

Overdrive pacing of early ischemic ventricular tachycardia: evidence for both reentry and triggered activity

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Arnar, David O., Dezhi Xing, and James B. Martins. Overdrive pacing of early ischemic ventricular tachycardia: evidence for both reentry and triggered activity. *Am J Physiol Heart Circ Physiol* 288: H1124–H1130, 2005; doi:10.1152/ajpheart.01162.2003.—Entrainment can be a useful method to identify reentry as a mechanism of ventricular tachycardia (VT). In this study, we evaluated the effect of gradually decreasing cycle lengths of overdrive pacing for stable VT induced in a canine model 1–3 h after coronary occlusion. Intact dogs underwent anterior descending coronary artery occlusion after instrumentation of the risk zone with 21 multipolar plunge needles, each recording 6 bipolar electrograms. Overdrive pacing was attempted if the animals had sustained hemodynamically stable VT, looking for evidence of entrainment. Subsequent three-dimensional mapping determined the mechanism of VT. Fifteen of the 21 dogs studied demonstrated entrainment with overdrive pacing by progressive QRS fusion alone (1), the first nonpaced QRS entrained to the paced cycle length only (7), or both (7). Five of these 15 dogs also had postpacing acceleration of the VT at a subsequent faster pacing cycle length. The mechanism of acceleration in four was a change to a VT with a focal origin. The prepacing mechanism in all 15 dogs was subsequently mapped to reentry. Regarding the six VTs, which demonstrated no evidence for entrainment, the site of earliest activity was mapped to a focal origin in all. These data showing entrainment of inducible reentrant VTs and lack of such for focal VTs support that the focal VTs seen in this study are unlikely the result of microreentry but possibly a mechanism as triggered activity.

ischemia; mapping; entrainment; mechanisms

VENTRICULAR TACHYCARDIA (VT) can be associated with acute myocardial ischemia. Ischemia of the left ventricle results in electrophysiological changes, which may contribute to both conduction delay and block (17). These provide conditions for reentrant VT to develop spontaneously during the acute phase of ischemia (11, 16, 17). In addition to reentry, VT with focal origin has also been seen to occur with acute ischemia (11, 12, 16). The mechanisms of VTs with focal origin may include triggered activity resulting from early (EADs) or delayed afterdepolarizations (DADs) and abnormal automaticity. It is possible that different mechanisms may contribute predominantly to ischemic VTs at various time intervals after coronary artery occlusion.

We have recently reported that the Purkinje system may contribute to the genesis of ventricular tachyarrhythmias occurring with acute ischemia and reperfusion. These VTs, which commonly have a focal origin, can occur spontaneously in the first 30 min of ischemia (1), with reperfusion after a brief (20

min) period of ischemia (3), and are also inducible with extrastimuli in the 1- to 3-h period after coronary artery occlusion (4). In addition to VTs with a Purkinje origin, focal VTs arising from the myocardium and VTs with a reentrant mechanism were seen in these studies. The underlying mechanisms of focal VTs in these studies are not clear. In all studies, there was an absence of substantial conduction delay in the vicinity of the focus of earliest activity, making macroreentry unlikely. Microreentry, on the other hand, could not be entirely excluded, although we have speculated that mechanisms, such as triggering or automaticity, might be more likely. Entrainment occurs because of a specific response of a tachycardia to overdrive pacing (21). Criteria for demonstrating entrainment of VT have been determined (14, 21), and entrainment of a tachycardia can be a useful method to identify reentry as a mechanism (19). The purpose of this study was to perform overdrive pacing of stable monomorphic inducible VT, occurring in the 1- to 3-h period after coronary artery occlusion in a canine model, in an attempt to further delineate the origin/mechanisms of these as either reentrant or focal. Our hypothesis was that VTs with a reentrant mechanism are entrainable by pacing at a rate slightly faster than the rate of VT, whereas those VTs with a focal origin do not show criteria of entrainment, suggesting reentry.

METHODS

Healthy dogs of either gender, weighing 18–24 kg, were used for these studies. The protocol was approved by the University of Iowa Animal Use and Care Committee and conformed to the guidelines of the American Physiological Society.

