Fractionated electrical activity and continuous electrical activity: fact or artifact?

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ENDOCAVITARY MAPPING during chronic ventricular tachycardia in patients with healed myocardial infarction and/or ventricular aneurysms has been used to locate the region from which ventricular tachycardia originates. During the process of mapping, bipolar electrograms with unusual configurations have been recorded from the chronically ischemic or healed infarcted regions, both with electrode catheters and with hand-held probes. Electrograms consisting of multiple "high-frequency" components with low amplitudes (<1 mV) and long durations that may exceed 100 msec have been termed "fractionated." Although fractionated electrograms have these qualitative descriptors, quantitative criteria to distinguish among various types of electrograms have not been established. Such quantification, however, is limited by the fact that electrogram amplitude and width can vary depending on the interelectrode distance, contact, and degree to which the signal is amplified. We have recently undertaken studies in normal subjects and in patients with infarction and ventricular tachycardia to develop such criteria using a 1 cm interelectrode distance and a fixed gain of 1 mV = 1 cm. With these methods normal electrograms had amplitudes greater than 3 mV, durations of 70 msec or less, and amplitude/duration ratios of 0.046 or more. Electrograms outside these values were termed "abnormal." Multicomponent electrograms that fell beyond 1 SD from mean values of abnormal electrograms (amplitude 1.4 ± 0.9 mV, duration 93 ± 40 msec, ratio 0.017 ± 0.012) were termed "fractionated." Although the pathophysiologic significance of the relationship between multicomponent "abnormal" and "fractionated" electrograms is unclear, our arbitrary criteria for fractionated electrograms were an amplitude of 0.5 mV or less, a duration of 133 msec or longer, and/or an amplitude/duration ratio of 0.005 or less. Whether quantifying the electrograms provides useful information beyond the qualitative descriptors requires investigation.

Sometimes the total electrogram may occur throughout the entire cardiac cycle, a phenomenon that has been called "continuous electrical activity." Fractionated electrograms (but not continuous activity) can also be recorded during sinus rhythm, in which case they may extend beyond the QRS complex of the surface electrocardiogram.

The detection of fractionated electrograms and continuous electrical activity in patients with ischemic heart disease has prompted a number of proposals concerning their possible significance: (1) the occurrence of fractionated electrograms during sinus rhythm may help to identify those patients who are prone to develop ventricular tachycardia; (2) the site at which fractionated electrograms are recorded during sinus rhythm may indicate the site of origin of ventricular tachycardia; and (3) the region at which continuous electrical activity is recorded during tachycardia defines the site at which the reentrant circuit is located. These proposals are all based on the assumption that fractionated electrograms are caused by slow, inhomogeneous conduction, a property that can cause reentry. That continuous electrical activity is synonymous with the location of the reentrant circuit is based on the fact that, during certain kinds of reentrant excitation, the impulse is continuously conducting through a circumscribed region (reentrant pathway) and that an electrode placed on such a pathway would record activity from one or another part of this pathway throughout the cardiac cycle.

These proposals are also a source of controversy. It has been suggested that fractionated electrograms and continuous activity may be artifacts, resulting from movement between the electrode and myocardium. Artifacts caused by movement should be particularly

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obvious because of the high amplification at which the electrograms are recorded (because of their low amplitude). Another suggestion has been that fractionated activity does not represent local electrical events but rather activity occurring far away from the recording electrodes. To demonstrate these points, Ideker et al.[1] recorded fractionated and continuous activity in a sponge sutured to the anterior surface of the canine left ventricle, and Gallagher et al.[2] recorded continuous activity from a bowl of Jell-o. Another suggestion has been that fractionated electrograms may be a product of the filtering characteristics of the amplifiers used to record them.[3] Some who concede that fractionated electrograms and fractionated activity might not be artifacts question whether their occurrence is predictive of tachycardia or indicates the location of reentrant circuits.[4] It is obvious, therefore, that there are important questions that must be resolved to determine the significance of these abnormal signals.

Are fractionated electrograms artifacts dependent on recording techniques?

