

Continuous Local Electrical Activity

A Mechanism of Recurrent Ventricular Tachycardia

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SUMMARY Although the mechanism of most episodes of recurrent ventricular tachycardia (VT) is believed to be re-entry, definitive proof of this hypothesis has heretofore been unavailable in man. Using programmed stimulation and ventricular endocardial mapping we studied three patients in whom the initiation of VT was dependent upon developing a critical degree of **fractionation** and delay in local left ventricular electrograms. When electrical activity spanned diastole, VT ensued. Maintenance of VT was associated

with continuous electrical activity resembling "local fibrillation" while termination of VT required cessation of this continuous activity. During sinus rhythm the electrogram recorded from the areas which subsequently developed continuous activity showed markedly **fractionated** and prolonged electrical activity exceeding 100 msec in duration. We feel these observations of the temporal relationship of continuous activity with the development of VT represent the first documentation of the re-entrant nature of this arrhythmia in man.

THE MECHANISM OF RECURRENT ventricular tachycardia (VT) is thought to be re-entry.¹⁻³ While reproducible initiation and termination of VT by programmed stimulation suggests a re-entrant mechanism,⁴ similar findings have recently been described for "triggered automatic" tachyarrhythmias.⁵⁻⁹ Proof of re-entry therefore requires the demonstration of a temporal relationship of the initiation and maintenance of the arrhythmia with the development of continuous electrical activity preceding the first and between subsequent complexes of the arrhythmia.¹⁰⁻¹⁴ This manuscript reports the first demonstration of continuous "re-entrant" activity in man and discusses the concept of "localized fibrillation" in the genesis of VT.

Methods

Three patients with recurrent sustained ventricular tachycardia underwent electrophysiologic evaluation of their arrhythmia in the nonsedated postabsorptive state after informed consent was obtained (table 1). Three or four electrode catheters were introduced percutaneously into the femoral and/or antecubital veins and fluoroscopically positioned in the high right atrium, at the A-V junction to obtain a His bundle recording, the coronary sinus, and the right ventricle. Another catheter was introduced percutaneously into a femoral artery and passed to the left ventricle. The inter-electrode distance of the catheters was 1 cm.

Programmed stimulation, including incremental ventricular pacing and the introduction of 1-3 (named S₂, S₃ or S₄ respectively) ventricular extrastimuli after every eighth spontaneous or paced (S₁) beat was performed with a custom-designed programmable stimulator. Current was delivered in 1.5 msec impulses at twice diastolic threshold using an isolated constant current source. Once the VT was initiated, endocardial mapping of the tachycardia was performed. Rapid ventricular pacing and the introduction of

1-3 programmed ventricular extrastimuli were subsequently used to terminate the arrhythmia. If these maneuvers failed, DC cardioversion was used (table 2).

Two surface electrograms (leads 2 and V₁) were simultaneously displayed with multiple intracardiac recordings on a multichannel oscilloscope (Electronics for Medicine DR-16) and recorded on magnetic tape. The amplifier gains for the local ventricular electrograms were not changed throughout the study. Data were later retrieved on photographic paper at a speed of 100-400 mm per second.

Results

Case 1

This 63-year-old male with healed inferior and anterior myocardial infarctions presented with recurrent syncope secondary to ventricular tachycardia. An infero-apical aneurysm was documented at catheterization.

During sinus rhythm fragmented electrical activity 112 msec in duration was recorded in the center of the aneurysm (fig. 1). This activity continued beyond the QRS which was 100 msec in duration. Ventricular tachycardia could be reproducibly initiated by multiple ventricular extrastimuli during sinus rhythm or ventricular pacing (fig. 2) and by rapid ventricular pacing. The initiation and maintenance of the tachycardia was associated with progressive fragmentation of electrical activity within the aneurysm, eventually leading to continuous activity throughout the cardiac cycle. This continuous activity resembled the "local ventricular fibrillation" described by Moe et al.¹⁵ Continuous activity was noted during multiple QRS morphologies suggesting different exit sites from the re-entrant circuit (fig. 2).

TABLE 1. *Clinical Data*

Age/Sex	Cardiac diagnosis	ECG
63/M	ASHD, ventricular aneurysm	Inferior and anterior infarctions
37/M	ASHD, ventricular aneurysm	Infero-posterior infarction
63/M	Congestive cardiomyopathy	IACD IVCD

Abbreviations: ASHD = atherosclerotic heart disease; IACD = intra-atrial conduction defect; IVCD = intraventricular conduction defect.

