Anterior Septal Coronary Artery Infarction in the Canine: A Model of Ventricular Tachycardia With a Subendocardial Origin

Ablation and Activation Sequence Mapping

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Background In humans, chronic ventricular tachycardia (VT) is usually associated with myocardial infarcts that involve the interventricular septum. In an effort to more closely mimic the anatomic substrate that gives rise to chronic VT in humans, we developed a canine model of VT in which the anterior septal coronary artery was ligated. The site of earliest activation, the subsequent activation sequence, and the mechanism of VT associated with the resultant ventricular septal infarct was then evaluated to determine if this model accurately reflected the characteristics of human VT.

Methods and Results Seventeen dogs underwent occlusion-reperfusion ventricular septal infarcts. Four to 7 days later, electrophysiological studies were performed. VT was initiated by programmed electrical stimulation and terminated by pacing at a cycle length of 50% to 75% of the VT cycle length. Electrophysiological studies were performed using a 256-channel mapping system. A total of 15 VT morphologies were mapped in 9 animals. Fourteen of 15 morphologies had septal subendocardial sites of earliest activation and 1 had a septal midwall site of earliest activation. VT ablation was performed using a nitrous oxide cryoprobe and confirmed the site of earliest activation by subsequently rendering VT noninducible. Electrophysiological studies demonstrated four distinct VT activation sequences: (1) circular reentrant (n=7), (2) concentric spread (n=5), (3) figure-of-eight (n=2), and (4) septal midwall (n=1).

Conclusions This canine model of ventricular septal infarction produces VTs with sites of earliest activation and activation sequences similar to those in humans. A reentrant mechanism as the basis of these arrhythmias is supported by the following observations: (1) all VT was initiated and terminated with programmed electrical stimulation; (2) VT activation sequences were consistent with reentry; and (3) precise interruption of the sequence terminated the VT and rendered it noninducible. (Circulation. 1994;90:2982-2992.)

Key Words • tachycardia • ischemia • heart diseases • infarction

Previously reported canine models of chronic ventricular tachycardia (VT) have involved ligation of the left anterior descending coronary artery and/or its branches.1,2 The resultant free wall infarcts produce VT with reentrant mechanisms but with a subepicardial site of earliest activation.1,2 A number of studies have demonstrated the site of earliest activation of chronic human VT is normally in the subendocardium3-6 and that the majority of human VT is associated with infarcts extending into the interventricular septum.7-16 Whereas the blood supply of the human interventricular septum arises from three to five large septal perforators that arise from the left anterior descending coronary artery, 75% of the canine interventricular septum receives its blood supply from a single artery, the anterior septal coronary artery.17 To more closely mimic the anatomic substrate that gives rise to chronic VT in humans, we developed a canine model of chronic VT by creating ventricular septal infarcts. The purpose of this study was to characterize the site of earliest activation, the activation sequence, and mechanism of VT after anterior septal coronary infarction in the dog.

Methods

Animal Preparation

All animals received humane care in compliance with the “Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication No 86-23, revised 1985). In addition, the study protocol was approved by the Washington University Animal Studies Committee.

Seventeen adult mongrel dogs weighing 22 to 27 kg were anesthetized with intravenous sodium pentobarbital (30 mg/kg), and mechanical ventilation was maintained by delivering 40% oxygen from a volume-cycled respirator (model MA-1; Bennett Respiration Products, Inc) through a cuffed endotracheal tube. After antibiotic prophylaxis (600 000 U penicillin G IM), a left thoracotomy was performed through the fourth intercostal space, and the heart was suspended in a pericardial cradle. The anterior septal coronary artery was identified at its origin near the bifurcation of the left main coronary into the left anterior descending coronary artery and the circumflex coronary artery (Fig 1). A rummell tourniquet was lowered onto a snare encircling the artery, and the artery was occluded. The tourniquet was released after 2 hours of total occlusion,
Fig 1. Drawing of the heart with the right ventricular free wall cut away to show the course and distribution of the anterior septal coronary artery (a). Occlusion-reperfusion infarcts of this artery were used to produce ventricular tachycardia in this study. Sections 1 through 5 at right are made at 1-cm intervals and show a typical infarction from base (section 1) to apex (section 5) traced from a postmortem specimen stained with 2,3,5-triphenyltetrazolium chloride. LAD indicates left anterior descending coronary artery.