The demonstration that fractionated electrograms can be recorded from sponges or bowls of Jell-o does not necessarily mean that those recorded from ischemic myocardium are caused by motion artifacts or represent distant activity. Fractionated electrograms, similar to those recorded in patients, have been found in regions of acute and chronic infarction in dogs, with both catheter electrodes and close bipolar electrodes fastened directly to the heart. Fractionated electrograms have also been recorded with close bipolar electrodes or with unipolar electrodes from isolated superfused preparations of canine myocardium obtained from areas of chronic or healed infarction in which mechanical motion is negligible and where nearly perfect contact can be ensured between electrode and tissue.[5] This demonstrates that fractionated electrograms can be real and can represent local activity under the electrode. In the study in isolated tissues, alteration of the filtering characteristics of the amplifiers did change the morphology of fractionated electrograms by including or excluding slow and high-frequency components, but fractionation was still obvious in recordings with a band pass above 0.6 Hz.[5] Thus, although the exact morphology of the electrograms may change at the different filter settings, fractionation cannot be created or abolished.

The demonstration that fractionated electrograms are real under these experimental conditions does not disprove suggestions that fractionated electrograms or continuous activity recorded from patients might result from motion artifact. Although catheter motion might cause what appears to be fractionation, for the following reasons we believe that in many instances fractionated activity is not an artifact of electrode movement. Fractionated electrograms, including continuous activity, occur almost exclusively in areas of scar tissue or at borders of aneurysms. They can be recorded during intraoperative mapping from the same regions where they were recorded during catheter mapping, even though electrode-tissue contact during intraoperative mapping is expected to be much better than with a catheter and the contraction of the empty ventricles on cardiopulmonary bypass is less vigorous. It is hardly likely that the same movement artifact would be observed under these different conditions. Slight repositioning of recording electrodes further toward the border with more normal myocardium (as little as several millimeters) usually results in a lesser degree of fractionated activity or in its disappearance; slight catheter movement would hardly be expected to alter motion characteristics. The fact that the characteristics of the electrogram can markedly change when the electrode is moved short distances within the scarred region during intraoperative mapping also argues against the electrogram representing distant activity and not local phenomena.

What causes fractionated electrograms?

If fractionated activity is not caused by motion, what then do fractionated electrograms tell us about the electrophysiologic traits of the regions from which they are recorded? Fractionated electrograms per se cannot be equated with slow conduction. In experiments on isolated preparations of ventricular muscle or Purkinje fibers, elevating K^+ to depress the conduction velocity simply reduced the amplitude and broadened the duration of the extracellular electrogram, but the slow conduction did not cause fractionated electrograms.[5, 6] In an experimental study on electrical activity in the muscle surviving on the epicardial aspect of canine infarcts, it was shown that fractionated electrograms usually appeared as the infarcts aged and their appearance corresponded to the ingrowth of fibrous tissue during infarct healing.[5] The connective tissue separates the myocardial fibers, decreases their interconnections, and distorts their orientation. Microelectrode studies have shown that because of this separation on a microscopic level, individual muscle bundles may be activated asynchronously and the individual components of the fractionated electrograms appear to represent electrical activity in the different surviving muscle bundles. Since action potentials recorded in the vicini-

ty of fractionated electrograms often had fast upstrokes, these individual components had a "high frequency." Since only a few bundles embedded in large amounts of connective tissue were present, the extracellular electrical field was small and high amplification was needed to see them.[5] Despite the nearly normal transmembrane potentials, activation of the region where fractionated activity was recorded was very slow. Slow conduction might be a result of the diminished intercellular coupling caused by the separation of the fibers. This finding of a structural basis for fractionated electrograms in infarcts should not be surprising, since Spach et al.[7] have shown that similar fractionated electrograms can be recorded from the distal Purkinje system, where individual Purkinje bundles are separated from one another, and from nonuniformly anisotropic atrium, where connective tissue separates muscle bundles.[8] In our recent study of the anatomy of subendocardial regions of patients with ventricular tachycardia, in which fractionated electrograms can be recorded, we have found this anatomic substrate — surviving myocardial muscle bundles separated by large amounts of connective tissue.[9]

