 2 regions studied and of the median, the 5th and 95th percentiles, and the differences between them.

By analyzing the variations in the morphology of the consecutive electrograms, we determined the regularity index (RI) that quantifies (between 0 and 1) the similarity between the electrograms for each channel.^{30,31} For repetitive signals in which the morphology of the activation waves is very similar, the index value is high, whereas this value decreases when the morphology is variable. To obtain the RI, bandpass filtering was used to remove baseline fluctuations and noise (40th-order FIR filter, bandpass 5–40 Hz, Kaiser window); after identifying local activations we calculated the signal centroid, which was defined as the point dividing the area of the signal module into 2 equal parts. Once the signals were normalized to avoid variations in amplitude, we analyzed similarities between successive activation waves detected in each channel during 4-s segments.

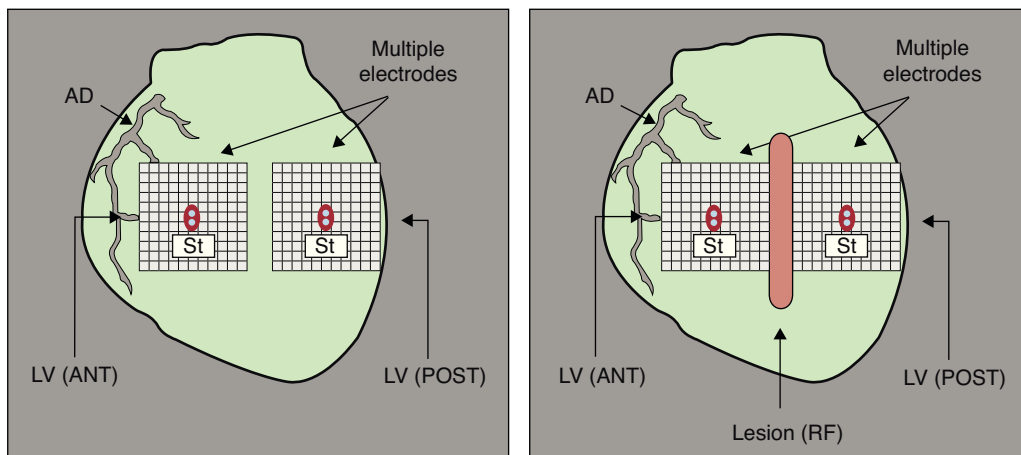


Figure 1. Diagram showing the location of the epicardial multiple electrodes on the left ventricular anterior and posterolateral walls and the site of the lesion. AD, anterior descending coronary artery; LV (ANT), left ventricular anterior wall; LV (POST), left ventricular posterior wall; RF, radiofrequency; St, stimulating electrode.

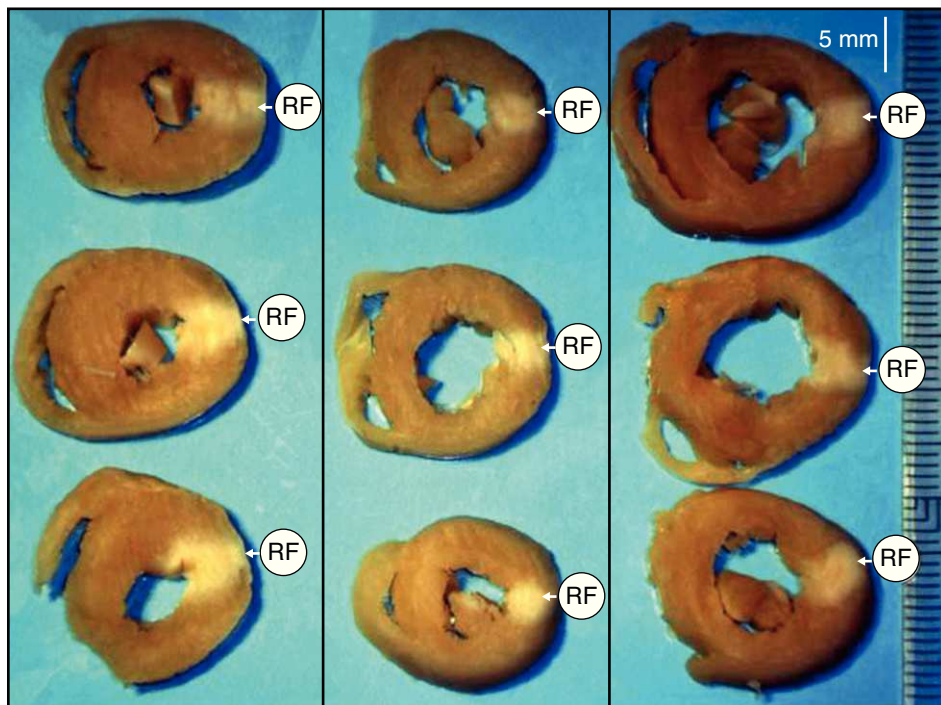


Figure 2. Cross-sections of hearts in 3 experiments in which the transmural nature of the radiofrequency lesions was macroscopically observed. RF, radiofrequency.