Surgical preparation. Anesthesia was induced with 500 mg thiopental sodium and 100–200 mg/kg iv α -chloralose as a bolus, and a continuous intravenous infusion of α -chloralose dissolved in polyethylene glycol at 8 mg·kg⁻¹·h⁻¹ was used for the maintenance of anesthesia. The animals were intubated and placed on a ventilator (Harvard Apparatus) with settings adjusted to achieve a physiological arterial PCO₂ (25–35 Torr) and to maintain normal PO₂ (80–150 Torr). NaHCO₃ was infused as necessary to maintain the pH within physiological range (7.30–7.45). Mean arterial blood pressure was continuously monitored via a femoral arterial line, and the femoral vein was cannulated for infusion of saline and the anesthetic agent.

A median sternotomy was done to expose the heart, and a snare was subsequently placed around the left anterior descending coronary artery immediately distal to the first septal perforator. Epicardial collateral vessels to the risk area were ligated. After the experiment, the animals were killed by induction of ventricular fibrillation.

Electrophysiological measurements. The right atrium was paced with a bipolar electrode using current at two times diastolic threshold

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with pulses of 2 ms duration and pacing at a cycle length (CL) of 300 ms. Surface electrocardiographic leads II and V5r were continuously monitored while the limb leads (I, II, III, aVR, aVL, aVF) and lead V5r were recorded. Ventricular pacing for VT induction was performed from the innermost pole of each of the 16-pole needles placed in three locations (apex, anterior base, and lateral wall) outside of the risk zone of the coronary artery occlusion. Cathodal stimuli (2 ms in duration at 4 times diastolic current of threshold) were applied to the pacing electrode while the anode was located in the abdominal subcutaneous tissue. Twenty-one multipolar plunge needles were inserted in and surrounding the risk zone of the left anterior descending coronary artery occlusion, as described previously in detail (1). Each needle recorded 6 bipolar electrograms from circumferential electrodes made from Teflon-insulated tungsten wire 1 mm apart, enabling recordings from a total of 126 sites. Details regarding the electrodes, including interelectrode and interbipole spacing, were as described previously (1, 3, 4).

Electrograms were recorded simultaneously on two separate computers, one for the three endocardial-most bipoles and the other for the three epicardial-most bipoles (1, 3, 4). Signals from the three endocardial-most electrodes were amplified by a gain of 100, bandpass filtered between 3 and 1,300 Hz, and sampled at 3.2 kHz. The epicardial electrograms were sampled at a frequency of 1 kHz/channel and bandpass filtered at 30–300 Hz. Three-dimensional activation maps were constructed from multiplexed signals. Data from both acquisition systems were incorporated for the construction of three-dimensional activation maps with a common surface electrocardiogram (lead II) recording pacing spikes allowing for alignment of signals from both computers.

Sixteen unipolar electrodes on each needle were used to select the six optimal bipolar electrograms, which were adjusted to maximize the capability to record Purkinje signals on the endocardial-most bipole. The adjustment was performed by sequential recordings on a storage oscilloscope for each bipole. A switching box was used to connect the selected bipoles to each amplifier. The length of the needles (22 mm with circumferential electrodes covering the proximal 16 mm of the needle shaft) traversed through the left ventricular wall into the left ventricular cavity. The epicardial-most bipole recorded an electrogram from the epicardium, and subsequent bipoles recorded electrograms sequentially through the myocardial wall. The endocardial-most bipole was used to record Purkinje potentials when they could be identified. Purkinje potentials were identified at their endocardial location according to previously published criteria from this laboratory, including 0.5-mV spikes lasting 1–2 ms preceding by 1–11 ms the larger and longer muscle spike and the surface QRS on the lead recording the earliest activity (1, 3–5). If a Purkinje potential was not identified for a given electrode, no activation time was assigned for the endocardial-most electrogram. Activation maps were constructed to determine the mechanism of VT as reentrant or to pinpoint a focal origin. The construction of the activation maps was described in detail previously (1).

VT induction was performed with the programmed extrastimulus technique at a drive CL of 300 ms. VT induction used up to four premature stimuli as follows. The first premature stimulus (S2) was fixed at 4 ms longer than the ventricular effective refractory period, and a second stimulus (S3) was employed at the same coupling interval. The S3 was shortened in 10-ms decrements until either VT induction or failure to capture occurred. If no VT was induced, the same procedure was followed for the third (S4) and fourth (S5) extra stimuli, as required. There was a pause of 1 s before the next drive started.