At the very least, therefore, fractionated electrograms indicate areas of abnormal anatomy and conduction that are suitable substrates for reentry. Experimental data suggest that the occurrence of fractionated electrograms depends on a specific anatomic substrate, one that produces nonuniform anisotropic conduction and slow regional activation. Myocardial infarction is a source of this substrate as well as a cause of ventricular tachycardia. However, the appearance of fractionated activity during sinus rhythm need not indicate a priori that the patient will have ventricular tachycardia. Fractionated activity might occur without the presence of reentrant circuits. Whether any specific measurements describing the fractionated activity (such as duration, number of components, etc.) will predict the eventual occurrence of tachycardia will require careful studies. Whether the site(s) at which fractionated electrograms are recorded during sinus rhythm in patients with histories of ventricular tachycardia indicate the sites where tachycardias originate must be determined by comparing these two in the same patients. Recent data from our laboratory have demonstrated that these abnormal electrograms are widespread and are not specifically predictive of the site of origin of ventricular tachycardia(s).[10]

Is continuous electrical activity during ventricular tachycardia an indication of reentrant excitation?

In their studies on coronary arterial ligation in the dog, Waldo and Kaiser[11] and Boineau and Cox[12] showed that extension of fractionated electrograms into diastole often coincided with the appearance of ventricular tachycardias or fibrillation. More recently, El-Sherif et al.[13] have used a composite electrode to record from a large area of an infarcted region in the dog and have found that electrical activity spanning the cardiac cycle was often associated with ventricular tachycardia. Mapping of activation sequences in regions where there was continuous activity sometimes showed reentrant excitation.[14, 15] Josephson et al.,[16] during endocavitary catheter mapping, found in some patients progressive fractionation of electrograms in areas of healed infarction or aneurysms during initiation of tachycardia and during sustained tachycardia. Initiation of the tachycardia was dependent on these electrograms spanning the cardiac cycle. This was the first demonstration of continuous activity in human beings. Of note was the finding that electrograms recorded from adjacent bipolar pairs on the same catheter did not show continuous activity, suggesting that this continuous activity was local. In addition, pacing at the same cycle length as the tachycardia failed to produce continuous electrograms. Furthermore, disturbance of the continuous electrograms by pacing during the tachycardia resulted in its termination. We have also noted similar observations during intraoperative mapping.

We agree that if one could record from an entire reentrant circuit, continuous electrical activity would be seen. If the circuit were relatively large, a composite electrode might be needed, but if the circuit were small it might fit under a relatively close bipolar electrode. However, this does not mean that finding continuous activity in a specific region indicates that the reentrant circuit is either present or located there, since continuous activity can also be caused by slow nonuniform conduction in the absence of reentry.[15] Can it, then, be determined whether the site at which continuous activity is recorded is the location of the circuit? If continuous activity stops spontaneously during tachycardia or can be interrupted by pacing techniques that do not terminate the tachycardia or alter its cycle length or QRS morphology, then the continuous electrical activity cannot be related to the reentrant circuit. One must also exclude the possibility that continuous electrograms may merely represent fractionated electrograms that are present during sinus rhythm with a duration that approximates the ventricular tachycardia cycle length.[1] Such electrograms would span the cardiac cycle during tachycardia and appear to be continuous.

We therefore suggest that the site at which continu-

ous activity is recorded *might* be the site of a reentrant circuit if the following criteria are met in an electrophysiologic study: (1) during protocols designed to initiate tachycardia there is an increase in fractionation and duration of the electrogram until, at some critical duration, tachycardia starts. (2) Continuous activity (with repetitive patterns) persists during tachycardia and interruption of continuous activity by pacing techniques changes tachycardia cycle length or QRS morphology, or terminates tachycardia. (3) During the cycles immediately preceding spontaneous termination of tachycardia there may be changes in the pattern of local continuous activity. (4) Continuous activity can be recorded only from a circumscribed area and not throughout the infarcted region. (5) When pacing the heart at the same cycle length as the tachycardia during which continuous activity was recorded, there is no continuous activity. This proof is more definitive if pacing a site close to the origin of tachycardia produces the same activation and contraction pattern as during the tachycardia. Pacing is necessary to eliminate the possibility that continuous activity reflects nonspecific rate-dependent alterations in conduction. (6) Finally, cooling, compression, or resection of the region of continuous activity stops the ventricular tachycardia while similar interventions in other regions do not. All of the above are compatible with the interpretation that continuous activity indicates reentry and have been observed in humans.[16] Ultimately, however, mapping excitation patterns with high-density electrode arrays in regions where continuous activity is recorded is required to demonstrate reentrant excitation.