Similarly, we constructed activation maps of the 2 regions studied at 100-ms intervals during 2-s windows in each phase before applying the stimulation protocols (at baseline, after the initial lesion was induced, and after enlargement). After constructing the isochrones, we quantified the activation fronts arriving in the 2 regions from each side of the electrode. When the front arrived simultaneously from both sides, entry was assigned to the highest number of electrodes activated.

Myocardial Capture During Ventricular Fibrillation

A sequential procedure was used, and the signals processed to characterize: a) possible synchronization between the stimuli and the signals recorded near the stimulation point; b) the existence of centrifugal activation patterns from the stimulating electrode (Fig. 4); and c) coincidence between the instant of activation in this region and the instant the stimuli were emitted. Once possible

capture episodes were identified, we manually edited the selected maps to confirm capture.

Statistical Analysis

Comparisons between the mean values of quantitative variables (within-subjects differences, repeated measures) were performed using a general linear model. A P -value of $<.05$ was used as a cutoff for statistical significance.

RESULTS

Modification of Myocardial Activation During Ventricular Fibrillation Caused by the Lesion

Figure 5 shows the averages of the median of the VF cycles in the 2 regions of the LV studied. No significant changes were observed after lesion induction and after enlargement.

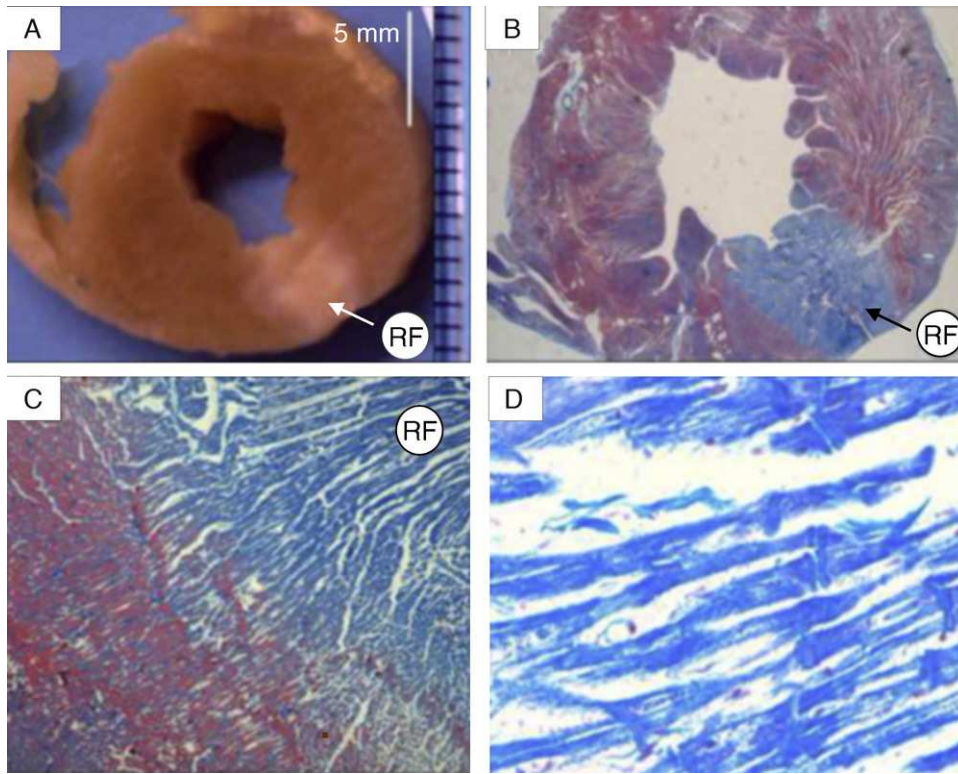


Figure 3. A, cross-section of a heart in which the transmural radiofrequency lesion can be observed. B, C, and D, histological preparations at different magnifications (B, $\times 2$; C, $\times 10$; D, $\times 20$) in which trichrome staining distinguishes the lesion site from adjacent undamaged myocardium. The higher magnification image shows the presence of contracture bands in damaged myocytes. RF, radiofrequency.

Figure 6 shows the averages of the differences between the 95th and 5th percentiles of the cycles in the 3 experimental phases in the 2 regions studied. After the lesion was induced we observed a small, statistically significant increase in the anterior LV.

Figure 7 shows the averages of the RI obtained in the 2 regions in each phase. This was significantly lower in the anterior and posterolateral regions after lesion induction and after enlargement.

Figure 8 shows the RI maps obtained in the 2 regions in 2 of the experiments. A decrease in RI can be observed in a large number of the electrodes after lesion induction and enlargement.

Once the activation maps were constructed during VF at baseline, and after lesion induction and enlargement ($n = 2640$), averages were calculated for the wavefronts arriving in the 2 study regions from each side of the multiple electrodes. Table 1 shows the averages obtained. In the anterior wall after lesion induction and elongation, there was a significant decrease of wavefronts from the right and lower regions, and increased wavefronts from the left region, opposite the lesion, and from the upper region. In the posterolateral wall there was an increase in wavefronts from the right region and a decrease in wavefronts from the left region, adjacent to the lesion. After lesion elongation, there was a significant decrease in those arriving from the upper region.

