Re-entrant Ventricular Arrhythmias in the Late Myocardial Infarction Period

1. Conduction Characteristics in the Infarction Zone

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SUMMARY Dogs 3–7 days following ligation of the anterior descending coronary artery represented a remarkably stable model for re-entrant ventricular arrhythmias (RVA) and allowed detailed electrophysiologic studies of the re-entrant mechanism. In these dogs, we could regularly illustrate the presence of continuous electrical activity originating from the infarction zone (IZ) and bridging the diastolic interval between the initiating and re-entrant beats as well as between consecutive re-entrant beats. Conduction in the IZ was highly complex, with multiple potentially re-entrant pathways, functionally dissociated areas, and areas of localized ventricular fibrillation. Conduction disorders in ischemic myocardium were consistently tachycardia-dependent with the spontaneous onset of RVA specifically associated with a Wenckebach-like conduction pattern in a potentially re-entrant pathway. Both manifest and concealed re-entry, as well as re-entrant beats with regular extrasystolic grouping, constant or variable coupling, uniform, multiform and bidirectional QRS configurations, were related to characteristic conduction patterns in the IZ. In summary, the study provides the first direct in vivo evidence of ventricular re-entry and demonstrates propensity for RVA and sudden death in the late myocardial infarction period.

ASHMAN AND HULL theorized that arrhythmias of myocardial infarction may be due to islands of partially isolated pathways in which conduction can occur in only one direction. Subsequent studies of myocardial infarction arrhythmias were, however, markedly influenced by the Harris and Rojas model in which two distinct phases of ventricular arrhythmias follow acute ligation of a major coronary artery. Several reports suggested that the early phase of ventricular arrhythmias, which is more serious and can degenerate into rapid ventricular tachycardia and fibrillation, is due to re-entry in ischemic myocardium. The late phase was explained on the basis of enhanced automaticity of Purkinje fibers. It is ironic that Harris and Rojas dismissed the possibility of re-entry in the early phase because local electrograms recorded from the ischemic zone failed to show continuous electrical activity between a supposedly re-entrant beat and the preceding impulse, a criterion they considered crucial for the diagnosis of re-entry.

In the series of experiments between 1969 and 1975, a number of investigators analyzed the early phase of myocardial infarction arrhythmias and almost all demonstrated slow desynchronized ventricular conduction in the ischemic zone while some studies showed a temporal relationship between progressive delay in activation of local electrograms and the onset of ventricular arrhythmias. Only one study did, in fact, demonstrate continuous electrical activity between the re-entrant beat and the preceding impulse. Unfortunately, all studies of the early phase of myocardial infarction arrhythmias dealt with a highly dynamic situation with an almost continuous change of the electrophysiological properties so that very few systematic studies could be performed. Indeed, in a relatively more stable acute ischemia model following the ligation of the anterior septal artery, El-Sherif et al. were able to demonstrate that conduction characteristics of the ischemic myocardium closely simulate those of the ischemic His-Purkinje system. They also strongly suggested that a conduction pattern in ischemic muscle with gradual increment of conduction delay reminiscent of the Wenckebach type of conduction characteristically preceded the spontaneous onset of re-entrant ventricular arrhythmias.

In the present study, we conducted a series of experiments in dogs 3–7 days following ligation of the anterior descending artery. We found that those dogs that survived the initial stage of myocardial infarction arrhythmias and were observed after the subsidence of the late stage of enhanced automaticity, still maintain a high propensity for re-entrant ventricular arrhythmias. These dogs represent a remarkably stable model for re-entry and one that would allow the application of various electrophysiologic maneuvers as well as pharmacologic interventions. We utilized a specially designed composite electrode in order to sample the electrical activity of a larger area of the epicardial surface of the infarction zone. This technique, in addition to multiple close bipolar recordings, allowed us to illustrate the presence of continuous electrical activity originating from the infarction zone and bridging the diastolic interval between the initiating and re-entrant beats as well as between consecutive re-entrant beats. These observations will be presented in a series of reports. This article describes conduction characteristics in the infarction zone. The following article will critically analyze the patterns of initiation and termination of re-entrant ventricular arrhythmias.

