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Virtual Electrode Polarization–Induced Reentrant Activity

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Abstract: It is known that electric shocks create a characteristic pattern of polarization ("virtual electrode polarization") in the myocardium but its roles on post-shock excitations remain to be clarified. We have optically mapped electrical activity of the left ventricular subepicardial layer of Langendorff-perfused rabbit hearts endocardialy frozen. Monophasic anodal and cathodal shocks were applied during the plateau or repolarization phase of the action potential. Electric shocks (20 V, 10 ms) resulted in a "dog-bone" pattern of polarization around the stimulation electrode and the withdrawal of the shocks were followed by "break excitations". Spread of the break excitations were partially blocked by refractory of the preceding excitation, and slow conduction around the functional line of block initiated reentrant excitations. These results suggest that break excitations arising from the virtual electrode polarization combined with spatial heterogeneity in repolarization of the preceding excitation play important roles in the genesis of post-shock reentrant activities.

Key words: membrane potential, electric field stimulation, optical mapping, reentry

Ventricular fibrillation is the result of one or more functional reentrant activities causing chaotic excitation of the heart. Application of a high-intensity electric field (shock) is the most effective procedure to extinguish reentrant activities and terminate fibrillation (electrical defibrillation). However, it is known that strong shocks may induce unexpected membrane potential aftereffects that initiate new arrhythmias (defibrillation failure). Recent experimental and computer simulation studies have demonstrated that strong shocks create a characteristic "dog-bone" pattern composed of positively and negatively polarized areas ("virtual electrode polarization") around the stimulation electrode (Wikswo et al, 1995; Efimov et al, 1998). The spatial pattern of polarizations induced by electric shocks has been well characterized but its roles on post-shock excitations remain to be clarified.

Recent advances in technology including development of voltage-sensitive dyes and high-resolution imaging techniques enable us to investigate changes in the membrane potential during strong shocks without artifacts due to electric field. In the present study, we have investigated, by use of high-resolution optical mapping, how the virtual electrode polarization is involved in the establishment of reentrant activities after defibrillation shocks.

Materials and Methods

Isolated rabbit hearts for optical signal recordings were prepared as discussed previously (Kodama et al, 1999; Kodama et al, 2000; Nihei et al, 2001). In brief, Japanese white rabbits weighing 1.5~2.0 kg were heparinized and anesthetized with pentobarbital sodium (30~40 mg/kg, i.v.). Then the hearts were removed and perfused in a Langendorff-apparatus. After producing complete atrio-ventricular block by ligating the proximal portion of the His-bundle, the heart was stained with a voltage sensitive dye, di-4-ANEPPS (Molecular Proves Inc., 2 μM). Diacetyl monoxiame (15 mM) was added to the perfusate to minimize mechanical movement because mechanical movement of the heart makes it difficult to analyze optical signal precisely. In order to prevent the intramural wave propagation, two-dimensional subepicardial sheet preparations were prepared by endocardial cryoablation (Kodama et al, 1999). TTC (Triphenyl Tetrazolium Chloride) staining confirmed that thin (~1 mm) subepicardial myocardial layers were viable after the procedure.

Our original high-speed digital video camera system was employed for detecting changes in optical membrane potential signals. Detailed experimental setups have been described previously (Kodama et al, 1999; Kodama et al, 2000; Nihei et al, 2001). Spatial and temporal resolutions of the video-imaging

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system was 0.12 mm/pixel and 1.3 ms/frame, respectively.

Basal stimuli (S1) were applied at the apex at a cycle length of 400 ms, and monophasic DC shocks (S2, 20V, 10 ms) were given at the anterior epicardial surface of the left ventricle during the plateau phase of the S1 action potential.

Results

Fig. 1A shows a typical example of virtual electrode polarization during anodal stimulus (S2, 20V) applied at the plateau phase of the S1 action potential. A characteristic "dog-bone"-shaped negatively polarized (hyperpolarized) area was induced with two positively polarized zones at both sides. Fig. 1B shows representative optical membrane potential signals obtained from positively polarized area (a) and negatively polarized area (b). The shock-induced positive polarization caused a marked prolongation of the repolarization phase of the action potential. In contrast, the negative polarization resulted in an immediate repolarization of the action potential and new excitation was induced after the withdrawal of the shock (break excitation). The activation of negatively polarized area was the result of partial or complete recovery of the excitability (recovery of Na^+ channels form voltage-dependent inactivation) in the negatively polarized area and electrotonically transmitted driving force from the positively polarized area. Cathodal monophasic shocks created a similar spatial polarization pattern of reversed polarity to that induced by anodal shocks, and the withdrawal of the shocks were followed by break excitations (data not shown).