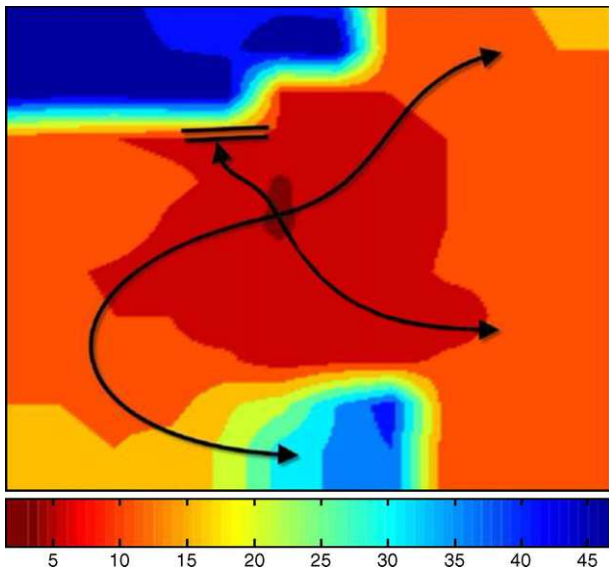


Figure 4. Activation map during ventricular fibrillation in which a centrifugal activation pattern can be observed from the central region to which the stimuli are applied. The color coding indicates local activation times and isochrones.

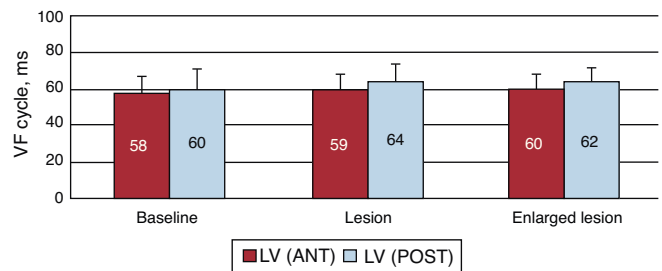


Figure 5. Mean (standard deviation) of the median of the intervals between successive activations during ventricular fibrillation obtained in the 2 study regions at baseline, after lesion induction, and after enlargement. LV (ANT), left ventricular anterior wall; LV (POST), left ventricular posterolateral wall; VF, ventricular fibrillation. Values in milliseconds.

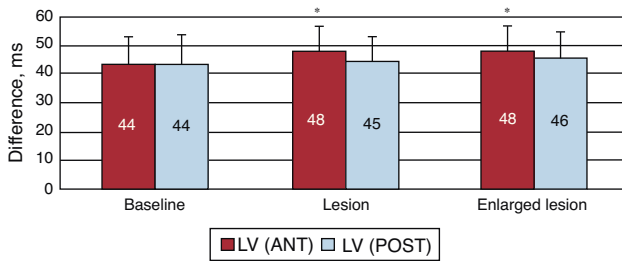


Figure 6. Mean (standard deviation) of the differences between the 95th and 5th percentiles of the histograms for the intervals between successive activations during ventricular fibrillation obtained in the 2 study regions in the 3 experimental phases. LV (ANT), left ventricular anterior wall; LV (POST), left ventricular posterolateral wall. Values in milliseconds. * $P < .05$ for baseline values.

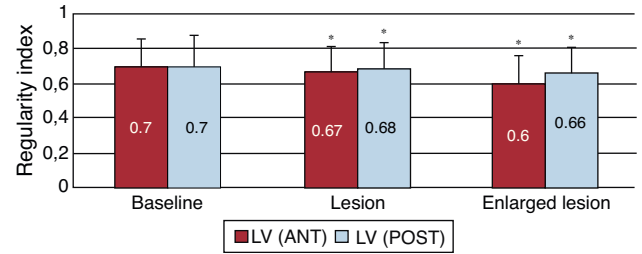


Figure 7. Mean (standard deviation) of the regularity index obtained in the 2 study regions in each experimental phase. LV (ANT), left ventricular anterior wall; LV (POST), left ventricular posterolateral wall. * $P < .05$ for baseline values.

We also quantified the maps with breakthrough and complete reentry patterns. Before lesion induction, the percentages of both types of maps were 33% and 8%, respectively. After lesion induction the percentages were 31% and 7%, respectively, and after lesion elongation they were 27% and 8%, respectively. The differences between the 3 phases were not statistically significant. On the maps showing evidence of complete re-entry the average number of turns or rotations was 1.2 (0.2) before lesion induction, 1.1 (0.2) after lesion induction, and 1.1 (0.1) after elongation (nonsignificant).

Myocardial Capture During Ventricular Fibrillation

To evaluate the algorithm used to identify capture, in 8 of the records obtained in different experiments we manually analyzed the activation maps of 2180 stimuli, identifying 22 captures. When this was done via an automated process, we detected activation patterns that met the criteria for possible capture on 581 occasions; 21 of the 22 manually identified captures were in this group. Thus, the algorithm had a sensitivity of 95% and