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TABLE 2. *Electrophysiologic Data*

VT Morphology	ERP-V*	Mean VT cycle length	Mode of initiation	Tachycardia Zone†	Mode of termination of VT
RBBB	180	375	2VPD RVP	S ₂ -S ₃ 200-280	2VPD RVP
RBBB	230	280	1VPD	S ₁ -S ₂ 290-260	spontaneously or cardioversion
RBBB	220	300 225	2VPD	S ₂ -S ₃ 230-260	spontaneously or RVP

*ERP-V = Effective refractory period of ventricle at paced cycle length of 600 msec.

†only includes data obtained by extrastimuli delivered during ventricular pacing.

Abbreviations: RBBB = right bundle branch block; RVP = rapid ventricular pacing; VPD = ventricular premature depolarization; VT = ventricular tachycardia.

During the tachycardia the catheter was positioned near the septum and the lateral wall of the aneurysm and more discrete electrograms were recorded during the cardiac cycle. Near the interventricular septum two sharp potentials were recorded in diastole, 100 and 20 msec prior to the QRS respectively, whereas the major potential recorded from the lateral aspect of the aneurysm occurred 75 msec after the onset of the QRS (fig. 3).

Partial penetration of the assumed re-entrant circuit by two ventricular premature depolarizations (VPDs) or rapid ventricular pacing was demonstrated by a change in morphology of the local recorded fragmented activity and a change in the QRS morphology and the ventricular activation pattern. Termination of the tachycardia was accomplished by the introduction of two ventricular premature depolarizations (VPDs) or by rapid ventricular pacing.

Case 2

This 37-year-old male was studied four weeks after an inferoposterior myocardial infarction with recurrent ventricular tachycardia and syncope. Cardiac catheterization revealed an inferoposterior dyskinetic segment of normal thickness, but without a discrete border.

During sinus rhythm the local ventricular electrogram obtained from the dyskinetic area showed fragmented activity 120 msec in duration (fig. 4). In addition, the posterior basal left ventricle as recorded from the coronary sinus was activated after the inscription of the QRS. Initiation of the tachycardia was dependent upon progressive fragmentation and delay of activity recorded in the aneurysm. When

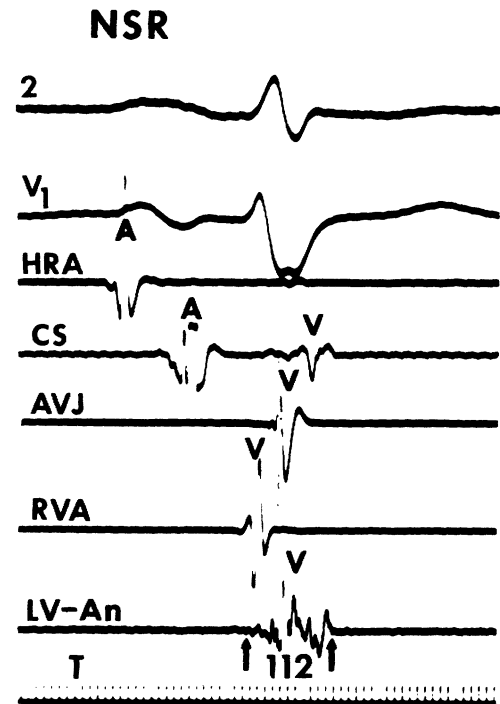


FIGURE 1. Intracardial recordings in case 1. From top to bottom are ECG leads II and V₁ and intracardiac electrograms from the high right atrium (HRA), coronary sinus (CS), atrioventricular junction (AVJ), right ventricular apex (RVA), and center of a left ventricular aneurysm (LV-An), and time lines (T). The electrogram in the LV-An is markedly fragmented and prolonged (112 msec).