Definitions. Definitions were as in previous studies from this laboratory (1, 3, 4), with VT defined as an abnormal QRS (different from the atrial paced) with atrioventricular dissociation. Only sus-

tained VT (lasting at least 30 s) was studied. The CL of VTs was averaged over the first 10 complexes after cessation of pacing.

VT was designated to have a focal origin when no electrical activity could be recorded on all adjacent sites in three dimensions between the latest activation of one QRS complex and the earliest of the next QRS. Moreover, conduction from the site of earliest activity to adjacent electrodes could not manifest conduction delay, which might account for a majority of the CL of the VT.

VT of Purkinje origin was defined as a focal endocardial mechanism with recording of a Purkinje potential before the QRS on the lead recording the earliest activity. Purkinje potentials had to be identified on electrograms during atrial pacing before and after coronary occlusion and during VT to be considered mechanistically involved.

Mechanisms of VT were defined as reentrant when the earliest activation site was located immediately adjacent to the site of the latest activation from the previous complex, and continuous diastolic activation was recorded between complexes. Reentrant mechanisms also demonstrated unidirectional and functional block to the subsequent earliest site of activation.

Entrainment of VT suggesting reentry was defined as follows in this study: fixed fusion of the surface QRS at a given paced CL with progressive fusion at faster-paced CL or first nonfused QRS entrained to the pacing CL. Also, resumption of the original VT morphology on cessation of pacing was required. We did not observe local conduction block or concealed entrainment because we paced only outside the ischemic zone.

Experimental protocol. After instrumentation of the risk zone with 21 multipolar plunge needles and before coronary artery occlusion, induction of VT was attempted with extrastimuli to exclude artifactual VT resulting from electrode instrumentation alone. None of the animals had inducible VT under these circumstances. The left anterior descending coronary artery was then occluded, collateral vessels in the risk zone were ligated, and VT induction was attempted using serial induction protocols during the time period from 1 to 3 h after occlusion. The time frame of 1–3 h was chosen because previous work from our laboratory has shown that the percentage of electrograms showing a significant drop in voltages (generally >45%) is relatively stable over this period after an initial increase over the first hour (2, 20). We also saw that activation times of ischemic (as assessed by a decrease of voltages of intramural electrograms by at least 45%) and nonischemic myocardium were stable during this 1- to 3-h period (20). Additionally, VT is reproducibly inducible in this model in the 1- to 3-h postcoronary occlusion period (2, 20). Pacing was performed from one of three additional electrodes placed outside the risk zone located in locations described above. A total of 21 dogs had hemodynamically stable enough VT to allow overdrive pacing, and those were included in the study. One VT/dog was subjected to an overdrive pacing attempt. Overdrive pacing was done from one of the three electrodes outside the ischemic zone, which were used for pacing during VT induction. Overdrive pacing was attempted from the same electrode, which induced that particular VT. No spontaneous sustained VT or VF was observed during the period of 1–3 h after coronary artery occlusion, although nonsustained VT was observed during the first 3 h after occlusion.

When stable monomorphic VT had been induced, overdrive pacing was attempted. Ventricular pacing began at the VT CL, with the pacing CL progressively shortened by 10 ms.

Analysis of the response to overdrive pacing and the subsequent VT mapping were done in a blinded fashion. Data are expressed as means \pm SE when appropriate, and a Student's *t*-test was used for comparison between groups with regard to the VT rates. The primary hypothesis was tested by a one-tailed Fischer's exact test.

RESULTS

A total of 21 dogs each had at least one episode of inducible sustained VT that was hemodynamically stable enough to allow overdrive pacing. The mean CL of all the VTs was 158 ± 8 ms.

Fifteen of the 21 dogs demonstrated entrainment with overdrive pacing (Table 1). Fourteen of the first 15 nonpaced QRS (resumption of the original VT morphology) were entrained to the pacing CL (Fig. 1A). Eight of the 14 demonstrated fixed progressive fusion with faster pacing CLs (Fig. 1B). During fixed fusion, the reentry circuit (orthodromically activated tissue) merged with pacing (antidromically activated tissue). In all 15, there was resumption of prepacing CL and VT morphology after cessation of pacing (Fig. 1). The prepacing mechanism of all 15 animals was subsequently mapped to reentry, with 14 having an epicardial reentrant circuit (Fig. 2), whereas 1 had transmural reentry, thus confirming the value of entrainment to confirm reentry as a mechanism of VT. The sites of reentry were located in the ischemic zone, as documented by voltage measurements (1, 4).