and the anterior septal coronary artery was reperfused. Lidocaine hydrochloride (1 mg/kg) and procainamide (12.5 mg/kg) were administered intravenously at the time of occlusion. A second dose of lidocaine was administered at the time of reperfusion. Intercostal nerve blocks were performed using 1% lidocaine, and the chest was closed. After surgery, the animals received supplemental oxygen for 12 hours, morphine sulfate (0.1 mg/kg) subcutaneously every 4 hours as needed for pain relief, and 600 000 U/d of penicillin G IM for 3 days.

Four to 7 days later, the animals were reanesthetized and ventilated in the same fashion as described above. A catheter was placed in the left femoral artery to monitor the arterial blood pressure. The chest was entered through a median sternotomy. Both vena cavae were encircled with tapes, and the azygous vein was ligated. The heart was exposed and suspended in a pericardial cradle. An asanguinous priming solution and a William Harvey oxygenator (model H-1500, Bard) were used for cardiopulmonary bypass. After heparinization (300 U/kg IV bolus) and direct cannulation of both cavae, normothermic cardiopulmonary bypass was established, and a mean arterial pressure of 60 to 80 mm Hg was maintained. The interatrial groove was dissected to expose the septal portion of the left atrium. The heart was arrested with electrically induced ventricular fibrillation, and a standard left atriotomy was performed. The left ventricular endocardial electrode mold containing multiple electrodes was introduced.
into the left ventricle through the left atriotomy to avoid the need for a ventriculotomy. The right ventricular endocardial mold was introduced through a right atriotomy across the tricuspid valve into the right ventricle. Sinus rhythm was restored after DC cardioversion. The entire epicardial surface of the heart was covered with a multipoint epicardial mold. A bipolar reference electrode and a pacing electrode were placed on the right ventricular free wall. A second bipolar reference electrode was placed on the right atrium to monitor atrial activation. A common reference electrode for all cardiac unipolar electrograms was sewn on the inside of the right hemithorax at a distance of at least 15 cm from the heart. Arterial blood gases, serum potassium, and hematocrit values were monitored at 20-minute intervals throughout the study. Sodium bicarbonate and potassium were administered as needed to maintain acid-base equilibrium and potassium level within normal limits.

Epicardial and Endocardial Electrodes and Mapping System

Unipolar data were recorded from 185 epicardial and endocardial sites (Fig 2). Intramural electrograms were recorded by use of multipoint plunge electrodes. All endocardial and epicardial molds were constructed using 2-mm silver beads for electrode points. The epicardial mold was constructed of foam rubber based on the epicardial structure of the normal canine heart. Sixty-one electrodes were arranged 12 mm apart with 5 electrode points each on 12 arrays placed equally within the cup-shaped mold; in addition, one point was placed at the apex of the mold. The elasticity of the mold provided optimal contact between the electrode points and the epicardial surface. The endocardial molds for the right and left ventricles were molded from fresh postmortem hearts and conformed to the internal anatomy of the right ventricle. Indentations accommodated the anterior and posterior papillary muscles; these, combined with an aortic outflow tract prominence, provided three-point fixation within the LV endocardial cavity. The LV electrode was inserted across the mitral valve. These epicardial and endocardial molds standardized 185 unipolar electrode positions on the epicardial and endocardial surfaces. Post. indicates posterior; Ant., anterior; FREE, free wall; and SEP., septum.