Material and Method

Experiments were performed on 50 adult mongrel dogs weighing 10–30 kg and anesthetized with intravenous sodium pentobarbital (30 mg/kg). In all dogs, a left-sided thoracotomy was performed under sterile conditions. In 45 dogs, the left anterior descending artery was ligated just distal to the anterior septal artery. The thorax was then closed in all dogs, with five dogs serving as sham controls. After three to seven days, the animals were restudied. A Harvard respirator, using room air, provided mechanical ventilation.

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through a cuffed endotracheal tube. Blood pressure in the femoral artery was monitored through a polyethylene catheter connected to a Statham transducer. A His bundle recording was obtained by an electrode catheter (5 French with ring electrodes 1 mm apart) inserted into a common carotid artery and advanced to the aortic root.17 A thoracotomy incision was made through the left fourth intercostal space. The pericardium was opened and the site of the myocardial infarction was roughly identified by the naked eye. A large composite electrode34 was applied to the epicardial surface of the infarction zone (IZ), and the adjacent normal zone (NZ). A description of this electrode is as follows (see fig. 1).

A teflon-coated silver wire (0.012 inches coated diam.) is woven through a rectangularly shaped paper tape (2 × 4 to 4 × 6 cm) so that part of the wire is on the nonadhesive side and part of it on the inner adhesive portion. The wire can be formed in two (fig. 1) or more rows depending on the configuration desired. Another strand of Teflon-coated wire is woven through puncture holes so that it forms the other portion of a bipolar recording electrode. In order to hold both wires in place and keep them impervious to body fluids, we used another piece of paper tape to seal the exposed wires in a sandwich fashion. The free end of each Teflon wire is connected to a pinjack so that a bipolar electrode can lead to a DC amplifier through a switch box. Using a sharp scalp knife, the Teflon coating is scraped off the wires at the points which contact the myocardium. The electrode can be secured to the myocardium with sutures at the corners. However, because of the malleability due to the embedded wires, it can also be secured to the myocardium by insertion under the pericardium. The composite electrode used in the study and shown in figure 1 is made of two separate portions in a single frame; each portion can serve as a bipolar electrode and both have the same configuration with an exactly similar array of wires. The composite electrode is placed in a circumferential fashion around the left ventricle with the two portions in an apical and basal position so that one portion is in contact with the epicardial surface of the IZ while the other portion overlies the epicardial surface of the adjacent NZ. Two composite electrograms are recorded reflecting the electrical activity on the epicardial surface of the IZ and the adjacent NZ respectively.

In every experiment, in addition to the composite electrode recordings, 2–5 close bipolar recordings (1 mm bipolar distance) were also obtained. In some experiments, the bipolar wires were threaded through the frame of the composite electrode so that the close bipolar pairs would record from the same area of the epicardial surface of the IZ covered by the composite electrode. In other experiments, pairs of plunge wire electrodes were placed separately immediately beneath the epicardial surface of the IZ through a 22-gauge needle. Close bipolar electrodes were made of Teflon-coated stainless steel wires (0.007 inches coated diam.).

In addition to these electrograms, two standard electrocardiographic leads were recorded, specifically, leads II and aV_R. All records were obtained on a multichannel oscilloscopic photographic recorder (E for M, Dr-8) at paper speeds of 25–200 mm/sec. Electrocardiograms were recorded with the preamplifier filters set for frequencies of 0.1–200 cycles/sec and bipolar electrograms were recorded with filter frequencies of either 40–200 cycles/sec or 12–200 cycles/sec. Recordings were stored on a magnetic tape recorder (Honeywell 5600) and replayed so that selected sections could be transferred to photographic paper for detailed analysis. Measurements were accurate up to ±3 msec at a paper speed of 200 mm/sec.

Atrial or ventricular pacing (2 msec duration, 150–300 pulses/min, and 2–10 volts) was achieved via two fine stainless steel wires (0.003 inches diam.) inserted by a 25-gauge hypodermic needle into the left atrial appendage or the right ventricular wall respectively. His bundle pacing was obtained through the same electrodes on the catheter recording the His bundle electrogram.17 Both regular pacing and premature stimulation were performed using a programmed digital stimulator that delivered rectangular impulses of 1.5 msec duration at approximately twice diastolic threshold. For slowing of the heart rate, two silver wires (0.012 inches in diam.) were inserted into the distal portion of the right or left vagosympathetic trunk.18 Vagal stimulation was accomplished by delivery of 0.05 msec square wave pulses of 1–10 V intensity at a frequency of 20 Hz. In some experiments, the sinus node was crushed to obtain a slower atrial or A-V junctional rhythm.