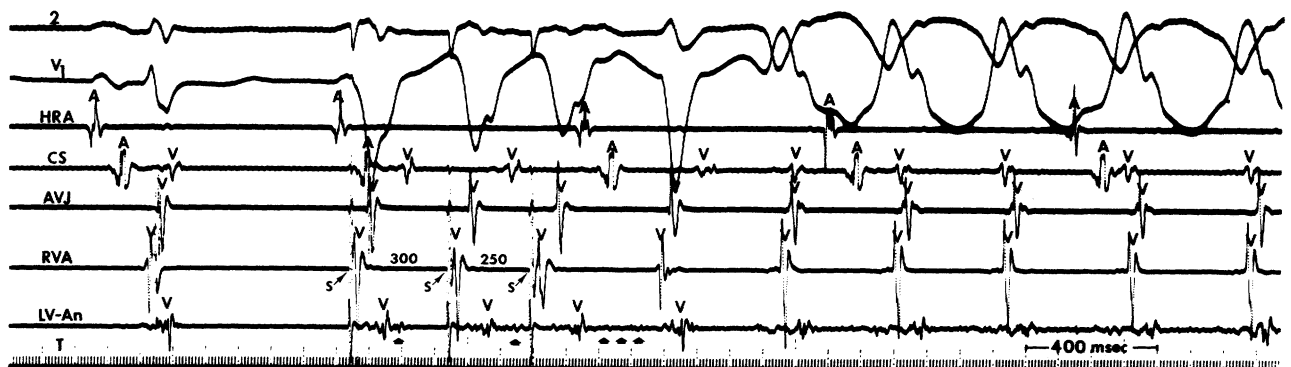


FIGURE 2. Relationship of progressive fragmentation and conduction delay to the initiation of ventricular tachycardia during sinus rhythm (case 1). The figure is organized similarly to figure 1. Fragmented depolarization is recorded in the LV-An during sinus rhythm (first beat). Three ventricular stimuli (S) are delivered at decreasing coupling intervals resulting in progressive desynchronization, fragmentation and conduction delay in the LV-An recording (broad arrow) leading to the development of ventricular tachycardia. During the tachycardia continuous low amplitude potentials are seen. Note the baseline LV-An electrogram is flat during sinus rhythm.

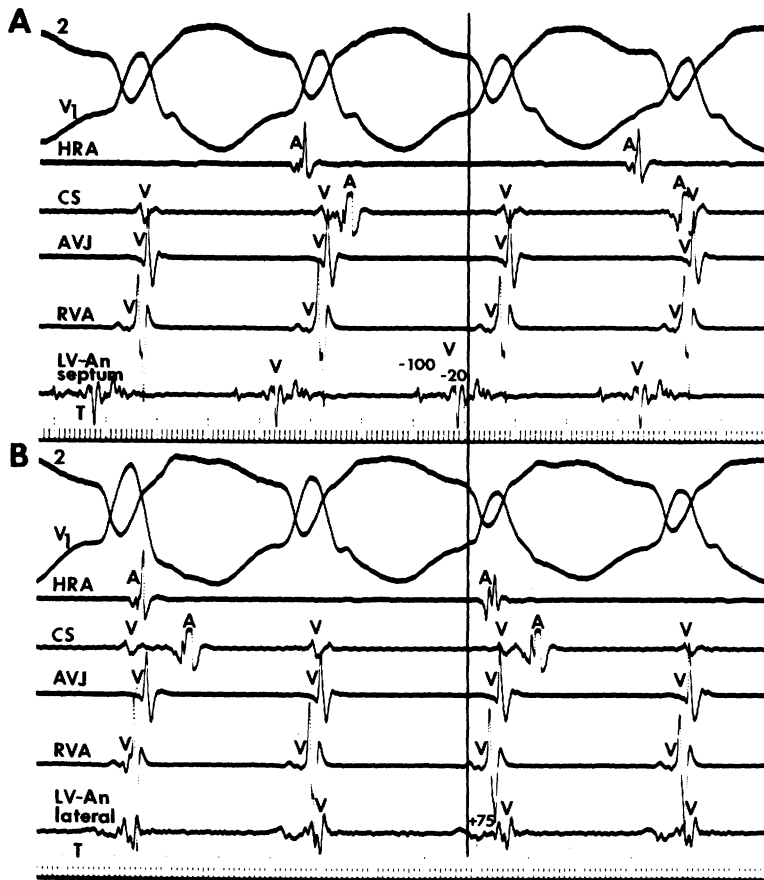


FIGURE 3. Local electrical activity in different parts of the aneurysm (case 1). The panels are organized as in figure 1. In panel A the LV-An catheter has been moved near the septum where the recorded electrical activity is primarily diastolic, with two discrete components occurring 100 and 20 msec prior to the onset of the QRS respectively. In panel B the LV-An catheter has been moved to the lateral aspect of the aneurysm where the major electrogram is recorded 75 msec after the onset of the QRS.