Fig 2. Diagram showing electrodes and electrode positions. Upper panels show the electrode molds; lower panels indicate electrode positions after the molds were in position. The epicardial (EPI) mold (A) was slipped over the epicardial surfaces. The right ventricular (RV-ENDO) electrode (B), designed to conform to the internal anatomy of the right ventricle (RV), was inserted across the tricuspid valve. The left ventricular (LV-ENDO) electrode (C) was molded from fresh postmortem hearts and conformed to the internal anatomy of the left ventricle (LV). Indentations accommodated the anterior and posterior papillary muscles; these, combined with an aortic outflow tract prominence, provided three-point fixation within the LV endocardial cavity. The LV electrode was inserted across the mitral valve. These epicardial and endocardial molds standardized 185 unipolar electrode positions on the epicardial and endocardial surfaces. Post. indicates posterior; Ant., anterior; FREE, free wall; and SEP., septum.
computers (Digital Equipment Corp) were linked to separate 128-channel, analog-to-digital converters capable of digitizing the unipolar data at a rate of 1000 samples per second. The two computers were linked to a single Microvox III computer (Digital Equipment Corp) used to display the waveforms and analyze the data. The time of the peak negative derivative (−dV/dt\text{max}) of the unipolar ECG was used as the time of local activation. With the 256-channel mapping system, unipolar data were recorded simultaneously from the 185 electrode positions evenly distributed over the endocardial and epicardial surfaces and standardized by the electrode forms. In addition, multipoint-needle plunge electrodes were used to map intramural activation. Up to 60 additional intramural points could be mapped simultaneously with the electrograms recorded from all of the endocardial and epicardial points.

Potential distribution mapping was used intraoperatively to localize the site of origin for the purpose of guiding ablation attempts. This method was chosen because it provides for rapid evaluation of large numbers of electrograms (details have been published previously). Activation times were determined using the time of the peak negative derivative of the unipolar complex as the time of local activation.

**Study Design**

After placement of the animals on normothermic total cardiopulmonary bypass, the endocardial and epicardial electrodes were positioned. Programmed electrical stimulation (Bloom model DTV-101) was performed to induce VT. Pacing was performed at a pulse width of 2 milliseconds at twice the late diastolic current threshold. A train of eight paced beats (S1) at a basic cycle length of 300 milliseconds was delivered, followed by a double premature stimuli (S2 and S3). The S3 interval was lowered by 5-millisecond decrements until non-capture of the S1 occurred, at which time the S3-S1 coupling interval was decremented by 5 milliseconds. This sequence was repeated until either the heart became refractory to the S1 or until VT occurred. If the heart became refractory to S1, then the S1 interval was reduced to 275 milliseconds. If no VT was induced at an S1 cycle length of 275 milliseconds, then an S1 cycle length of 250 milliseconds was used. Ablation of VT was attempted in animals with repeatedly inducible VT. Repeatedly inducible VT was defined as VT of a single surface ECG morphology, which could be induced at least 25% of the time at a single programmed electrical stimulation setting. All morphologies of repeatedly inducible VT were terminated by pacing the ventricle at a cycle length 50% to 75% of the VT cycle length. Potential distribution maps were constructed for repeatedly inducible VT, and the site of earliest activation was identified. Cryolesions were made using a nitrous oxide cryo-probe with a 4-mm base and a 3-mm tip. The freezing time was 4 minutes for each lesion, and the probe reached a temperature of −60°C. An attempt was made to have the animal in sustained VT while the cryolesions were placed, since termination of VT during placement of the cryolesions was taken as evidence of accurate localization of the site of earliest activation. After placement of the cryolesions, reinitiation of VT was attempted both at the original settings and through the entire programmed electrical stimulation protocol. If VT could be reinitiated with the same surface QRS morphology as the original VT, additional cryolesions were placed at the initial site of earliest activation. However, if repeatedly inducible VT with a different surface QRS morphology was initiated during restesting, it was mapped and cryolesions were directed at this new site of earliest activation. Repositioning of the molds after ablation was facilitated by the shape of the molds, which conform to the internal anatomy of the left and right ventricles and provided three-point fixation. Ablation was successful if no VT of any morphology could be induced. For 9 animals after induction of VT and mapping, a ventriculotomy was made through the ventricular free wall opposite the point recording the earliest activation of the VT as determined by potential distribution mapping. The myocardium adjacent to the electrode point recording earliest activation was identified by carefully peeling back the electrode form. VT was reinduced after the ventriculotomy to verify that the ventriculotomy itself had not rendered the VT noninducible. The cryoprobe was placed at the site of the earliest activation, and the cryolesion was made while the animal was in sustained VT.