In 5 of the 15 dogs that demonstrated entrainment, subsequent overdrive pacing at a faster rate accelerated the VT CL compared with the prepacing CL. None of the VTs had pace acceleration with the first overdrive pacing attempt. Only one of the mechanisms postpacing remained epicardial reentry, although a different reentrant circuit was seen; two had changed to a focal Purkinje VT (Fig. 3), one to a focal epicardial VT, and another had multiple foci of early activity.

Table 1. Responses of inducible early ischemic VTs (n = 21) to overdrive pacing

VT Mechanism	VT-CL	Pace CL	Entrainment	Acceleration of VT With Subsequent Faster Overdrive Pacing
Epireentry	180	170-160	Fusion	No
Epireentry	150	140-130	First	No
Epireentry	185	170-100	First	No
Epireentry	160	140-120	Fusion, first	No
Epireentry	140	140-130	Fusion, first	No
Epireentry	160	150-100	First	No
Epireentry	140	140-110	Fusion, first	No
Transreentry	160	150-130	First	No
Epireentry	120	120-110	Fusion, first	No
Epireentry	125	110-90	Fusion, first	No
Epireentry	140	130-90	Fusion, first	Acc, Purkinje
Epireentry	220	180-150	First	Acc, endo
Epireentry	250	220-120	First	Acc, Purkinje focal
Epireentry	130	110-100	Fusion, first	Acc, epireent
Epireentry	125	110-90	First	Acc, multiple focal
Purkinje focal	220	130-120	None	Acc, Purkinje focal
Purkinje focal	180	170-130	None	No
Purkinje focal	150	130-120	None	No
Epi focal	115	110-100	None	No
Purkinje focal	115	110-100	None	No
Epi focal	150	130-120	None	No

Data are for 21 experiments. VT, ventricular tachycardia; CL, cycle length (msec); Epi, epicardium; fusion, fixed progressive fusion; first, first nonfused VT complex entrained to the pacing CL; trans, transmural; Acc, acceleration of VT; endo, endocardium; multiple, multiple origins, including Purkinje fibers.