fragmentation spanned diastole and became continuous, ventricular tachycardia was initiated. Such fragmentation was produced by VPDs (fig. 5), bundle branch re-entry,¹⁶ and rapid ventricular pacing. With rapid ventricular pacing at a cycle length of 300 msec progressive **fractionation** and conduction delay appeared in a Wenckebach fashion which resulted in ventricular tachycardia if pacing was discontinued at the end of the Wenckebach cycle (fig. 6). Continued pacing produced concealed re-entry, then immediate termination of the tachycardia. Pacing at longer cycle lengths failed to produce great enough delays or ventricular tachycardia. Termination of the tachycardia was always dependent upon cessation of local continuous activity (fig. 7). A flat baseline was seen prior to the initiation and subsequent to the termination of the tachycardia in the left ventricular electrogram in which continuous activity was recorded. Of note is the fact that the area demonstrating the most delayed activation during sinus rhythm (posterior basal left ventricle) demonstrated slight fragmented activity, but was delayed proportionally to the extent of fragmentation and delay in the aneurysm in response to VPDs (figs. 5, 6) although to a lesser extent. This suggests that ventricular activity recorded from the posterior basal left ventricle resulted from exit at the distal posterior part of the aneurysm.

Case 3

The final representative case is a 62-year-old male with recurrent ventricular tachycardia and congestive cardiomyopathy. Although no catheterization was performed, the

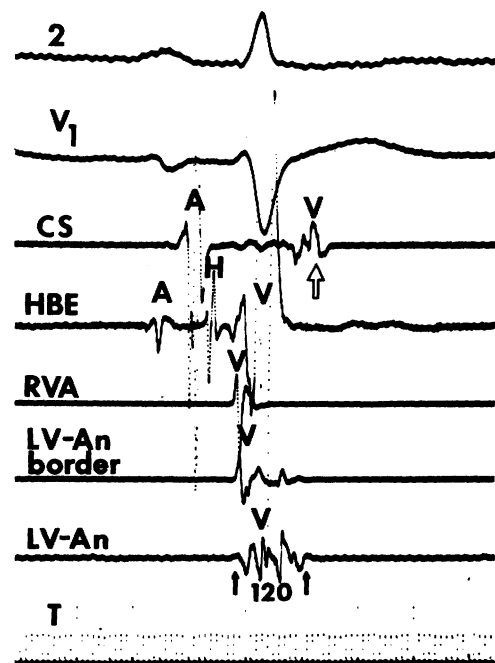


FIGURE 4. Intracardiac recordings in case 2. From top to bottom are ECG leads II and V₁ and intracardiac electrograms from the coronary sinus (CS), His bundle electrogram (HBE), right ventricular apex (RVA), border of left ventricular aneurysm (LV-An), and from the LV-An 1 cm from the border. The electrogram in the LV-An recording is fragmented and 120 msec in duration, extending beyond the end of the QRS. Note the ventricular electrogram in the CS recording occurs after inscription of the QRS (open arrow).

