**E.J.Ciaccio, J.Coromilas, A.L.Wit**

# NEW METHODS TO PINPOINT REENTRANT CIRCUITS CAUSING VENTRICULAR TACHYCARDIA

*Columbia University College of Physicians and Surgeons*
*New York, USA*

**Abstract** Following myocardial infarct (heart attack) in human patients, it is a common problem for arrhythmias to develop due to presence of diseased and dead tissue in the infarct area. Activation mapping is an important procedure to detect and localize the arrhythmogenic zone. However, currently this requires induction of tachycardia and extensive recording time in patients undergoing electrophysiology (EP) study, which is inconvenient for the patient and can be debilitating. In this work we describe new methods of analysis for detection of arrhythmogenic zones using signals acquired during the normal sinus rhythm. Examples of the analysis are given using a postinfarction canine model in which induction of ventricular tachycardia is possible using programmed electrical stimulation. Firstly, signals from the heart surface are acquired from the experimental animals at 196-312 sites. These signals are analyzed, and various parameters of electrogram shape, namely the activation time and the electrogram duration, are mapped. The area of the map with unique electrogram properties is shown to coincide with the focal area of the arrhythmia. Potentially, this technology can be applied to clinical data for rapid localization of the arrhythmogenic zone. This would be useful for clinical ablation therapy to prevent reinduction of tachycardia in postinfarction patients.

## Introduction

Following myocardial infarct (heart attack) in human patients, it is a common problem for arrhythmias to develop due to presence of diseased and dead tissue in the infarct area. Commonly, and infarct border zone forms, which is a thin layer of surviving cells superficial to the infarct location. These cells typically have abnormal properties of electrical conduction and are interspersed with dead cells and connective tissue. The result is that activation across this area of the heart tends to be slow and irregular. When a premature electrical stimulus arrives of natural or artificial origin, conduction slows and/or blocks at the abnormal region. If there is sufficient delay, the activation wavefront can reenter previously excited regions; a process called reentry. If the reentrant loop, or circuit, around which the activation wavefront propagates is such that the cycle time is less than the timing of the normal pacemaker of the heart, the reentrant circuit which capture the activation of the heart from the pacemaker. Hence, reentrant activity is rapid, i.e., tachycardia ensues. Typically this occurs around an infarct region located in the right or left ventricle, and the arrhythmia is called reentrant ventricular tachycardia.

Reentrant ventricular tachycardia is a serious condition because there abnormal conduction and inefficient pumping of blood to the systemic and pulmonary systems. Normally, activation across the entire ventricles is rapid and nearly simultaneous, resulting and forceful and uniform contraction of the ventricles during systole, and refill of the ventricular cavities during diastole. During reentrant ventricular tachycardia, the activation wavefront slowly travels in one or more loops around the ventricle, causing slow and irregular contraction of the chamber and inefficient pumping of blood. Moreover, the rapid cycle time adds to the inefficiency, because the ventricular chambers have less time to refill with blood after each systolic cycle. To cure this conduction, the abnormal (arrhythmogenic) region must be altered so that a reentrant circuit can no longer be induced there with premature extrastimuli. Antiarrhythmic drug therapy maybe useful in some but not all cases. Surgery is an option to remove the compromised tissue, but it can be risky and cause morbidity to the patient. A less invasive option is ablation therapy, in which energy is imparted to the arrhythmogenic region via a catheter which is inserted usually through the femoral artery and positioned in the appropriate ventricle near the infarct location. A problem with this therapy is the difficulty in isolating and localizing the arrhythmogenic zone. In this paper we describe new methods to pinpoint arrhythmogenic regions where reentrant circuits causing ventricular tachycardia form.