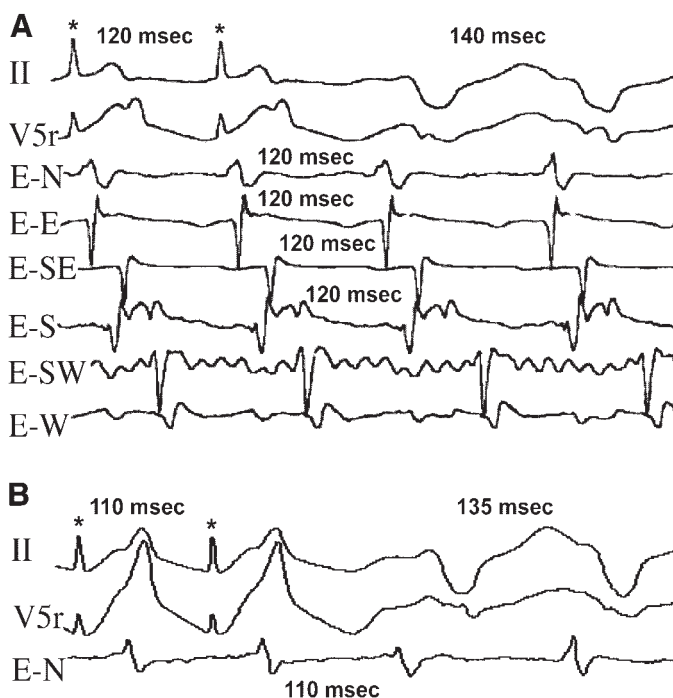


Fig. 1. A: ventricular tachycardia (VT) entrainment. Surface ECG leads II and V5r show fixed fusion with paced (*) complexes. In these paced complexes, the orthodromic wavefront in the epicardial electrograms located north (E-N), east (E-E), southeast (E-SE), and south (E-S) within the reentry circuit is activated indirectly after delay from the wavefront, which is directly activated via epicardial electrograms southwest (E-SW) and west (E-W) in the circuit. E-SW and E-W are activated earlier in the paced complexes. The first nonfused VT complex is entrained to the pacing CL of 120 ms because of orthodromic activation via an area of slow conduction. E-SW and E-W are delayed in the VT complexes (last two) because activation is not altered by pacing. CL of VT resumed at 140 m. B: same VT as in A demonstrating entrainment with pacing at a shorter CL than previously. When the morphology of the paced complexes is compared with those in A, progressive fusion is noted. The pacing (*) CL is at 110 ms, with fixed fusion more reflective of larger mass of tissue antidromically activated. The first nonfused complex returns to a CL of 110 ms because of orthodromic activation. The original VT CL of 135 ms resumes upon cessation of pacing.

Four of these dogs had the faster VT subsequently degenerate to ventricular fibrillation. The VTs in which CL accelerated with overdrive pacing (173 ± 25 ms) had an initial CL no different from those that did not accelerate with overdrive pacing [153 ± 7 ms; $P =$ not significant (NS)].

The prepacing mechanism in all remaining six dogs where neither fusion nor entrainment of the first nonfused complex was seen was a focal origin originating in the ischemic zone, as documented by voltage measurements (Fig. 4); this lack of occurrence of entrainment criteria was significantly different, $P < 0.05$, from 7 of 15, which showed two criteria of entrainment suggesting reentry. Although not all six had pacing from multiple sites, the VT shown in Fig. 4 had no evidence of entrainment from three separate ones. In addition, half of the six had multiple episodes of the same VT induced and paced, demonstrating reproducibility. Of these six focal VT's, four had a Purkinje origin (Fig. 5), whereas two had an epicardial origin. The CL of focal VT was no different (155 ± 16 ms) from the reentrant VT's (159 ± 10 ms, $P =$ NS). The observation that the focal VTs seen in this model could not be entrained suggests that they are unlikely the result of micro-

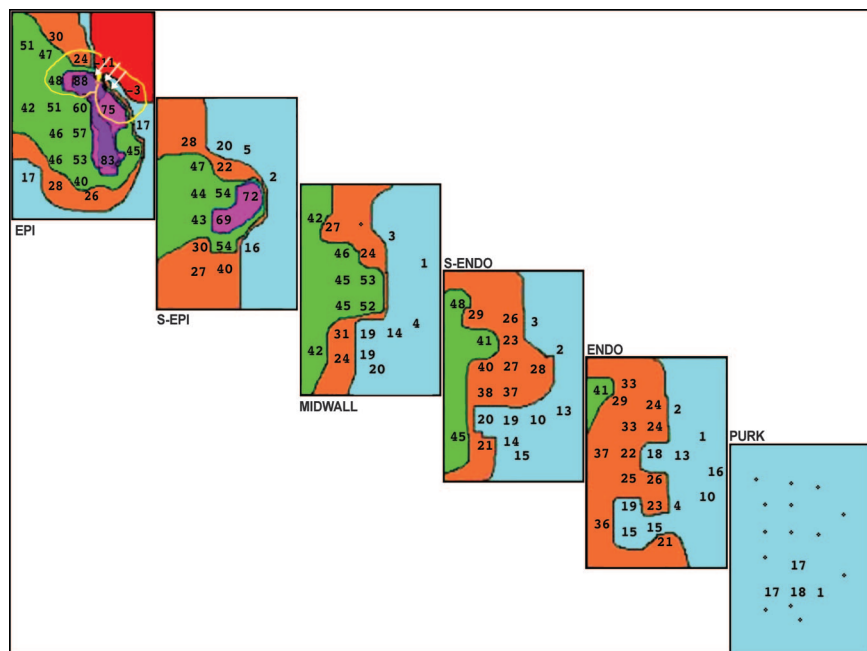


Fig. 2. Activation map of the first nonfused complex in Fig. 1A. Each rectangle represents a layer in the anterior wall of the heart extending from the epicardium (EPI) to the Purkinje layer (PURK). Myocardial activation is shown in colored isochrones, each of which represents 20 ms of activation. The earliest activation is in red with subsequent light blue, orange, green, purple, and navy blue. The earliest activation in this complex is in the epicardium (-11 ms) close to the pacing site at the base of the heart, likely as a result of reentrant activation from the previous complex. Although the rest of the myocardium is activated rapidly from the earliest site in the epicardium, there is significant conduction delay in the epicardium that suggests double-loop reentry. The black area represents unidirectional conduction block around which the double loop converges to activate across the area of block. Electrograms E-N, E-E, E-SE, and E-S from Fig. 1A are located superior to the area of block, whereas E-SW and E-W are located inferior to the thick solid lines (arrows).