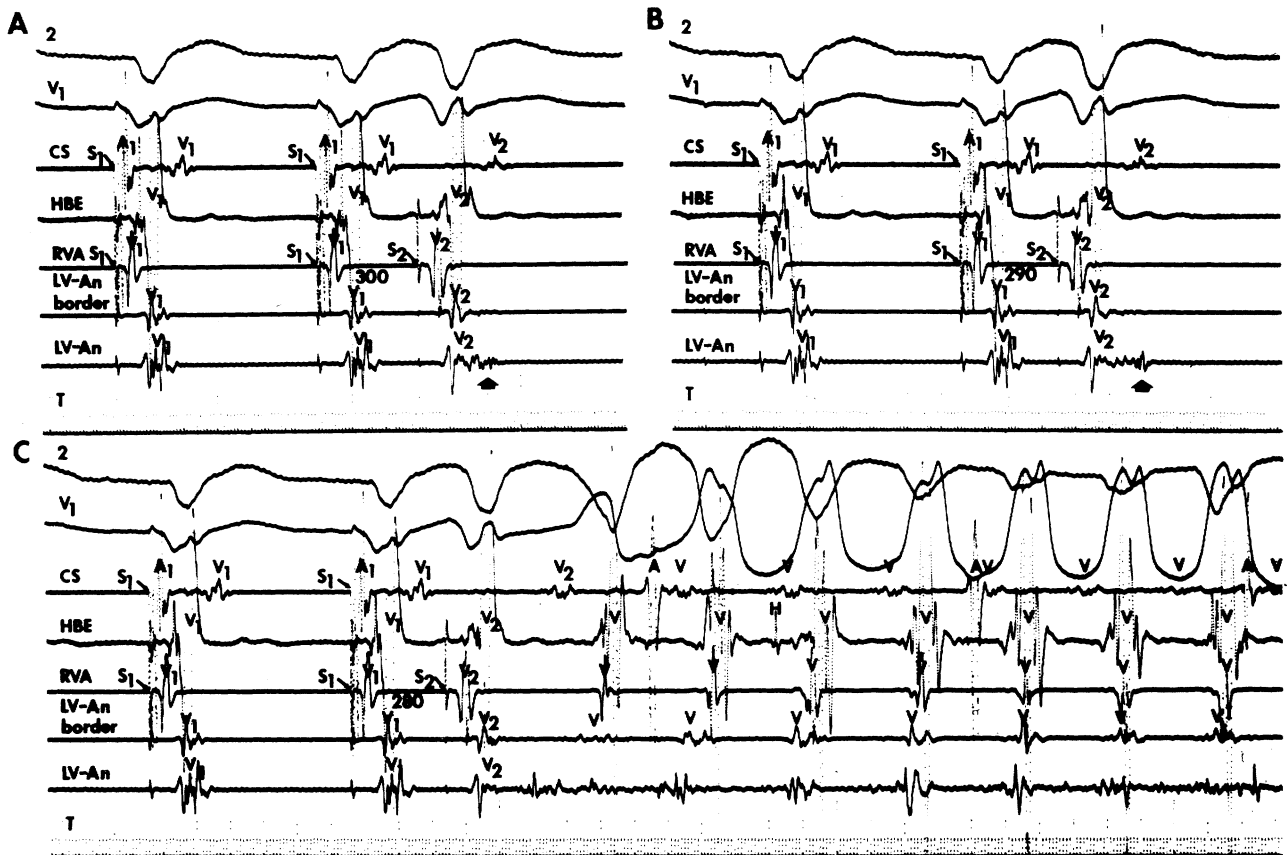


FIGURE 5. Initiation of ventricular tachycardia by ventricular premature depolarizations (case 2). The panels are organized as in figure 4. In panels A through C progressively premature ventricular stimuli (S_2) were delivered during a ventricular paced cycle length of 600 msec (S_1 - S_1). An increasing degree of fragmentation and delay is noted in the LV-An as the S_1 - S_2 coupling interval is decreased (broad arrow). At an S_1 - S_2 of 280 msec continuous **fractionated** activity develops and ventricular tachycardia ensues (panel C).