## Materials and Methods

Although human clinical data is available for retrospective study, in our laboratory, prospective studies can be done using a canine model of postinfarction reentrant ventricular tachycardia. In this option the LAD is ligated to cause an infarct in the left ventricle. Four to five days post infarction, the animal is prepared for electrophysiologic analysis. Sodium pentobarbital is administered (10mg/kg), the chest is opened and positive pressure ventilation is applied. In this model, the infarct border zone typically occurs on the epicardial surface, which is convenient for analysis by the open chest method. An array of 196-312 bipolar electrodes is positioned over the left ventricle superficial to the infarct location, and is sutured there to maintain constant positioning. An example array is shown in Figure 1 and signals acquired with it during normal sinus rhythm are shown in Figure 2. These surface signals (called electrograms) are acquired first during the normal sinus rhythm at the beginning of each experiment. Thereafter, attempts are made to induce ventricular tachycar-

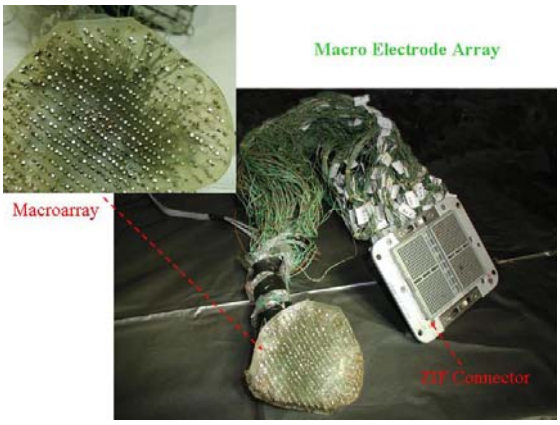


**Figure 1.** *Image of a multielectrode array used to acquire signals from the anterior left ventricular surface in the open chest canine heart*

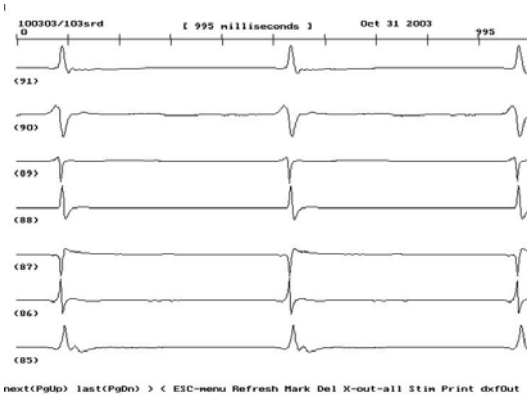


**Figure 2.** *Examples of actual surface signals (electrograms) acquired with this array during the normal sinus rhythm. The sinus rhythm cycle length in this animal is approximately 450ms (see scale at top of panel).*

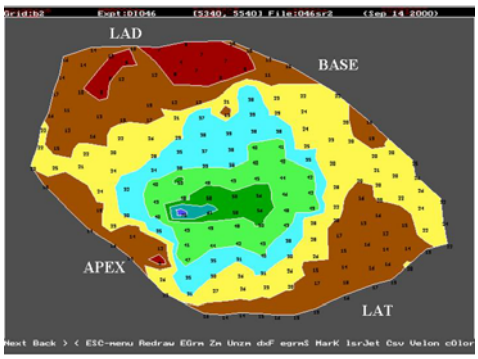


**Figure 3.** *Sinus rhythm activation map with 10ms isochrones, denoted by colors. The relationship of the map to the geometry of the heart is denoted*