reentry. Pacing did not result in a change of VT CL or morphology except in one dog in which the VT accelerated, but the earliest focus of activity during the VT remained focal Purkinje without development of ventricular fibrillation.

DISCUSSION

These results showing significant lack of entrainment with focal VTs support our speculation that the focal VTs seen in this model are unlikely to be reentrant and other mechanisms, such as triggered activity, may be a more plausible explanation. Additionally, these data with entrainment of stable inducible VT and subsequent three-dimensional mapping to confirm the VT mechanism as reentry further validate entrainment as a valuable method to determine a mechanism of VT.

On the basis of the resolution of the mapping system used (needles spaced at 10 mm and intraelectrode bipole spacing 1 mm), it is difficult to completely exclude microreentry as a

mechanism of VT with a focal origin in this model. The interneedle spacing was 10 mm, but microreentry may involve even smaller areas than that (16). The lack of entrainment during overdrive pacing of focal VTs helps to exclude microreentry if entrainment was expected to be observed with this mechanism. Prominent fusion of the surface QRS may not be observed because of the limited size of the antidromic limb of the circuit or if the surface QRS during pacing has the same morphology as the VT, such as in concealed entrainment or pacing near the exit site. However, microreentrant circuits may have excitable gaps, which might allow capture and entrainment of the first nonpaced QRS (23).

These results showing that VTs with a focal origin, including a focal Purkinje origin, that could not be entrained are consistent with a nonreentrant mechanism underlying these inducible VTs. Because automatic VTs are not inducible, this strongly implicates triggered activity as a potential mechanism

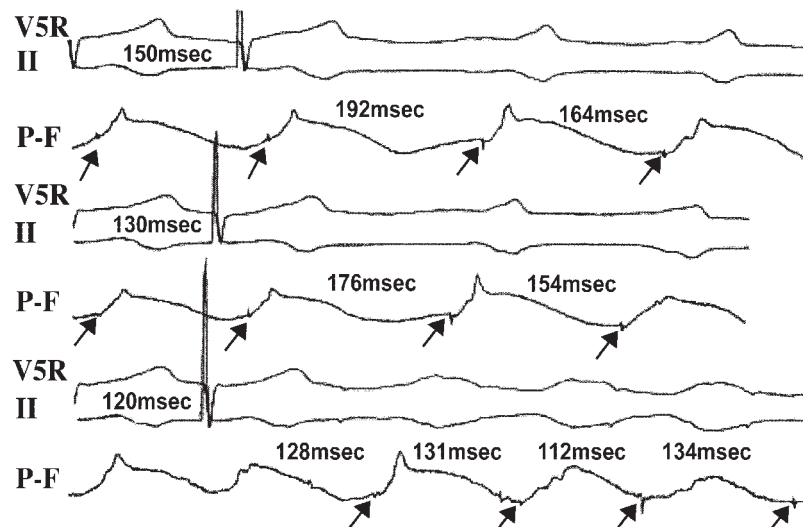
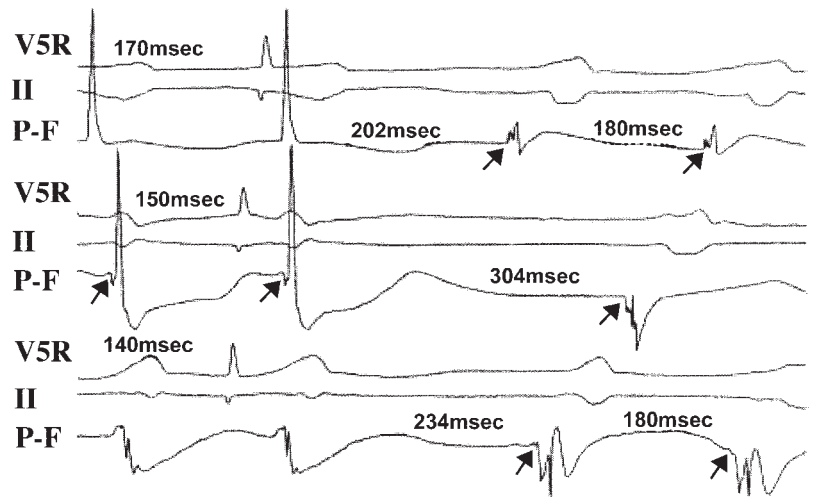