In 3 animals, a transmural or transtricuspid approach was used to avoid a ventriculotomy. Typical surface ECG recordings from an experiment are shown in Fig 3. At the end of each experiment, the animals were euthanized with an overdose of sodium pentobarbital (≥120 mg/kg IV). The infarct size and distribution were verified by staining with 2,3,5-triphenyltetrazolium chloride (TTC).

To determine the dimension of the cryolesions, a single animal without an infarction was placed on normothermic...
The site of earliest activation occurred on the left ventricular (LV) endocardial surface, and the electrogams correspond to the points on the activation map of the LV endocardial (LV-ENDO) surface. The times of subsequent activation of the remaining myocardial surfaces, right ventricular (RV) endocardial (RV-ENDO), and epicardial (EPI) are indicated, and the subsequent activation sequence is demonstrated by the isochron maps. From the site of earliest activation (A), the activation wavefront moves in a clockwise circular direction with the latest time (I) adjacent to the site of earliest activation (A). Earliest activation on the RV endocardium occurs 23 milliseconds after the activation of point A and proceeds from the posterior (Post) aspect of the RV endocardium anteriorly (Ant). There are two areas of block, one inferior and one superior. Earliest activation on the epicardium occurs at 21 milliseconds, and epicardial activation proceeds in a concentric spread pattern. The activation sequence recorded from the RV endocardium and epicardium do not indicate the site of earliest activation or mirror the activation sequence on the LV endocardium. Sep indicates septum; FW, free wall.

Results

Fifteen morphologies of repeatedly inducible sustained VT were mapped in 9 animals, including 5 animals with one VT morphology, 2 animals with two VT morphologies, and 2 animals with three VT morphologies. The mean VT cycle length was 184±33 milliseconds. Postmortem examination and TTC staining revealed septal infarctions in all the animals in which VT could be induced. The earliest point of activation recorded from the endocardial and epicardial molds occurred over the endocardial surface of the septum in all 15 morphologies of VT. In 1 animal there was near simultaneous activation of the right and left ventricular endocardial septal surface; in this animal intramural mapping with plunge electrodes revealed a septal midwall site of earliest activation. In the remaining 14 morphologies of VT, the site of earliest activation occurred on either the right (n=3) or left (n=11) endocardial septal surface.

Patterns of Activation

Isochron activation maps were constructed for each morphology of VT. Four distinct activation patterns were observed emanating from the site of earliest activation.

In seven morphologies of VT all with earliest activation on the left ventricular endocardium, the activation sequence was characterized by a circular reentrant pattern (Fig 4). A single activation wavefront spread in only one direction for the site of earliest activation and circled around the left ventricular endocardium in either a clockwise or counterclockwise direction, with the latest activation times recorded immediately adjacent to the earliest site of activation. There was always an isoelectric gap. The activation sequence of the epicardium was uniformly characterized by a concentric spread pattern of
activation. The right ventricular endocardial activation sequence, although frequently more complex than the epicardial concentric spread pattern of activation, failed to mirror or suggest the pattern of activation of the left ventricular endocardium.