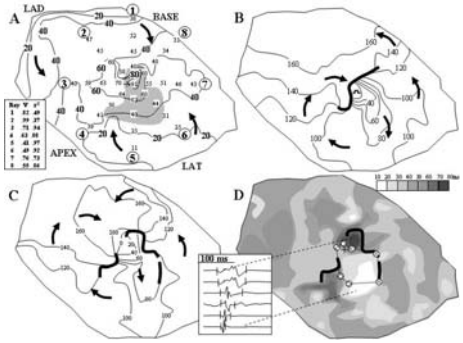


**Figure 4.** *Procedure for sinus rhythm analysis. A. sinus rhythm activation map and vectors for linear regression. B. activation map of the premature stimulus cycle leading to tachycardia. C. activation map of ventricular tachycardia arising from the premature stimulus cycle shown in panel B. The pattern of activation shows that tachycardia is caused by a reentrant circuit. D. the sinus rhythm electrogram duration map. Lighter shades of gray denote shorter sinus rhythm electrogram duration and vice versa. Short sinus rhythm electrogram duration coincides with the area which is bounded by functional arcs of conduction block during reentrant ventricular tachycardia. These arcs are overlaid on the map to show position.*

dia by pacing the heart followed by introduction of a premature stimulus. The pacing procedure is done automatically using programmed protocols embedded in a PC-type computer and a constant-current generator. The heart is paced with a constant current that is twice the current necessary to capture activation of the heart at the stimulus site. The stimulus pulse is 2ms wide. Typically the basic cycle length for pacing, called S1, is slightly shorter than the normal heart rate for the canine, and is between 250 and 300ms. Following 10 basic stimuli, a premature (early stimulus) is applied, normally in the range of 140 to 200ms. This extrastimuli caused slow conduction and often block to occur in the arrhythmogenic zone because the cells there are compromised and the path for activation is circuitous. If conditions are such that there is sufficient delay in the infarct border zone so that one area can reexcite via the same wavefront, reentry occurs, which will be sustained so long as certain conditions are met, such as that the cycle length for reentry is shorter than the heart rate during normal sinus rhythm. Signals are acquired during basic pacing, the extrastimuli cycle, and ventricular tachycardia, if it is induced.

Activation maps are made from all of these data. They are constructed as follows. Each electrogram signal is marked during each cardiac cycle at the point of greatest slope in the signal associated with the largest peak amplitude. This time is considered, to a first approximation, to be the time at which the activation wavefront propagates beneath the recording electrode during each heart beat. It is based on theoretical considerations which have been described in detail elsewhere (Spach). This times, called activation marks, are used to construct an isochronal map called an activation map. Firstly, the times of activation for one cardiac cycle for all recording sites are printed on a computerized grid. The locations of the printed times correspond to the locations of the corresponding recording electrode in the array that is positioned and sutured over the left ventricular surface of the heart. Therefore, one can observe areas of early activation (earlier activation times) and later activation (later activation times) on the map. Isochrone lines can be drawn on the map, which separate clusters of activation times within the same range. For example, isochronal spacing of 10ms separate clusters of sites having activation times

separated by 10ms. A typical sinus rhythm activation map is shown in Figure 3, with heart landmarks shown. Early activation proceeds from the LAD border (red). Latest activation is toward the center (green and blue).

We use sinus rhythm activation maps in the following manner of analysis to detect and pinpoint areas of arrhythmogenic activity where reentrant circuits can form. Firstly areas of latest sinus rhythm activation are determined from the sinus rhythm activation map. From such locations, areas with a uniform and sharp activation gradient are ascertained. The sinus rhythm activation gradient is computed as follows. The times of activation at 4-6 recording sites along a curved line positioned over the computerized mapping grid are recorded and a linear regression is computed. If the coefficient of regression r2 is greater than 0.9, and the slope of the regression line is less than 0.75mm/ms, it is predicted that a reentrant circuit can form at the location of the curved line, i.e., it is an arrhythmogenic zone. To determine the borders of the zone, the electrogram duration is mapped (see Figure 4). The electrogram duration is defined as the interval of the electrogram, encompassing the local activation time, at which electrogram deflections are contiguous with no isoelectric interval of greater than 10ms. The boundary of the arrhythmogenic area is predicted to coincide with the locations at which electrogram duration is short and bounded by areas of longer duration. Sinus rhythm characteristics were measured for a series of experiments to determine and predict the area of arrhythmogenicity which would lead to reentrant ventricular tachycardia in postinfarction canine heart experiments.