Fig. 2 illustrates formation of functional reentry from virtual electrode-induced break excitation. In this case, an anodal shock was applied during the repolarization phase of the S1 action potential. By the end of the shock, typical virtual electrode-type distribution of positively and negatively polarized areas were created (Fig. 2A), and after the withdrawal of shocks, negatively polarized areas were activated by an electrotonic driving force from neighboring positively polarized area and break excitation initiated new multiple wavefronts at the boundary between positively and negatively polarized areas (Fig. 2B). Some wavefronts propagated rapidly across the area that had been recovered from refractory (bottom right area in Fig. 2C), whereas conduction of other wavefronts was delayed or partially interrupted in the area that remained in the refractory period (upper left area in Fig. 2C). Slow conduction combined with unidirectional conduction block in the partial refractory region provided a substrate for functional reentry and in the case shown Fig. 2 and 3 spiral-type reentrant excitations were initiated (Fig. 2D-F and Fig. 3).

Discussion

In the present study, application of high-intensity monophasic shocks to the ventricular myocardium resulted in characteristic distribution of membrane potential polarizations

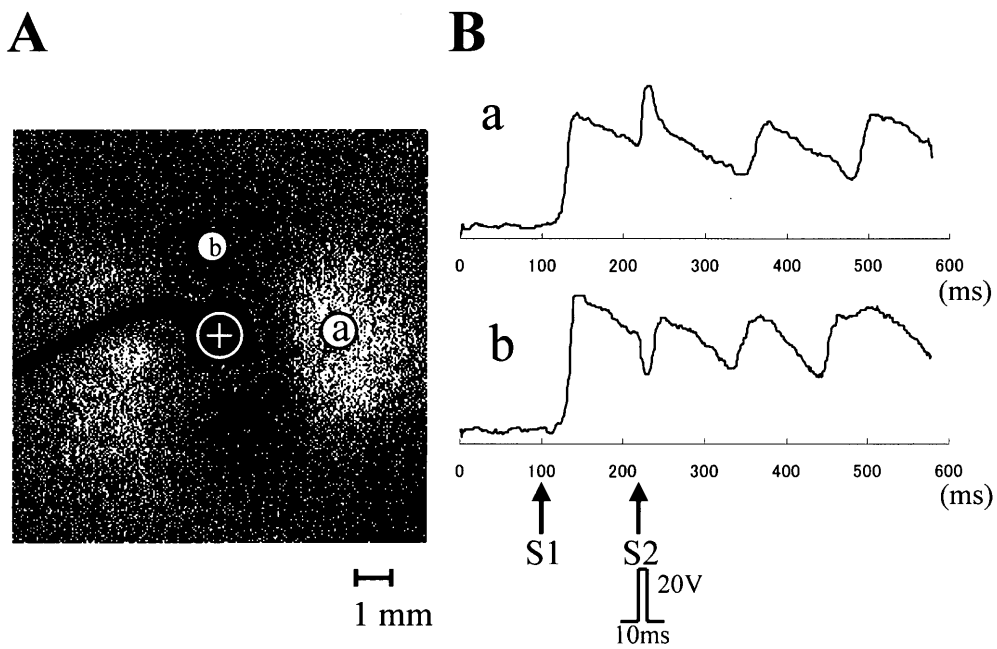

Fig. 1 The spatial pattern of polarization (virtual electrode polarization) optically recorded from the rabbit ventricular epicardium at the end of 10 ms monophasic anodal shock (+20 V, S2). The shock was applied at the plateau phase of the basic (S1) action potential through a unipolar electrode (black square in panel A). A, fluorescence membrane potential image at the end of the shock. White color corresponds positive polarization (depolarization) and black color represents negative polarization (hyperpolarization). B, optical membrane potential signals obtained from depolarized (a) and hyperpolarized (b) areas.