In five morphologies of VT, the activation sequence on the endocardial surface of earliest activation was characterized by a concentric spread of activation from the site of earliest activation, which occurred on either the left ventricular endocardium (n=2) or the right ventricular endocardium (n=3). In the example shown in Fig 5, the site of earliest activation was recorded from the left ventricular endocardial septal surface. Subsequent activation spread radially from that point. Although the concentric spread pattern of activation was recorded emanating from the site of earliest activation and ablation attempts directed at this site were successful, right ventricular endocardial and intramural mapping demonstrated a more complex activation pattern. Right ventricular endocardial activation occurred 20 milliseconds after earliest activation was recorded on the left ventricular endocardium. Activation of the right ventricular endocardium then proceeded in a circular reentrant pattern in a counterclockwise loop, with the latest recorded activation on the right ventricular endocardium adjacent to the point of right ventricular endocardial wave front breakthrough and opposite the site of earliest overall activation on the left ventricular endocardial septal surface. Intramural mapping with plunge electrodes demonstrated electrical activity between the latest point of right ventricular endocardial activation and the site of earliest recorded activation on the left ventricular endocardial surface, thus demonstrating a return pathway. This global pattern of activation is consistent with a reentrant mechanism.

In two morphologies of VT, both with earliest points of activation recorded on the left ventricular endocardium, the activation sequence was characterized by a figure-of-eight pattern (Fig 6). From the site of earliest activation, the wave front split into two arcs, one clockwise and one counterclockwise, circling around two putative arcs of conduction block and eventually reuniting to form a common return limb back to the site of onset. This sequence of activation followed the figure-of-eight pattern recorded from the epicardial surface of dogs after left anterior descending coronary artery infarction as described by El-Sherif et al and is consistent with a reentrant mechanism.

A pattern of activation in which earliest recorded activation occurred in septal midwall was observed in 1 animal with a single morphology of VT (Fig 7). In this animal there was near simultaneous activation of the right and left endocardial septal surfaces. Intramural septal mapping with multipoint plunge electrodes revealed a midwall septal site of earliest activation. Activation proceeded in a concentric spread pattern from this site of earliest recorded activity. Following wave front breakthrough onto the right and left ventricular endocardial septal surfaces, the remaining activation sequence continued in a concentric spread pattern.

Four animals had more than one morphology of VT. To be characterized as a distinct morphology of VT, a subsequent morphology induced in an animal had to have a different QRS morphology on surface ECG, earliest site of activation, activation sequence, and cycle length. An example is shown in Fig 8. This example demonstrates the characteristics necessary for two morphologies of VT to be characterized as different. The first morphology with a cycle length of 179 milliseconds has a circular reentrant pattern of activation with a clockwise loop. A subsequent morphology of VT initiated in this animal has a different site of earliest activation, and the activation sequence proceeds in a
Results of Ablation Attempts

Ablation of VT was attempted using a nitrous oxide cryoprobe (Frigidaire Corp) with a 3-mm tip and a 4-mm base. Cryolesions were placed at the site of earliest recorded activation, the presumed exit point from an area of slow conduction. VT was successfully ablated in 14 of 15 morphologies using 2 to 14 cryolesions (4 ± 3 cryolesions per morphology). Two techniques of cryoaulation were used. In 6 of 9 animals in the study, ablations were performed through ventriculotomies. In the remaining 3 animals, a transatrial or transatrial approach was used. The ventriculotomy technique was chosen because it allowed precise placement of cryolesions immediately adjacent to the electrode from which earliest activation was recorded. In addition, cryolesions were placed in an open, dry field. VT was induced after ventriculotomy to ensure that the ventriculotomy itself was not responsible for terminating the arrhythmia. In the ventriculotomy group, 2 to 4 cryolesions per morphology of VT were required for ablation. The transmural or transtrial approach was used in 3 animals. The first animal in which a transmural/transtricuspid approach was used had 2 morphologies of VT. The first morphology was induced with earliest activation recorded on the right ventricular septal surface. This morphology of VT was successfully ablated with 2 cryolesions. An additional morphology of VT was then induced with earliest recorded activation on the left ventricular endocardial surface adjacent to the base of the posterior papillary muscle. Despite a total of 5 cryolesions directed at this point, the VT was still inducible. At this point in the experiment, the animal's condition deteriorated, and the study was terminated. It was noteworthy that this morphology of VT could be repeatedly terminated by application of the normothermic cryoprobe to the site of earliest activation. The earliest site of activation of this morphology of VT was near the apex of the left ventricular cavity. Difficulty was encountered in keeping the left ventricular cavity dry and the ventricular walls away from the cryoprobe during freezing. Rapid thawing may have contributed to the difficulty in achieving ablation of this morphology of VT. This is supported by the repeated termination of VT by the application of the normothermic cryoprobe, indicating that the earliest site of activation had been correctly localized. The second animal in which VT ablation was attempted using a transmural approach required a total of 9 cryolesions placed over the posterior left ventricular endocardial septal surface from which earliest activation was recorded. Again, warming of the cryolesion by the myocardium and the intracavitary blood may have contributed to the increased number of cryolesions required as compared with the ventriculotomy group. A morphology of VT was induced in 1 animal in which earliest recorded activation was in the midportion of the interventricular septum, a transmural-transtricuspid approach to ablation was used. In this animal, a total of 14 cryolesions, 7 on each side of the septum, were required for ablation. The difficulty in ablating this morphology of VT is consistent with the midwall site of earliest activation, demonstrated by intramural mapping, since the cryolesions only penetrate 6 mm. In all of the morphologies of VT studied, either cryoaulation (14 of 15) or termination of sustained VT by application of the normothermic cryoprobe (1 of 15) confirmed the site of earliest activation as determined by intoraoperative mapping. The sites of earliest activation of all morphologies of VT are summarized in Fig 9.