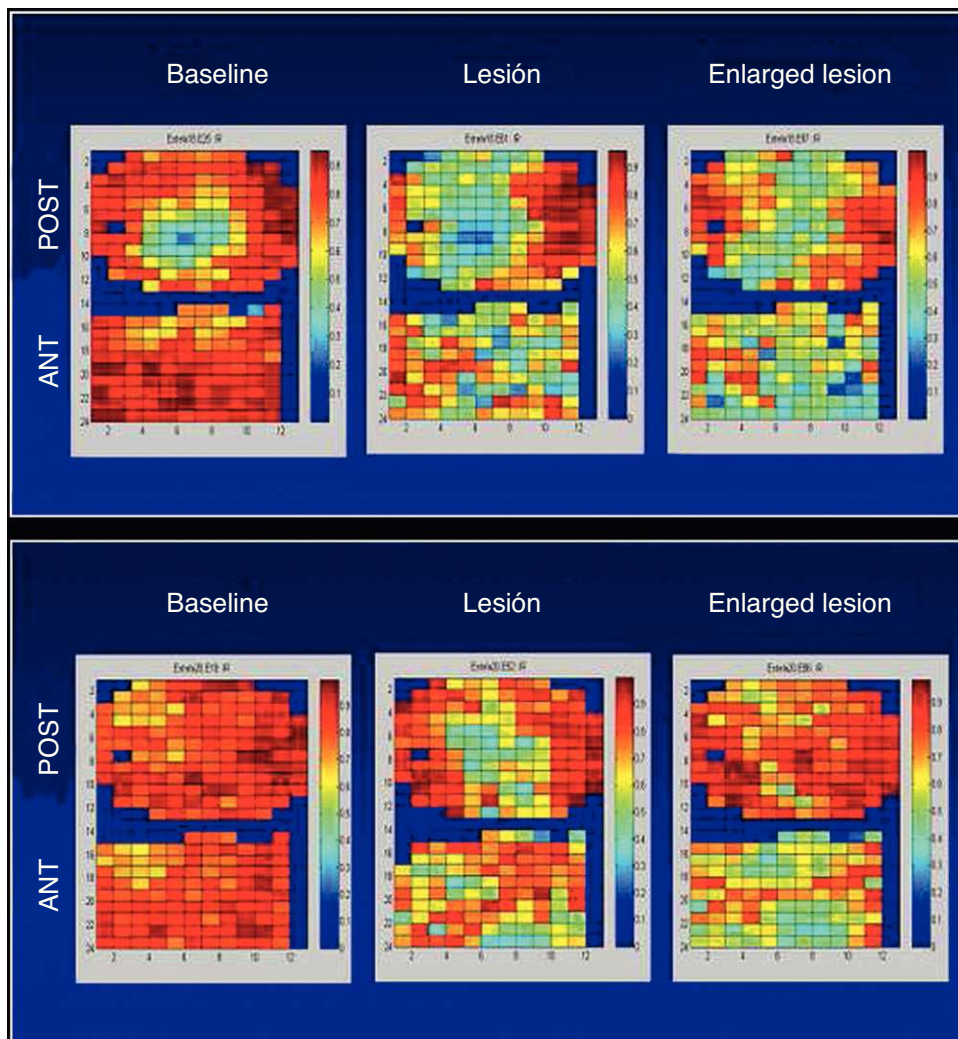


Figure 8. Representation, color coded, of the regularity indices obtained in each of the 2 electrodes of the 2 multiple electrodes located on the left ventricular anterior and posterolateral walls at baseline, after lesion induction and after enlargement. ANT, anterior; POST, posterolateral.

Table 1

Mean (Standard Deviation) of the Number of Activation Fronts Arriving in the Regions Encompassed by the Multiple Electrodes Located in the Left Ventricular Anterior and Posterolateral Walls From Each of the Sides Formed by the Multiple Electrodes in the 3 Experimental Phases

	Baseline	Lesion	Enlarged Lesion
<i>Anterior wall</i>			
Upper	4.8 (1.9)	5.5 (2.1) ^a	5.2 (2.2) ^a
Right	3.2 (1.6)	2.9 (1.7) ^a	2.2 (1.4) ^{a,b}
Lower	3.4 (2.1)	3.1 (2.1) ^a	2.4 (1.9) ^{a,b}
Left	4.5 (2.1)	5.6 (2.9) ^a	7.1 (3.2) ^{a,b}
<i>Posterolateral wall</i>			
Upper	4.2 (2)	4.2 (2.1)	3.8 (2.2) ^{a,b}
Right	3.6 (1.8)	4.4 (2.1) ^a	5.1 (2.3) ^{a,b}
Lower	5.5 (2.3)	5.5 (2.4)	5.6 (2.7)
Left	3.8 (1.8)	3.3 (2) ^a	2.6 (1.7) ^{a,b}

^a $P < .05$ for baseline values.

^b $P < .05$ for initial lesion.

specificity of 79%. The negative predictive value was high (99%) and its application significantly reduced the number of maps that had to be manually analyzed, with a low probability of excluding stimuli with capture.

Table 2 shows the number of captures observed in each phase. There were no significant differences at baseline and after lesion induction in any cycle. After lesion elongation, the number of captures at cycles 10% longer than the VF was significantly higher than those obtained at cycles 10% shorter than the VF and those obtained at baseline. However, the number of captures obtained was similar to the number of captures obtained at baseline at cycles 10% shorter than that of the arrhythmia. Table 3 shows the averages of the episodes for each experiment in which at least 3 consecutive captures were observed. It can be seen that there are few episodes of this type and that there were no statistical differences between the 3 cycles at baseline and after lesion induction. Following lesion enlargement the average increased slightly and was significantly higher for cycles 10% longer than the VF. At cycles 10% shorter than that of the VF, the number of episodes with capture was lower after lesion induction and enlargement. None of the capture episodes led to the interruption of the VF.