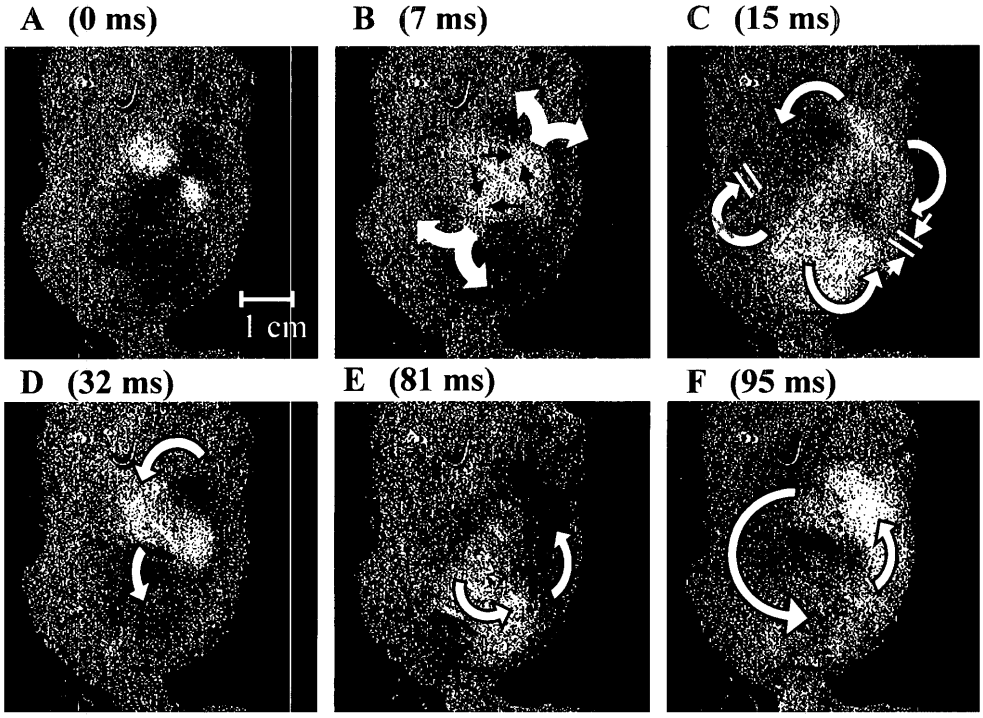

Fig. 2 Initiation of spiral-type reentrant excitation from virtual electrode polarization. A 10 ms monophasic shock was applied at the left ventricular epicardial surface at the repolarization phase of the basic action potential. Fluorescence membrane potential images were obtained at the end of the shock (a), 7 ms (b), 15 ms (c), 32 ms (d), 81 ms (e) and 95 ms (f) after the shock termination. White color corresponds positive depolarization and black color represents hyperpolarization. (see text for explanation).

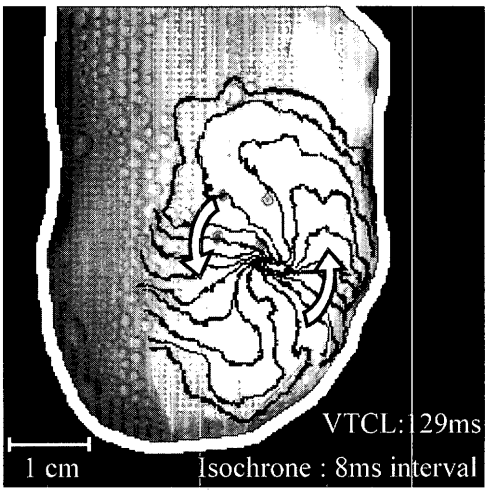

Fig. 3 Activation sequence (8-ms isochrones) during shock-induced spiral reentry shown in Fig. 2.

(positively and negatively polarized areas) around the stimulation electrode. Such virtual electrode effects may be the result of differences in intramyocardial and extramyocardial conductivity. Sepulveda et al (Sepulveda et al, 1989) previously demonstrated using a two-dimensional bidomain mathematical model, areas of opposite polarizations could be induced by epicardial stimuli due to unequal anisotropic properties of intracellular and extracellular spaces in the myocardium.

In this study, virtual electrode-induced negatively polarized areas were quickly activated after the withdrawal of shocks by an electrotonically transmitted driving force from neighboring positively polarized area and break excitation initiated new wavefronts at the boundary between positively and negatively polarized areas. These patterns of break excitations were essentially similar to those reported by previous mathematical simulations and experimental studies (Wikswo et al, 1995; Efimov et al, 1998).

The wavefronts of virtual electrode-induced break excitations are complex in the structure and independent of the repolarization wave tails of preceding basic excitations, and this may produce transient wavebreaks and result in functional reentry (Roth, 1995). In this study, functional line of conduction block was formed in the limited area of the break excitation wavefrants as a result of wavebreaks and slow conduction around the line of block initiated spiral-type reentrant activities.

The virtual electrode effect has dual roles in defibrillation. Due to this effect, a monophasic defibrillation shock of any polarity can erase preexisting fibrillatory activity by rapidly resetting the phase and inducing positive and negative polarization in neighboring areas. However, at the same time, this effect may create a new arrhythmia via induction of virtual electrode-induced break excitations (Efimov et al, 1998).

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