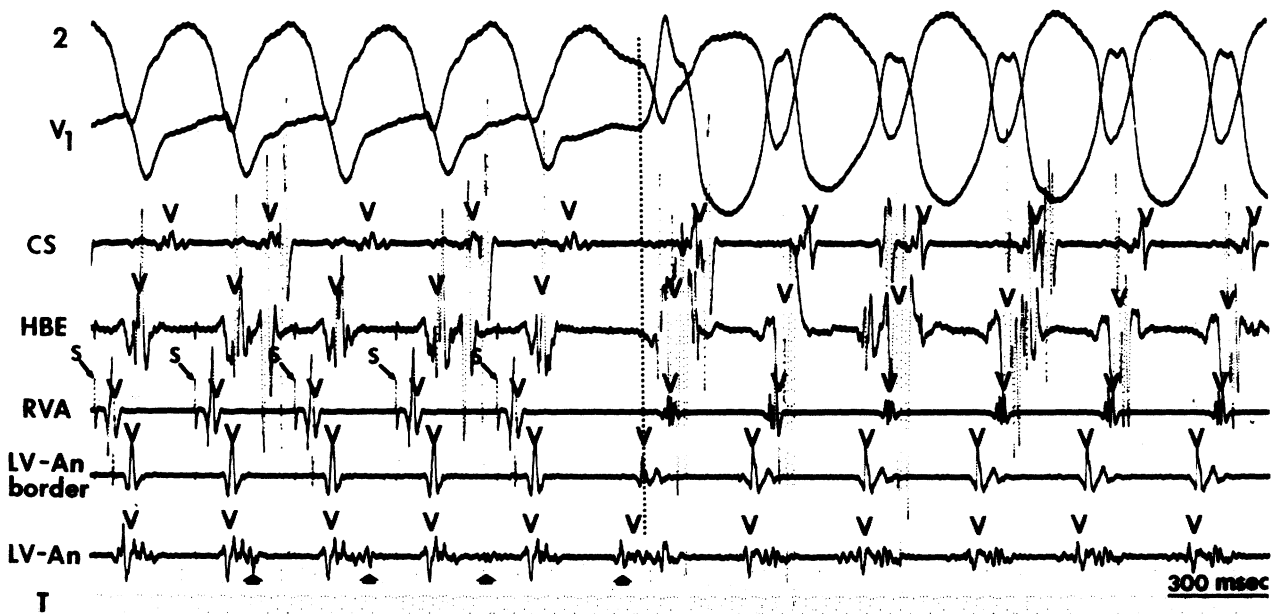


FIGURE 6. Ventricular tachycardia induced by ventricular pacing (case 2). The figure is organized as in figure 5. Ventricular pacing from the right ventricle (S) produces gradual fragmentation and delay in the LV-An (broad arrows) which results in ventricular tachycardia when pacing is discontinued. During ventricular pacing the electrogram in the LV-An occurs late in the QRS but appears prior to the first beat of the tachycardia; thus re-entry must be occurring in the area recorded by the LV-An electrogram.

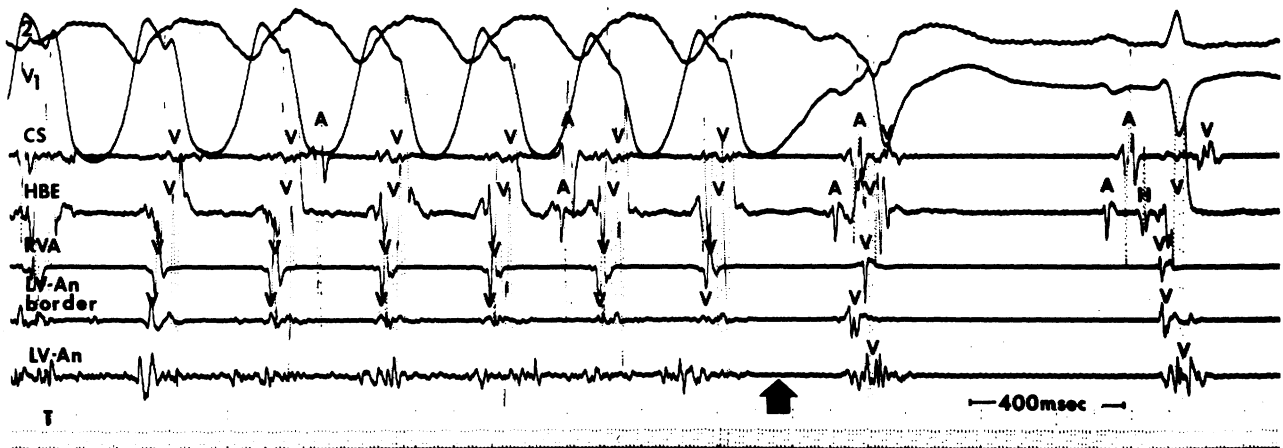


FIGURE 7. Spontaneous termination of ventricular tachycardia (case 2). Spontaneous termination of the tachycardia appears coincident with cessation of continuous activity (arrow). The last ventricular ectopic impulse results from block in the re-entrant circuit and exit via another pathway. Note the flat LV-An baseline subsequent to termination of the tachycardia.

echocardiogram revealed a diffusely hyokinetic, dilated, thin-walled left ventricle.