After lesion induction, the overall number of activation fronts detected in the mapped regions did not vary significantly, although there was a significant decrease in those from the region ipsilateral to the lesion. Using a random sample of 50 captures from each of the 3 phases of the protocol, we analyzed the characteristics of the activation map prior to capture. In these maps, the number of activation fronts ipsilateral to the region where the lesion was located significantly decreased after lesion induction and after enlargement (baseline=9%, after lesion induction=2%, and after elongation=0%; $P < .01$).

Table 2

Mean (Standard Deviation) of Number of Stimuli With Capture During Ventricular Fibrillation Obtained in Each Case During Stimulation With Cycles 10% Shorter Than, Equal to, or 10% Longer Than the Fibrillation Cycle in the 3 Study Phases

	Baseline	Lesion	Enlarged lesion
Cycle 10% shorter	89 (54)	68 (51)	49 (34)
Equal cycle	84 (58)	70 (42)	79 (50)
Cycle 10% longer	56 (35)	42 (22)	85 (41) [*]

^{*} $P < .05$ for baseline values and for cycles 10% shorter.

Table 3

Mean (Standard Deviation) of the Number of Episodes With 3 or More Consecutive Captures During Ventricular Fibrillation Obtained in Each Case During Stimulation With Cycles 10% Shorter Than, Equal to, or 10% Longer Than the Fibrillation Cycle Through the 3 Study Phases

	Baseline	Lesion	Enlarged lesion
Cycle 10% shorter	1.8 (1.9)	0.1 (0.1) ^a	0.1 (0.1) ^a
Equal cycle	1.1 (0.6)	0.8 (0.4)	0.8 (0.9)
Cycle 10% longer	0.6 (0.7)	1 (1)	3.0 (2.8) ^{a,b}

^a $P < .05$ for baseline values.

^b $P < .05$ for cycles 10% shorter.

Figure 9 shows the maps corresponding to one of the capture episodes produced after lesion induction during stimulation from the LV anterior wall. The upper left part shows the map prior to capture indicating the activation region where the electrode was located before stimulation. To the right is the capture that created a centrifugal activation pattern from the region of application. At the lower left is another map with capture and to the right there is the loss of capture due to the activation of the central region by a front reaching this region prior to the stimulus.

DISCUSSION

The main results of this study are as follows: a) the induction of a lesion in the LV free wall increases the heterogeneity of myocardial activation during VF and modifies the arrival of fronts in adjacent regions; b) stimulation during VF using trains of high-frequency stimuli causes occasional captures during at least 3 consecutive stimuli, and c) lesion elongation slightly increases consecutive captures when using cycles slightly longer than those of the arrhythmia.

Modification of Myocardial Activation During Ventricular Fibrillation Caused by the Lesion

Radiofrequency catheter ablation is a widely used technique for treating several types of arrhythmias and its effects on the substrate and the transmission of impulses during atrial fibrillation have been extensively studied.³² The effects of ablation on VF have been studied less.^{15–21} In patients with idiopathic or primary VF associated with long QT or Brugada syndrome, selective applications of RF in the Purkinje network, right ventricular outflow tract, and the extrasystole site of origin have been effective in preventing arrhythmic events.¹⁸

In experimental models using isolated rabbit hearts, ablation of the anterior papillary muscle terminated VF during propranolol infusion and reduced its inducibility.²¹ The induction of lesions encompassing the posterior region of the septum and ventricular walls, the anterior region of the septum and walls, or the midseptal region modified or interrupted activation in large areas of the myocardium, excluding them from the activation process during VF. They were not essential for sustaining VF.²⁰

In this study using a similar experimental model, the lesion was located between the papillary muscles but without reaching the atrioventricular groove, which probably caused the lack of change in the average cycle of the arrhythmia, although the arrival of activation wavefronts in the regions explored was modified, with decreased entry from the lesion site mainly due to increases in regions opposite to the site. The transmural nature of the lesions was demonstrated macroscopically in all cases by visualizing their extension from the epicardium to the endocardium. Histological analysis was performed in one third of the cases and it cannot be