Fig. 3. Pace acceleration. Two paced complexes (pacing site from ventricular base) and occurrence of more rapid VT of Purkinje origin are shown. Three panels of electrograms are shown, each consisting of surface leads V5R and II and the electrogram from the new site of origin of the accelerated VT in the Purkinje layer (P-F). Each of the 3 panels with acceleration of the paced cycle length (CL; 150–120 ms) shows no fusion of QRS and successive shortening of the return cycle (192–128 ms) and acceleration of VT (164–131 ms). The PF recording with Purkinje potentials (arrows) is located at the new focal origin of the accelerated VT.

Fig. 4. No evidence of entrainment. Two paced complexes and resumption of VT during attempts to entrain VT with right bundle branch block and northwest axis morphology at a CL of 180 ms are shown. Surface leads V5R and II are recorded with Purkinje recordings (arrows) from focal origin (P-F) of VT. *Top*: attempts at overdrive pacing the VT at a CL of 170 ms from lateral wall did neither fuse nor entrain (202 ms) the QRS. *Middle*: pacing at a CL of 150 ms from the apex did not fuse or entrain (304 ms) the QRS. *Bottom*: attempted overdrive pacing at CL of 140 ms from base again did not fuse or entrain (234 ms) the QRS.



of focal VTs in this study. Both EADs or DADs can contribute to sustained triggered activity. In this study and others from this laboratory (1, 3, 4), it is unlikely, however, that EADs contribute to VT development, since the right atrium was paced at CL 300 ms and EADs are bradycardia dependent. Given this, we speculate that triggered activity resulting from DADs is a likely mechanism of the focal VTs induced.

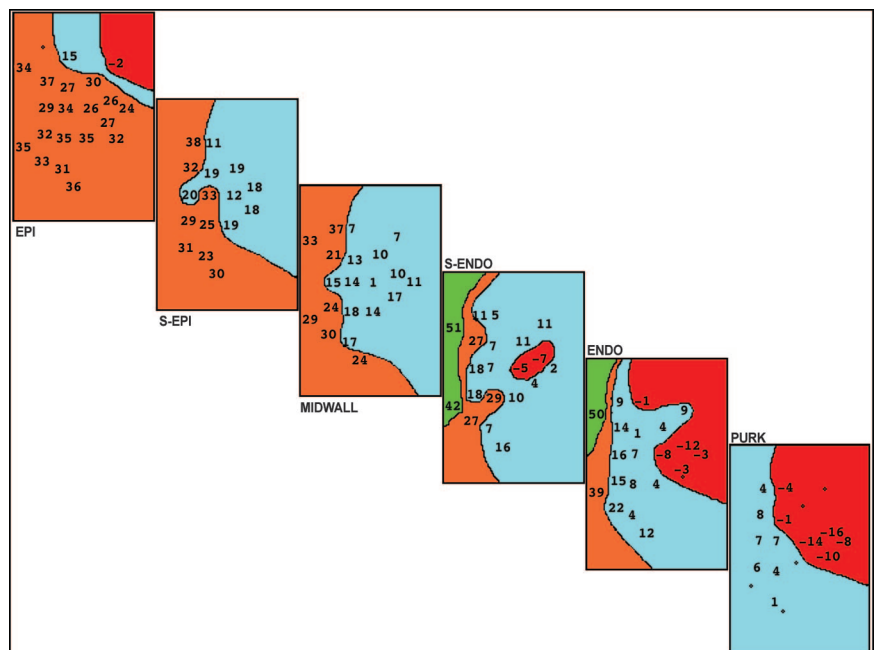
In another study using this same model, Xing and Martins (22) resected endocardial ventricular tissue and free-running Purkinje fibers from normal and ischemic sites both at the origin and remote from the origin of VT inducible at 1–3 h after coronary artery occlusion. Subsequent offline three-dimensional mapping of stored electrograms from the in vivo study identified the sites of origin and mechanism of the VTs. DADs and triggered activity were more commonly seen in the ischemic sites than nonischemic endocardium, but the highest frequency of DADs and triggered activity was seen in Purkinje tissue, which was a source of focal VTs in vivo before the

