In vivo validation of the coincidence of the peak and end of the T wave with full repolarization of the epicardium and endocardium in swine

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OBJECTIVES/BACKGROUND Previous *in vitro* studies have suggested full repolarization of the epicardium coincides with the peak of the T wave (T_{peak}) and that of the M cells coincides with the end of the T wave (T_{end}). However, *in vivo* validation of the theory is lacking.

METHODS Monophasic action potentials (MAPs) were recorded using the CARTO mapping system from 51 ± 10 epicardial sites and 64 ± 9 endocardial sites of the left ventricle in 10 pigs and from 41 ± 4 epicardial sites and 53 ± 2 endocardial sites of the right ventricle in two of the 10 pigs. End of repolarization (EOR) times over the epicardium (EOR_{epi}), endocardium (EOR_{endo}), and over both (EOR_{total}) were obtained. QT_{peak} and QT_{end} intervals were measured from simultaneously recorded 12-lead ECG.

RESULTS Minimal and maximal EOR_{total} were observed in the left ventricle in all pigs. Minimal EOR_{total} was on the epicardium in five pigs, and maximal EOR_{total} was on the endocardium in nine pigs. Minimal, mean, and maximal QT_{peak} intervals all were significantly smaller than maximal EOR_{epi} (322 ± 23 ms, $P < .01$). No significant difference was found between maximal QT_{end} interval (338 ± 30 ms) and maximal EOR_{endo} (339 ± 24 ms, difference = 1 ± 19 ms, $P = .92$), between maximal QT_{end} interval and maximal EOR_{total} (341 ± 24 ms, difference = 2 ± 18 ms, $P = .69$), or between minimal QT_{peak} interval (283 ± 28 ms) and minimal EOR_{total} (282 ± 20 ms, difference = 0 ± 15 ms, $P = .95$).

CONCLUSIONS In *in vivo* pig models, T_{peak} does not coincide with full repolarization of the epicardium but coincides well with the earliest EOR, whereas the T_{end} corresponds with the latest EOR. These findings suggest that not only the transmural gradients but also the apicobasal repolarization gradients contribute to genesis of the T wave.

KEYWORDS T wave; QT interval; Repolarization; Monophasic action potential

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Introduction

Increased dispersion of ventricular repolarization is associated with the development of ventricular tachyarrhythmias, as suggested by previous experimental studies.[1–3] Other studies demonstrated that dispersion of repolarization may result from differences in action potential duration among cells originating from different myocardial layers, epicardial and endocardial cells, and subendocardially located M cells.[4,5] Further *in vitro* studies suggested that full repolarization of the epicardium coincides with the peak of the T wave (T_{peak}) and that of the M cells coincides with the end of the T wave (T_{end}) on the pseudo-ECG.[6] The apicobasal voltage gradient was demonstrated to contribute little to genesis of the T wave.[7,8] However, this theory was based on *in vitro* studies of canine arterially perfused ventricular

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wedge. Other *in vivo* studies have failed to find the existence of marked transmural dispersion of ventricular repolarization.[9–12] The coincidence between T_{peak}/T_{end} and full repolarization of the epicardium/endocardium has never been validated *in vivo.*

Monophasic action potential (MAP) is the generally accepted method of choice for evaluating ventricular repolarization.[13,14] To study the global dispersion of ventricular repolarization, we developed a MAP mapping technique that combines MAP recording and electroanatomic mapping (CARTO, Biosense Webster, Waterloo, Belgium) techniques.[15–18] In the present study, we simultaneously recorded 12-lead ECG and MAP from both epicardium and endocardium using the CARTO mapping system to evaluate global ventricular repolarization in open chest pigs and thereby to validate whether full repolarization of the epicardium on MAP recordings is consistent with T_{peak} and that of the endocardium with T_{end}.