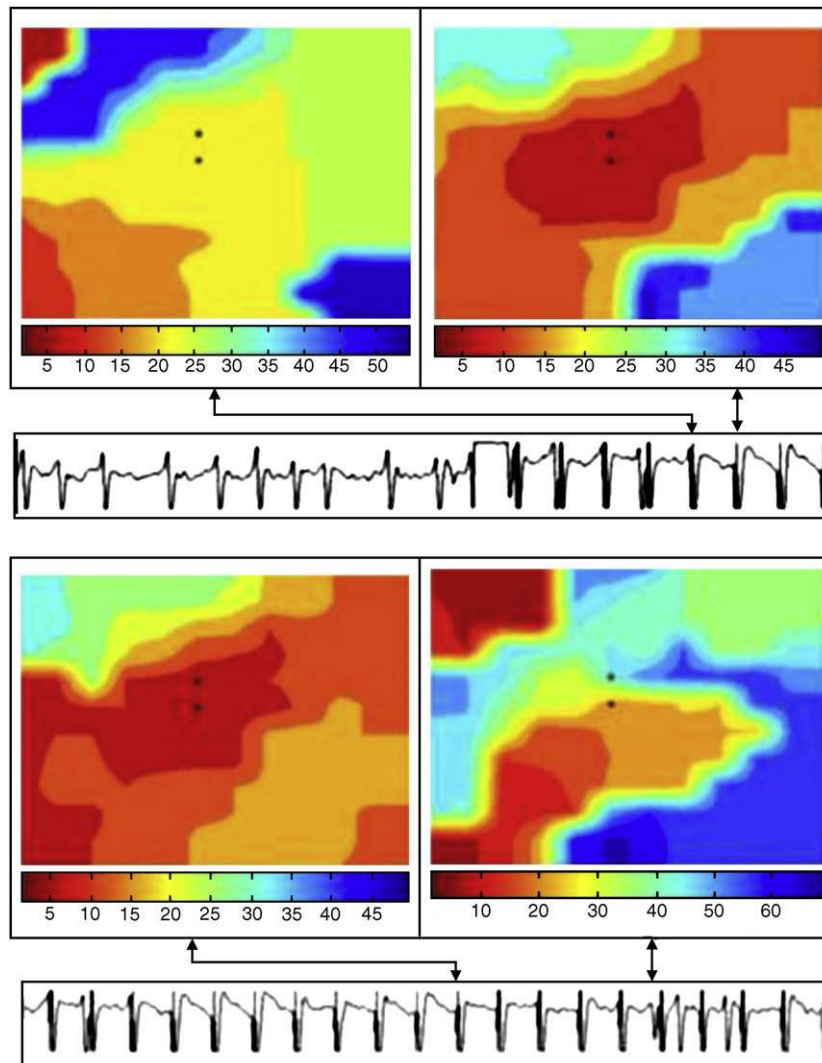


Figure 9. Activation maps for 1 of the capture episodes obtained after lesion induction. The recording obtained with 1 of the electrodes indicates the time corresponding to each of the maps. The color coding indicates local activation times and isochrones. The stimulating electrode is positioned in the central area of the multiple electrode, located on the left ventricular anterior wall.

excluded that in the remaining cases limited areas of undamaged myocardium may have persisted in the lesions. In relation to the stability of the preparations used in the study, there was no control group. However, in previous studies that used a similar experimental preparation^{3,20} it was found that the electrophysiological properties of the ventricular myocardium were stable for up to 2 h, both in terms of refractoriness and conduction velocity. It was also found that in the VF recordings obtained over long periods, if coronary perfusion was maintained, both the cycles between successive activations and the dominant frequency were stable, except immediately after induction of arrhythmia.

Myocardial Capture During Ventricular Fibrillation. Effects of the Lesion

Kenknight et al.³³ observed regional myocardial capture during VF in a porcine model by emitting trains of stimuli with cycles between 80% and 115% of the average cycle during the arrhythmia. These results supported the existence of an excitable gap during VF as previously demonstrated during atrial fibrillation in a canine model.^{26,37} Nanthakumar et al.²⁴ performed rapid pacing from 1 or

2 lines of ventricular epicardial electrodes documenting myocardial capture during the arrhythmia. This was consistent with Pak et al.²³ who synchronized activation fronts with the aim of terminating VF. Subsequently, Ravi et al.³⁴ used synchronized stimulation techniques to create lines of block during VF in isolated perfused rabbit hearts. Johnson et al.²² applied stimulation during VF to compare the effectiveness of adaptive or fixed pacing algorithms without observing significant differences. In the present study we used fixed stimulation protocols at 3 different stimulation cycles: one that was the same as that of the arrhythmia, one slightly longer, and one shorter. The identification of captures during VF is a laborious process given the large number of stimuli emitted. To facilitate the task we used a semi-automatic sequential procedure that excluded stimuli without capture with a low probability of error. It was observed that the capacity to capture at baseline was limited, as indicated by the low number of episodes in which there were at least 3 consecutive captures. If the maps that fulfill the criteria for capture are observed in isolation, this does not exclude the possibility that the emission of stimuli may have coincided with a spontaneous activation that began in the center of the region explored, due to the breakthrough of a front from subendocardial regions. This coincidence is less likely

when repeated captures are observed and for this reason they more accurately reflect the capacity to capture myocardium during the arrhythmia.