resection of the tissue. They concluded that myocardial ischemia can promote DADs in endocardial tissues and that triggered activity resulting from DADs occurs frequently in ischemic tissue and especially at Purkinje sites of focal VT. This supports our hypothesis that DADs and triggered activity but not microreentry may underlie a significant portion of focal VTs seen in this model. Others have shown that microreentry is unlikely to be involved in the generation of sustained VT during the late phase of acute ischemia (7).

The response of reentrant VTs to overdrive pacing further validates the use of entrainment in determining the mechanism of a tachyarrhythmia (14, 19, 21), since each of the 15 VTs, which had a VT with a reentrant mechanism, demonstrated entrainment with overdrive pacing. In addition, in 5 of the 15 reentrant VTs, pace acceleration of the VT was noted with pacing at faster CL.

Antitachycardia pacing (ATP) is a form of overdrive pacing, which can be an effective therapy for monomorphic VTs and is

Fig. 5. Map of Purkinje VT, which showed no evidence of entrainment after pacing from the apex, as shown in Fig. 4. In contrast to epicardial reentrant VT shown in Fig. 2, the early activity was in the Purkinje layer –16 ms before the QRS, and surrounding activation was all within ms of the earliest site. These activations cannot support microreentry as a mechanism for a VT with a CL of 180 ms. See Fig. 2 for details.



a standard feature of implantable cardioverter defibrillators. ATP is an attractive alternative to shocks because of less patient discomfort and less battery draining. ATP can, however, cause acceleration of VTs in some of these patients. The faster the CL of VT the more likely pace acceleration is to occur (10, 15), and in this study there was a trend toward the VTs that pace accelerated to be faster than those that did not. Spontaneous VT may be less likely to accelerate with ATP than inducible VT, since inducible VT is generally faster than spontaneous VT (9, 18).

Several mechanisms have been proposed to account for pace acceleration of VT in experimental models of healed infarct scars or a model with fixed anatomic obstacles (6, 8, 13). These include a change in the reentrant circuit to one with a different path, initiation of double-wave reentry, an alteration of a functionally determined circuit, and changes in exit sites from a reentrant loop rather than in the pathway of the circuit.

In this study, however, we observed another potential mechanism of acceleration by overdrive pacing on hemodynamically stable VT during 1–3 h of early ischemia. We saw development of focal sites of early activity upon cessation of pacing in four of five animals that had reentry before overdrive pacing. Presumably, the acutely ischemic substrate has latent foci of triggered activity, which may be induced by rapid pacing. However, we did not observe the development of reentry with attempted overdrive pacing of focal VTs. In fact, only one of the focal VTs accelerated without a change in mechanism. The fact that VTs with a focal origin might occur as a result of pace acceleration of reentrant VTs might also imply that antiarrhythmic therapy in patients with frequent pace acceleration should also involve agents that are effective against VT with a focal origin. This might include agents with calcium channel or β -adrenergic receptor-blocking properties, among others.

In this study, we did not pace from every conceivable site possible, so it may be that entrainment could have been observed in a VT with a focal origin. We hasten to point out that the focal VTs were studied with the same protocol as were the reentrant ones; this same protocol was not able to identify any evidence for entrainment in the group with focal VT.

In conclusion, the lack of entrainment in the inducible VTs with focal origin supports the view that a mechanism such as triggered activity resulting from DADs may be responsible for the focal VTs seen. VTs in this study with a reentrant mechanism were entrained consistently. An additional observation from this study was that pace acceleration occurred in some with a change in mechanism from reentry to one with a focal origin. This change in mechanism from reentry to focal VTs offers a potential alternative explanation for pacing-induced acceleration of early ischemic VTs.

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