Slow fragmented activity of longer duration (180 msec) than the QRS was recorded by a catheter placed at the inferoseptal area of the left ventricle (fig. 8). Rapid ventricular pacing or two VPDs reproducibly initiated the tachycardia which was related to the development of continuous fragmented activity in this area. Rapid ventricular pacing (cycle length 200 msec) resulted in termination of the arrhythmia. Termination was associated with the alteration of the fragmented activity during pacing. When pacing produced morphologic changes in the continuous activity suggesting an alteration of re-entrant pathways, cessation of pacing caused a final re-entrant beat, then termination (fig. 9). The final re-entrant complex resulted from pacing-induced disruption of the primary re-entrant circuit responsible for the tachycardia, with slow conduction and exit through another site. This produced a different QRS in the last complex. Re-entrant activity could no longer be sustained and both the continuous activity and tachycardia stopped.

Discussion

Reproducible initiation and termination of a tachyarrhythmia has been considered presumptive evidence that the underlying mechanism of the arrhythmia is re-entry.¹⁻⁴ This concept remained unchallenged until several investigators recently demonstrated that under certain experimental conditions, automatic arrhythmias, especially those due to afterpotentials, could be triggered and terminated by appropriate stimulation.⁵⁻⁹ While the relevance of such triggered automaticity to sustained ventricular arrhythmias in man remains unclear, the initiation and termination of an arrhythmia can no longer be taken as *prima facie* evidence for re-entry.

Thus, other requirements must be satisfied in order to firmly prove a re-entrant mechanism. Other commonly accepted requirements for re-entry include: a) electrophysiologically heterogeneous tissue; b) unidirectional block in one or more pathways in that tissue; and c) slow conduction through an alternative pathway allowing enough time

for the initially blocked pathway to recover excitability. In the absence of intracellular recordings with microelectrodes, the criteria which can be fulfilled in the intact heart are slow conduction and electrophysiologic heterogeneity. This can be accomplished by the demonstration of

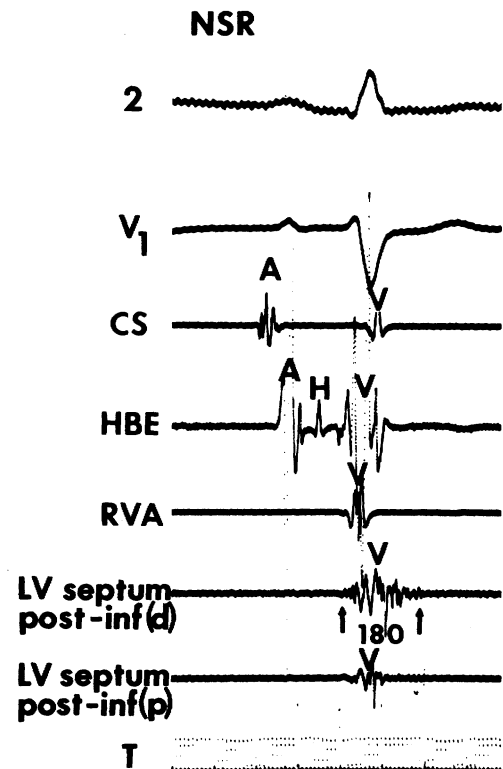


FIGURE 8. Intracardiac recordings during sinus rhythm in case 3. From top to bottom are ECG leads II and V₁ and electrograms from the coronary sinus (CS), His bundle area (HBE), right ventricular apex (RVA) and from the proximal (p) and distal (d) pair of electrodes of a catheter positioned at the posterior-inferior (post-inf) left ventricle (LV) near the septum. LV (p) and (d) were recorded 2 cm apart. Fragmented depolarization 180 msec in duration is seen in the distal LV electrogram and extends well beyond the end of the QRS.



FIGURE 9. Termination of ventricular tachycardia by rapid ventricular pacing (case 3). The figure is organized as in figure 8. Ventricular tachycardia (VT) is noted in the first five beats at which time rapid ventricular pacing (S) is begun. The morphology of continuous activity noted in the distal LV electrogram during VT is altered during pacing. When pacing is discontinued, termination of both the continuous activity and VT occur after a final re-entrant complex with different morphology.

slow, fragmented activity in response to changes in rate or premature stimuli. Continuous electrical activity would therefore represent a manifestation of re-entry.¹⁰⁻¹⁴

Slow, fragmented, and asynchronous epicardial and intramural activation has been observed in acutely ischemic myocardium in experimental animals.^{11, 12} In these studies extension of fragmented activation beyond the T wave or continuous diastolic activity was associated with the development of ventricular arrhythmias. These findings were reminiscent of the "localized fibrillation" noted by Moe, Harris and Wiggers¹⁵ in noninfarcted canine hearts in response to premature ventricular stimuli.