**Results and Discussion**

In Figure 4 is shown an example of sinus rhythm activation mapping analysis. In panel A the sinus rhythm activation map is shown with selected activation times printed on the computerized grid. Late activation occurs at time 91ms on the grid, and several vectors are projected away from this site to compute a linear regression. The vector with sharpest gradient (lowest value) and highest r2 value is that labeled 5 (values of 0.41mm/ms and 0.97 respectively). Therefore, it would be predicted based on sinus rhythm activation times that at this vector location would be present arrhythmogenic tissue from which a reentrant circuit causing ventricular tachycardia could form. Ventricular tachycardia was actually induced in this experiment by a premature stimulus as shown in panels B-C. In panel B, the activation map for the premature stimulus cycle is shown. The stimulus site is marked near the center of the grid, and proceeds toward the LAT margin. Block occurs in the opposite direction as denoted by the thick curvy line. The activation wavefront bifurcates and proceeds around the block line, propagating toward the LAD margin. It then turns in toward the block line, and because there has been sufficient time (160ms) for recovery of excitability, it breaks through the unidirectional arc of conduction block reenters the previously excited area to begin a reentry cycle. The arrows denote the course of propagation of the activation wavefront during the premature excitation cycle (panel B). A reentry cycle is shown in panel C, with the thick curvy lines denoting locations of functional arcs of conduction block on the computerized grid. These arcs are more or less stabilized during ventricular tachycardia when cycle length is relatively short, but disappear during the normal sinus rhythm when cycle length is longer. In the tachycardia activation map, activation proceeds toward the LAT margin of the grid when the wavefront is propagating between the functional lines of block. The wavefront bifurcates and travels as two distinct wavefronts toward the LAD margin. They coalesce, and traverse the region between the functional arcs of conduction block. The cycle length of this tachycardia is approximately 200ms (see isochrones). This process is known as reentry with a double loop (figure-8) pattern of conduction. In panel D is shown the sinus rhythm electrogram duration map, with the locations of the arcs of block from ventricular tachycardia overlying the computerized map grid. Electrogram duration is relatively short between the locations of the arcs of conduction block. Shorter electrogram duration is denoted by lighter gray shading, and examples of electrogram duration marks are given in the inset. At the borders between short and long duration surrounding vector 5, are the locations of the arcs of conduction block forming during reentrant ventricular tachycardia. Hence, the arrhythmogenic zone is predictable from sinus rhythm analysis.

Although this example was provided from data acquired using a canine model, there is potential application to clinical analysis of patients with postinfarction tachycardia. In clinical cases the infarct border zone is typically endocardial, not epicardial as in the canine. However, clinical data from the endocardial surface of the heart is relatively easy to obtain using a mapping catheter which is inserted prior to or simultaneously with the ablation device during clinical EP study. The canine model is similar to clinical tachycardia in many ways including the ability to induce reentrant ventricular tachycardia by premature artificial stimulation, and modification of the conductive properties of the tissue with antiarrhythmic drugs. If sinus rhythm analysis could be applied to human studies, it would be of potential benefit for therapy, because the arrhythmogenic zone could be pinpointed without the need to induce tachycardia. Currently, in many cases tachycardia cannot be induce during clinical study because it is difficult to reproduce the nature stimulus properties from which tachycardia is initiated when using artificial programmed stimulation. Furthermore, even when tachycardia is inducible, if there is hemodynamic compromise, there is often insufficient time to map the tachycardia activation pattern before the arrhythmia must be terminated. Future applications of this work will be used in retrospective clinical data as a precursor to the development of a clinical trial.

**Acknowledgements**

Supported by an Established Investigator Award from the American Heart Association and Whitaker Foundation Research Award to Dr. Ciaccio, and NIH-NHLBI Program Project Grant HL30557.

**E-Mail:** ejc6@columbia.edu