Methods

Subjects and anesthesia

Ten healthy pigs (weight 47–53 kg) were premedicated with pancuronium bromide 0.1 mg/kg, thiopental 5 mg/kg, and atropine 0.015 mg/kg. Anesthesia was maintained with a 10 ml/hour infusion of a mixture of fentanyl 1 mg and pancuronium bromide 20 mg. Intubation and artificial ventilation of the pigs were performed during the study. Volume-controlled ventilation of 8 L/min, 20 breaths/min, positive end-expiratory pressure of 5 cmH_2O, and FiO_2 of 0.5 was used. Thoracotomy and pericardectomy were performed to expose the heart. The study was approved by the local ethics committee, and the electrophysiologic procedures were in accordance with local institutional guidelines.

CARTO system

The system has been described in detail previously.[19] In brief, the torso of the subject is covered by three magnetic fields of different frequencies. A location reference (Ref-Star, Biosense Webster) is fixed on the subject's back, while a mapping catheter (Navi-Star, Biosense Webster) navigates within the cardiac chambers or on the surface of the heart. The magnetic sensors in the tip of the mapping catheter and the location reference continuously compare the intensities of the three magnetic fields, ensuring that the location of the mapping catheter can be accurately determined and displayed in real time. Three-dimensional maps of endocardial or epicardial activation can be constructed from accurately localized electrograms recorded using the mapping catheter. The accuracy of spatial localization has been verified to be 0.7 mm *in vivo.*[19]

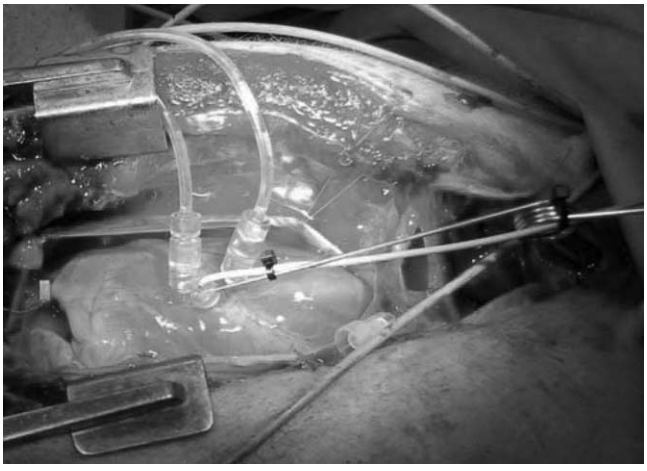

Figure 1 Epicardial mapping with a modified-tip Navi-Star catheter mounted on an elastic handle. Myocardial temperature was kept constant by drips of warm saline controlled by a temperature monitor.

MAP recording

Both endocardial and epicardial mapping were performed after thoracotomy and pericardectomy. In two pigs, both the right and left ventricles were mapped. In the remaining eight pigs, only the left ventricle was mapped. A modified-tip, 7Fr Navi-Star catheter (Biosense Webster) was used, which has a contact ball of 0.5-mm length and 1-mm diameter at the end of the tip electrode.[18] For endocardial mapping, the catheter was introduced into the left ventricle via the right femoral artery. For epicardial mapping, the catheter was mounted on an elastic handle of an epicardial mapping probe (EP Technologies, Sunnyvale, CA, USA). Two saline lines were hung over the left and right ventricles with warmed saline drip to maintain the myocardial temperature constant and to facilitate electrical contact of electrodes with the epicardium. A thermometer (myocardial needle temperature probe) was inserted into the myocardium of the right ventricular outflow tract for monitoring of myocardial temperature during the entire experiment (Figure 1). The temperature and speed of the saline drop were adjusted if necessary.

MAP signals were recorded between the 4-mm tip electrode (exploring electrode) and the 2-mm ring electrode 1 mm proximal to the tip (indifferent electrode) at a filter bandwidth of 0.05 to 400 Hz. A unipolar electrogram from the indifferent electrode was recorded at a filter bandwidth of 0.5 to 120 Hz. When the amplitude and morphology of the MAP in the real-time monitor window of the CARTO system appeared satisfactory,[13] the data were captured in a sampling window for further inspection. The accepted signals were stored simultaneously at a sampling frequency of 1 kHz. Caution was taken to place the mapping catheter perpendicularly against the endocardium/epicardium and to avoid "ST-segment" elevation, that is, >20% amplitude of the ventricular deflection on the unipolar electrogram from the indifferent electrode. At least one MAP was recorded in a 2-cm^2 area during epicardial and