Most recently in a series of experiments using a composite ischemic zone (IZ) electrogram in a chronically (3-7 day) infarcted dog model fragmentation and slowing of conduction as well as the production of continuous electrical activity in response to pacing and premature stimulation have been demonstrated.^{13, 14} The relationship of these conduction changes to the development of ventricular arrhythmias was clearly demonstrated. Depending upon the recording site of simultaneous close bipolar electrodes, discrete activity in diastole corresponding to activation of that part of the re-entrant circuit in close proximity to the electrode pair was recorded.

In each of our patients the arrhythmia could be reproducibly initiated by programmed stimulation. Re-entry was confirmed as the mechanism by demonstrating that the onset of the tachycardia depended upon the development of continuous fragmented activity prior to the first beat of the tachycardia. Furthermore, maintenance of the tachycardia required the perpetuation of such activity; the cessation of continuous activity resulted in termination of the arrhythmia. These findings represent the first proof of re-entry in man.

Continuous Electrical Activity — Re-entry versus Localized Fibrillation

The continuous fragmented activity produced by electrical stimulation in our study resembles the localized fibrillation described by Moe et al.¹⁵ as well as the re-entrant activity described by Boineau,¹¹ Waldo¹² and others.^{13, 14} Another interpretation of our records might be that the fragmented activity is an artifact. Our data suggest that this is not the case:

a) this activity was reproducibly initiated and terminated; b) a flat baseline was recorded both prior to and immediately after termination of VT in the electrode recording continuous activity; and c) rapid ventricular pacing did not produce continuous activity unless VT was initiated.

We therefore feel that the fragmented activity represents continuous circulating activity through an electrophysiologically heterogeneous area.¹¹⁻¹⁴ The geometric and spatial arrangements of the actual and potential re-entrant circuits caused the recording of apparent continuous activity in the area. Hence the activity recorded by our electrodes (1 cm interelectrode distance) must represent an actual composite recording of the electrical activity within the re-entrant circuit analogous to the composite electrogram previously described.^{13, 14} Similar fragmentation has been recorded in the acutely ischemic dog using catheters at high gain to record simultaneous His bundle electrograms.¹⁷ This assumption is further supported by recording discrete electrical activity after moving the catheter to one or another side of the original area recording continuous activity. These more discrete electrograms reflect activity in part of the re-entrant circuit. Furthermore, re-entry more readily explains why the cycle lengths of the ventricular tachycardias exceeded the refractory periods of normal myocardial tissue and how programmed stimulation could terminate the arrhythmia. Thus, the body of evidence supports the concept that fragmented activity represents slow conduction over multiple pathways.

Localization of the Site of Re-entry

Temporal dispersion of activation and recovery are required for re-entry. These requirements may be met in the setting of a variety of cardiac disorders; two of our patients had coronary artery disease and one had a congestive cardiomyopathy. A finding common to each of these patients was fragmented electrical activity of long duration (> 100 msec) recorded during sinus rhythm in the area, demonstrating continuous activity during ventricular tachycardia. During sinus rhythm this activity extended beyond the inscription of the QRS.

Investigators employing epicardial mapping have noted a late potential recorded following the QRS and have postulated this delayed potential is a marker for the re-

entrant site;^{18, 19} however, continuous activity was never demonstrated. This delayed potential may be the result of slow endocardial or intramyocardial conduction with delayed breakthrough on the epicardium and need not indicate a site of re-entry. This point is demonstrated in case 2 in whom the posterior left ventricle was depolarized well after the inscription of the QRS during sinus rhythm but was distant from the site at which continuous activity was recorded. The limitations of epicardial mapping in localizing the site of re-entry have been shown in studies in which the site of origin predicted by epicardial mapping was distant from the true site of origin documented by simultaneous endocardial and intramural mapping.^{20, 21} While the sub-epicardium may be the site of re-entry in some cases of ventricular tachycardia, mapping the entire thickness of the myocardium is required to determine accurately the site of origin of the arrhythmia. In our patients we believe the site of re-entry was endocardial but we cannot be certain without intramural and epicardial mapping, which can only be performed at open heart surgery.

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