The induction of linear lesions modified the activation patterns, particularly the arrival of the fronts from the lesion site; these decreased after lesion induction and enlargement at the expense of simultaneous changes in arrival from other sites. The capacity to achieve capture after lesion induction remained limited and did not prevent the perpetuation of the arrhythmia. Nevertheless, the extended lesion modified the capacity to obtain successive captures, showing a slight increase when using cycles 10% longer than those of the arrhythmia. The presence of the lesion and the decrease in the arrival of fronts from the lesion site may have reduced interference from fronts which, by arriving at the stimulation site before the next stimulus was emitted, may have prevented the perpetuation of myocardial capture. This is one of the mechanisms involved in the loss of myocardial capture during fibrillatory processes when stimulating at cycles slightly longer than those of the arrhythmia.^{26,27}

Moreover, after the lesion was elongated, when stimulating at cycles shorter than those of the arrhythmia, there was a slight decrease in the number of captures, although the differences did not reach statistical significance. One possible explanation is that after the lesion was induced the lower limit of the excitable gap may have increased, thus reducing the possibility of capture. This change could be due to increased irregularity of the activation and action of the stimuli themselves, which in turn would shorten the upper limit of the excitable gap to generate reentrant activations that may interfere with the captures caused by successive stimuli. By stimulating with cycles longer than those of the arrhythmia, the upper limit of the excitable gap would be determined more by the spontaneous arrival of the activation fronts, including those reaching the region later, thus increasing the likelihood that the stimuli coincided with the excitable gap.

Clinical Implications

Electrical stimulation is useful to interrupt ventricular tachycardia and in fact implantable cardioverter-defibrillators have a stimulation mode to control these arrhythmias. Regional myocardial capture during VF has been studied less and therefore its effects and the factors that promote or limit it are beginning to receive attention. The present study is framed within this field and describes some of the limitations of capture procedures using high-frequency pacing. The results obtained may be of use in guiding future research on myocardial capture during VF using programmed stimulation procedures.

Study Limitations

The features of the model used enabled the analysis of VF and the effects of the lesions without interference from metabolic deterioration that accompanies the onset of VF. However, the analysis of the results is restricted to situations similar to the initial moments of the arrhythmia when this occurs in a clinical setting.

CONCLUSIONS

RF lesions increase the heterogeneity of myocardial activation during VF and modify the arrival of activation fronts in adjacent areas. High-frequency pacing during VF leads to occasional captures during at least 3 consecutive stimuli. Enlarged lesions slightly increase the capacity to capture by using cycles slightly longer than those of the VF.

FUNDING

This study was funded by research grants from the *Instituto de Salud Carlos III* FIS PI06/0758-PS09/02417 and RETIC REDINSCOR RD06/0003/0010, from the *Generalitat Valenciana* PROMETEO 2010/093, and from the *Sociedad Española de Cardiología*.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Weiss JN, Qu Z, Chen PS, Lin SF, Karagueuzian HS, Hayashi H, et al. The dynamics of cardiac fibrillation. *Circulation*. 2005;112:1232–40.
- Vaquero M, Calvo D, Jalife J. Cardiac fibrillation: from ion channels to rotors in the human heart. *Heart Rhythm*. 2008;5:872–9.
- Chorro FJ, Trapero I, Guerrero J, Such LM, Cánoves J, Mainar L, et al. Modification of ventricular fibrillation activation patterns induced by local stretching. *J Cardiovasc Electrophysiol*. 2005;16:1087–96.
- Liu YB, Pak HN, Lamp ST, Okuyama Y, Hayashi H, Wu TJ, et al. Coexistence of two types of ventricular fibrillation during acute regional ischemia in rabbit ventricle. *J Cardiovasc Electrophysiol*. 2004;15:1433–40.
- Chow AW, Segal OR, Davies DW, Peters NS. Mechanism of pacing-induced ventricular fibrillation in the infarcted human heart. *Circulation*. 2004;110:1725–30.
- Tabereaux PB, Dossdall DJ, Ideker RE. Mechanisms of VF maintenance: wandering wavelets, mother rotors, or foci. *Heart Rhythm*. 2009;6:405–15.
- Ten Tusscher KHW, Mourad A, Nash MP, Clayton EH, Bradley CP, Paterson DJ, et al. Organization of ventricular fibrillation in the human heart: experiments and models. *Exp Physiol*. 2009;94:553–62.
- Adgey AAJ, Spence MS, Walsh SJ. Theory and practice of defibrillation: (2) Defibrillation for ventricular fibrillation. *Heart*. 2005;91:118–25.
- Chorro FJ, Trapero I, Such-Miquel L, Pelechano F, Mainar L, Cánoves J, et al. Pharmacological modifications of the stretch-induced effects on ventricular fibrillation in perfused rabbit hearts. *Am J Physiol Heart Circ Physiol*. 2009;297:H1860–9.
- Mowrey KA, Efimov IR, Cheng Y. Membrane time constant during interval defibrillation strength shocks in intact heart: Effects of Na⁺ and Ca²⁺ channel blockers. *J Cardiovasc Electrophysiol*. 2009;20:85–92.
- Sánchez-Muñoz JJ, García-Alberola A, Martínez-Sánchez J, Peñafiel-Verdú P, Caro-Martínez C, Manzano-Fernández S, et al. Extrasistolia ventricular desencadenante de la fibrilación ventricular. *Rev Esp Cardiol*. 2010;63:798–801.
- Lawo T, Deneke T, Schrader J, Danilovic D, Wenzel B, Buddensiek M, et al. A comparison of chronaxies for ventricular fibrillation induction, defibrillation, and cardiac stimulation: unexpected findings and their implications. *J Cardiovasc Electrophysiol*. 2009;20:315–7.
- Alzueta J, Linde A, Barreda A, Peña J, Peinado R. Registro Español de Desfibrilador Automático Implantable. VI Informe Oficial del Grupo de Trabajo de Desfibrilador Automático Implantable de la Sociedad Española de Cardiología (2009). *Rev Esp Cardiol*. 2010;63:1468–81.
- Tang L, Hwang GS, Song J, Chen PS, Lin SF. Post-shock synchronized pacing in isolated rabbit ventricle: evaluation of a novel defibrillation strategy. *J Cardiovasc Electrophysiol*. 2007;18:740–9.
- Haïssaguerre M, Shoda M, Jais P, Nogami A, Shah DC, Kautzner J, et al. Mapping and ablation of idiopathic ventricular fibrillation. *Circulation*. 2002;106:962–7.
- Weerasooriya R, Hsu LF, Scavee C, Sanders P, Hocini M, Cabrera JA, et al. Catheter ablation of ventricular fibrillation in structurally normal hearts targeting the RVOT and Purkinje ectopy. *Herz*. 2003;28:598–606.
- Kohsaka S, Razavi M, Massumi A. Idiopathic ventricular fibrillation successfully terminated by radiofrequency ablation of the distal Purkinje fibers. *Pacing Clin Electrophysiol*. 2007;30:701–4.
- Wright M, Sacher F, Haïssaguerre M. Catheter ablation for patients with ventricular fibrillation. *Curr Opin Cardiol*. 2009;24:56–60.
- Pak HN, Oh YS, Liu YB, Wu TJ, Karagueuzian HS, Lin SF, et al. Catheter ablation of ventricular fibrillation in rabbit ventricles treated with beta-blockers. *Circulation*. 2003;108:3149–56.
- Chorro FJ, Blasco E, Trapero I, Cánoves J, Ferrero A, Mainar L, et al. Selective myocardial isolation and ventricular fibrillation. *Pacing Clin Electrophysiol*. 2007;30:359–70.
- Pak HN, Kim GI, Lim HE, Fang YH, Choi JI, Kim JS, et al. Both Purkinje cells and left ventricular posteroseptal reentry contribute to the maintenance of ventricular fibrillation in open-chest dogs and swine. Effects of catheter ablation and the ventricular cut-and-sew operation. *Circ J*. 2008;72:1185–92.
- Johnson PL, Newton JC, Rollins DL, Smith WM, Ideker RE. Adaptive pacing during ventricular fibrillation. *Pacing Clin Electrophysiol*. 2003;26:1824–36.
- Pak HN, Okuyama Y, Oh YS, Hayashi H, Liu YB, Chen PS, et al. Improvement of defibrillation efficacy with preshock synchronized pacing. *J Cardiovasc Electrophysiol*. 2004;15:581–7.
- Nanthakumar K, Johnson PL, Huang J, Killingsworth CR, Rollins DL, McElderry HT, et al. Regional variation in capture of fibrillating swine left ventricle during electrical stimulation. *J Cardiovasc Electrophysiol*. 2005;16:425–32.