Discussion

Intraoperative mapping during surgery for VT in humans demonstrates that VT originates in the subendocardium in the majority of cases, and epicardial activation wavefront breakthrough cannot be relied on to correspond with the subendocardial site of origin. Well-characterized canine models of chronic VT have
produce a canine model of VT with a subendocardial origin, it was necessary to produce an interventricular septal infarction. A single artery, the anterior septal coronary artery, is the blood supply for 75% of the canine interventricular septum and therefore this was the vessel we chose to occlude to produce the infarcts that we studied. Previous studies using anterior septal coronary artery infarction and ligation include those of Lumb et al.23 and Hashiba et al.24 who used anterior septal artery ligation in the dog to study bundle branch block and complete atrioventricular (AV) block. In a series of studies, El-Sherif, Scherlag, and Lazarra25-28 used ligation of the anterior septal coronary artery to study a variety of conduction defects including Mobitz type II, rate-dependent bundle branch block and paroxysmal AV block. All of these studies were performed primarily to study the conduction defects associated with acute ischemia of the basal interventricular septum. Further studies used this model to study ventricular arrhythmias after acute myocardial ischemia, demonstrating that the ventricular arrhythmias arose from the basal portion of the septum and that they had a reentrant mechanism.29 Using plunge electrodes and pace mapping 24 hours after anterior septal coronary artery infarction, Spear et al.30 demonstrated that ventricular arrhythmias arose from the subendocardium. Spielman et al.31 reported that anterior septal infarctions in the dog produced VT that was initiated by programmed electrical stimulation and had a subendocardial origin. Based on these studies, we proceeded to develop a model of chronic VT using anterior septal coronary artery ligation.

Four patterns of activation were observed; all of the activation patterns described have also been observed during intraoperative mapping during surgery for VT in humans. Two morphologies of VT demonstrated a figure-of-eight pattern of activation (Fig 6) similar to that observed in humans during intraoperative studies.21,22 This activation pattern was recorded from the left ventricular endocardium; it was characterized by two large arcs of activation that both circled back toward the site of earliest activation so that the latest activation times were adjacent to the site of earliest activation. Seven morphologies of VT, all with earliest activation recorded from the left ventricular endocardium, had a circular reentrant pattern of activation (Fig 4). The circular reentrant pattern was characterized by the spread of the activation wave front in one direction, from the site of earliest activation, around the left ventricular endocardium to the latest area of activation, which was always adjacent to the site of earliest activation. This pattern is similar to that recorded by Harris et al.32 during intraoperative mapping in humans in which they described a circular activation sequence characterized by a broad wave front of excitation that circled around the ventricle. They also recorded incomplete circular activation in which there was a measurable isoelectric gap, presumably representing an area of slow conduction during which electrical activity could not be recorded. This most closely resembles the circular reentrant pattern described in this study. The circular reentrant pattern of activation may also represent an incomplete figure-of-eight pattern of activation. An incomplete figure-of-eight pattern of activation, also described in humans, is characterized by two arcs of