Conclusion

We conclude that fractionated electrograms and continuous electrical activity are real phenomena that result from an anatomic substrate in which muscle fibers are separated by scar tissue to produce slow and nonuniform anisotropic conduction. Careful consideration of recording procedures can eliminate motion artifacts. All electrograms that are fractionated and/or continuous, however, may not be related to reentrant phenomena. Recognition of the limitations of recording methods and use of stimulation techniques with analysis of the response of the electrograms to these stimulation techniques can in many instances exclude "continuous electrical activity," which is unrelated to the mechanism of tachycardia. The demonstration of localized continuous electrical activity that is inextricably related to the *initiation* and *maintenance* of ventricular tachycardia as outlined above strongly suggests that such activity is a reflection of reentrant excitation.

References

1. Ideker RE, Lofland GK, Bardy GH, Smith WM, Worley SJ, Wallace AG, Cox JL, Gallagher JJ: Late fractionated potentials and continuous electrical activity caused by electrode motion. PACE **6:** 980, 1983
2. Gallagher JJ, Kasell JH, Cox JL, Smith WM, Ideker RE, Smith WM: Techniques of intraoperative electrophysiologic mapping. Am J Cardiol **49:** 221, 1982
3. Waxman HL, Sung RJ: Significance of fragmented ventricular electrograms observed using intracardiac recording techniques in man. Circulation **69:** 1349, 1980
4. Brugada P, Abdollah H, Wellens HJJ: Significance of continuous electrical activity during ventricular tachycardia. Circulation **68** (suppl III): III-422, 1983 (abst)
5. Gardner PI, Ursell PC, Fenoglio JJ Jr, Wit AL: Anatomical and electrophysiological bases for electrograms showing fractionated activity. Circulation **66** (suppl II): II-78, 1982
6. Spach MS, Barr RC, Serwer GA, Kootsey JM, Johnson EA: Extracellular potentials related to intracellular action potentials in the dog Purkinje system. Circ Res **30:** 505, 1972
7. Spach MS, Barr RC, Johnson EA, Kootsey JM: Cardiac extracellular potentials: analysis of complex wave forms about the Purkinje network in dogs. Circ Res **33:** 465, 1973
8. Spach MS, Muller WT, Dolber PC, Kootsey JM, Sommer JR, Mosher CE: The functional role of structural complexities in the propagation of depolarization in the atrium of the dog: cardiac conduction disturbances due to discontinuities of effective axial resistivity. Circ Res **50:** 175, 1982
9. Fenoglio JJ Jr, Pham TD, Harken AH, Horowitz LN, Josephson ME, Wit AL: Recurrent sustained ventricular tachycardia: structure and ultrastructure of subendocardial regions where tachycardia originates. Circulation **68:** 518, 1983
10. Cassidy DM, Vassallo JA, Buxton AE, Doherty JU, Marchlinski FE, Josephson ME: The value of catheter mapping during sinus rhythm to localize site of origin of ventricular tachycardia. Circulation **69:** 1103, 1984
11. Waldo AL, Kaiser GA: A study of ventricular arrhythmias associated with acute myocardial infarction in the canine heart. Circulation **47:** 1222, 1973
12. Boineau JP, Cox JL: Slow ventricular activation in acute myocardial infarction: a source of reentrant premature ventricular contraction. Circulation **48:** 702, 1973
13. El-Sherif N, Scherlag BJ, Lazzara R, Hope RR: Re-entrant ventricular arrhythmias in the late myocardial infarction period. 1. Conduction characteristics in the infarction zone. Circulation **55:** 686, 1977
14. El-Sherif N, Smith A, Evans K: Canine ventricular arrhythmias in the late myocardial infarction period: epicardial mapping of reentrant circuits. Circ Res **49:** 255, 1981
15. Wit AL, Allessie MA, Bonke FIM, Lammas W, Smeets J, Fenoglio JJ Jr: Electrophysiologic mapping to determine the mechanism of experimental ventricular tachycardia initiated by premature impulses: experimental approach initial results demonstrating reentrant excitation. Am J Cardiol **49:** 166, 1982
16. Josephson ME, Horowitz LN, Farshidi A: Continuous local electrical activity: a mechanism of recurrent ventricular tachycardia. Circulation **57:** 659, 1978