25. Pak HN, Liu YB, Hayashi H, Okuyama Y, Chen PS, Lin SF. Synchronization of ventricular fibrillation with real-time feedback pacing: implication to low-energy defibrillation. *Am J Physiol Heart Circ Physiol*. 2003;285:H2704–11.
26. Allesie M, Kirchhof C, Scheffer GJ, Chorro F, Brugada J. Regional control of atrial fibrillation by rapid pacing in conscious dogs. *Circulation*. 1991;84:1689–97.
27. Kirchhof C, Chorro F, Scheffer GJ, Brugada J, Konings K, Zetelaki Z, et al. Regional entrainment of atrial fibrillation studied by high-resolution mapping in open-chest dogs. *Circulation*. 1993;88:736–49.
28. Gu Y, Patwardhan A. Multiple spatially distributed stimulators and timing programs for entrainment of activation during ventricular fibrillation. *Biomed Sci Instrum*. 2002;38:295–9.
29. Chorro FJ, Guerrero J, Cánoves J, Trapero I, Mainar L, Pelechano F, et al. Modificaciones de las características espectrales de la fibrilación ventricular en las lesiones producidas con radiofrecuencia. Estudio experimental. *Rev Esp Cardiol*. 2008;61:394–403.
30. Faes L, Nollo G, Antolini R, Gaita F, Ravelli F. A method for quantifying atrial fibrillation organization based on wave-morphology similarity. *IEEE Trans Biomed Eng*. 2002;49:1504–13.
31. Ravelli F, Faes L, Sandrini L, Gaita F, Antolini R, Scaglione M, et al. Wave similarity mapping shows the spatiotemporal distribution of fibrillatory wave complexity in the human right atrium during paroxysmal and chronic atrial fibrillation. *J Cardiovasc Electrophysiol*. 2005;16:1071–6.
32. Calkins H, Reynolds MR, Spector P, Sondhi M, Xu Y, Martin A, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhythm Electrophysiol*. 2009;2:349–61.
33. KenKnight BH, Bayly PV, Gerstle RJ, Rollins DL, Wolf PD, Smith WM, et al. Regional capture of fibrillating ventricular myocardium. *Circ Res*. 1995;77:849–55.
34. Ravi K, Nihei M, Willmer A, Hayashi H, Lin SF. Optical recording-guided pacing to create functional line of block during ventricular fibrillation. *J Biomed Opt*. 2006;11:021013.