Fig 7. In a single morphology of ventricular tachycardia, a septal midwall site of earliest activation was found. Intramural mapping of the ventricular septum with plunge electrodes demonstrated a midwall septal site of earliest activation with concentric spread from the point of earliest activation to the subendocardium. There was near simultaneous activation of the left and right ventricular (LV and RV) endocardial surfaces. The remainder of the activation sequence was characterized by concentric spread of the activation wave front from the site of endocardial wave front breakthrough. LAD indicates left anterior descending coronary artery.

been described that are produced by occlusion and reperfusion of the left anterior descending coronary artery. These infarcts create the substrate for an inducible VT with a reentrant activation sequence, and the subepicardial origin corresponds to the site of reentry where the wave front exits from an area of slow conduction.1,2 Unlike the canine model, a number of studies have mapped the origin of chronic human VT to the subendocardium. The majority are associated with infarcts extending into the interventricular septum.3-16 To
Fig 8. Example of two morphologies of VT initiated in a single animal. For the first morphology of VT, the site of earliest activation is recorded from point A. The activation sequence then proceeds in a clockwise direction around the LV endocardium, with the latest time recorded at point I adjacent to the site of earliest recorded activation. The cycle length of this morphology of VT was 179. Lettered electrogars shown to the left of the activation map of the first morphology were recorded from the corresponding points on the activation map; times of local activation are indicated by arrowheads. After the placement of cryolesions at point A, VT of this morphology was no longer inducible. However, a second morphology of VT was induced. The activation sequence map of the second morphology of VT shows that the earliest recorded activation occurred at point A'; a more anterior-superior septal location than the site of earliest activation of the first morphology. Again, a circular reentrant activation sequence is demonstrated, with the latest activation time recorded from point H' adjacent to the earliest site of activation. However, in the second morphology of VT, activation proceeds in a counterclockwise direction as opposed to the clockwise activation sequence of the first morphology. The cycle length of the second morphology was 203 milliseconds, longer than the cycle length of the first morphology (179 milliseconds). Cryolesions directed at point A' ablated this morphology. See Fig 4 for definitions of abbreviations.

activation, one clockwise and one counterclockwise, circling around two arcs of conduction block and eventually reuniting to form a common return limb. However, in an incomplete figure-of-eight pattern of activation, because of more rapid conduction in one of the arcs of activation, the opposite arc of activation is blocked and therefore diminished in size.21,22 Because of the limits of resolution of the mapping system used in our study, some of these circular reentrant activation patterns we observed may represent incomplete figure-of-eight patterns. In addition, the basilar location of the infarct may also permit only one arc of activation spreading toward the apex because the opposite arc of activation, which would spread toward the base, had inadequate tissue to complete its return limb. Both the figure-of-eight and circular reentrant patterns of activation support a reentrant mechanism of the VT. A concentric spread pattern of activation also observed in humans was the pattern of activation of five morphologies of VT; this activation pattern was characterized by the radial spread of the activation wave front from the point of earliest activation.21,22 Although the activation sequence would suggest an ectopic pacemaker as the mechanism for the tachycardia, using global activation mapping as well as intramural mapping with plunge electrodes, we were able to identify nearly continuous electrical activity and a global activation sequence consistent with reentry in the example shown in Fig 5. In a single morphology of VT in this study, intramural mapping of the interventricular septum with plunge electrodes demonstrated a midwall septal site of earliest activation with concentric spread from that point (Fig 7). There was near simultaneous activation of the left and right ventricular endocardial septal surfaces. The remainder of the activation sequence was characterized by the concentric spread of the activation wave front from the site of endocardial wave front breakthrough.
Intraoperative interventions confirmed the site of earliest activation of all the morphologies of VT in this study. VT was rendered noninducible by the application of cryolesions in 14 of 15 morphologies and in the remaining morphology, VT was repeatedly terminated by application of the normothermic cryoprobe. Intraoperative intervention allowed for precise confirmation of the site of earliest activation because the diameter of the cryolesions was essentially equal to the interelectrode distance, the resolution of the mapping system. Cryoablation was selected as a technique of ablation for two reasons. First, the cryolesions do not have a great deal of penetration (6 mm), and therefore ablation using this method could confirm that the site of earliest activation was in the subendocardial region. Second, cryoablation is not arrhythmogenic. Previous studies have shown that programmed electrical stimulation did not elicit tachycardia in dogs after ventricular cryolesion placement. The only arrhythmias noted in these animals were frequent ventricular premature beats. Enhanced automaticity as the mechanism for arrhythmias that appear after cryosurgery was suggested by their ECG features.2 The activation sequence patterns observed, the initiation of the tachycardia by programmed electrical stimulation, and the ablation of tachycardia by strategic placement of the lesions on the endocardial surface all support a reentrant mechanism. This suggests that the site of earliest recorded activation of the VT represents the exit from the central common pathway of the reentrant circuit in which conduction is slow and fragmented and undetectable by the methods used in this study.

Multiple VT morphologies were found in 4 animals, including 2 animals with three morphologies each and 2 animals with two morphologies each. After successful ablation of the first VT morphology, VT with a different surface QRS morphology could be initiated. When the new VT morphology was initiated during postablation programmed electrical stimulation, it was mapped and ablation attempted. To be characterized as a distinct morphology, this new morphology had to have a different site of earliest activation, cycle length, and activation sequence (Fig 8). The first morphology of VT had a shorter cycle length (164±11 milliseconds) than subsequent morphologies (210±29 milliseconds, P=.03). This suggests that in some animals there are multiple potential reentrant pathways and the VT with the shortest cycle length will dominate.

The resolution of the mapping in this study was limited by the interelectrode distances, =8 mm for the endocardial molds and =12 mm for the epicardial molds. The interelectrode distances were determined by the desire to map global myocardial activation combined with intramural mapping, simultaneously using the 256-channel mapping system. Although increased electrode points could have been used with the present system if multipass mapping (alternating recording from different electrode arrays during sustained monomorphic VT) was used, the short cycle length made this technique unacceptable because a small change in the cycle length could alter the apparent activation sequence. To accurately determine the site of earliest activation, global activation sequence, and therefore to determine the mechanism, this mapping technique was chosen despite the limitations. A second weakness of this study was the use of unipolar mapping. This technique was chosen because previous studies have demonstrated that potential distribution mapping using unipolar electrode points can rapidly and accurately localize the site of earliest activation, and this technique was used to locate the site of earliest activation intraoperatively for the purposes of ablation.18,19 However, it can be difficult to determine the site of earliest activation from electrograms with QS patterns found adjacent to the infarct and the site of earliest activation. This study used the peak negative derivative (−dV/dt max) of the unipolar electrogram as the site of local activation of the myocardial tissue adjacent to the electrode. Intraoperative interventions that terminated the VT support the interpretation of the electrograms in the study. Future studies using shorter interelectrode distances and bipolar mapping may provide additional information concerning this model of VT.

Anterior septal coronary artery infarction in the dog produces VT with origins and activation sequences similar to those in humans. A reentrant mechanism is supported by the following observations: (1) all VT was initiated and terminated with programmed electrical stimulation; (2) activation sequences were consistent with reentry; and (3) precise interruption of the sequence terminates VT and renders it noninducible. Because of its similarity to the architecture of the infarct and the activation patterns of VT in humans, this model may be superior to left anterior descending coronary artery infarct models for the evaluation of surgical and catheter ablation techniques as well as pharmacological interventions.

**Acknowledgments**

This study was supported in part by National Institutes of Health grants R01-HL-33722 and R01-HL-32257.

**References**


*Circulation*. 1994;90:2982-2992
doi: 10.1161/01.CIR.90.6.2982

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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