**Procedure**

Recordings were obtained during spontaneous sinus rhythm, vagal-induced cardiac slowing, and atrial, His bundle or ventricular pacing, with either gradual or abrupt increase of the heart rate. The effect of premature beats with variable coupling and of either atrial, His bundle or ventric-
ular origin was also tested. The onset and termination of ventricular arrhythmias were monitored in the ECG leads as well as the corresponding changes in the IZ and NZ electrograms. If ventricular fibrillation did occur, the experiment was terminated and defibrillation was not attempted. In all experiments, gross postmortem examinations of the infarcted heart were performed to assess the infarction size. The anterior descending artery was probed, then split open at the site of ligature to make sure that the vessel was completely occluded. Correlations were made between the electrographic recordings and postmortem findings.

**Results**

In all experiments, the left anterior descending artery showed complete occlusion. Gross postmortem examination of the heart in the five sham experiments showed no evidence of myocardial damage and there were no abnormal electrophysiologic findings. In five of the 45 experiments in which the anterior descending artery was occluded, there was no gross evidence of subepicardial damage and only small areas of subendocardial infarction were noted (mottling of the subendocardial surface). In each of these five dogs, there was a large anastomatic vessel arising from the posterior descending artery and curving around the cardiac apex to fill the anterior descending artery distal to the ligation. These five experiments also revealed no abnormal electrophysiologic findings. In the remaining 40 experiments, transmural infarction of variable size (3–8 cm² on the epicardial surface) was evident on gross postmortem examination. The IZ consistently showed an irregular contour with a ragged irregular border between the infarcted and viable muscle. In these 40 experiments, the electrophysiologic study revealed characteristic disorders of conduction in the IZ as shown by the changes in the IZ electrograms.

**Tachycardia-dependent Conduction Disorders in the IZ**

The conduction disorder in the IZ was consistently tachycardia-dependent, meaning that conduction worsened at higher, but not necessarily high rates, and improved at relatively slower rates. In 60% of the experiments, there was a 1:1 conduction pattern in the IZ at the spontaneous sinus rhythm. In the rest of the experiments, a variable degree of

![Figure 2](http://circ.ahajournals.org/)

**Figure 2. Tachycardia-dependent conduction disorders in the infarction zone.** Panel A shows the infarction zone composite electrogram (IZeg) and the normal zone electrogram (NZeg) during spontaneous sinus rhythm. Panel B illustrates a 2:1 block of the late part of the IZeg (i.e., the IZ potential) during atrial pacing at a cycle length of 185 msec. In panel C, at a cycle length of 210 msec, the IZ potential showed an alternating 2:1 block and 3:2 Wenckebach-like conduction pattern with the potential fractionating into a series of multiple asynchronous spikes during the second beat of the Wenckebach cycle (marked by an arrow). Panel D illustrates a regular 4:3 Wenckebach-like conduction pattern of the IZ potential at a cycle length of 245 msec which resulted in concealed quadrigeminy. The latter is only revealed by a change of the NZeg (marked X). Hbeg = the His bundle electrogram; H = the His bundle potential. In this and subsequent figures the timelines are set at 1 sec intervals.
conduction block was present in one or more parts of the IZ. Figure 2 illustrates typical tachycardia-dependent changes of conduction from an experiment that was showing a 1:1 conduction pattern in the IZ at spontaneous sinus rhythm. Both the IZ and NZ composite electrograms (IZeg and NZeg) were recorded with the preamplifier set for frequencies of 12-200 cycles/sec. The NZeg represented electrical activity of the NZ that closely bordered the IZ. Figure 2, panel A, was recorded during spontaneous sinus rhythm. The NZeg was a sharp deflection with a duration roughly equal to the QRS duration in surface leads. The IZeg consisted of a multiphasic deflection with a duration longer than the QRS duration in surface leads. Thus, part of the IZeg was inscribed in the early part of diastole during the ST-T segment.

In all experiments, it was observed that the first part of the composite IZeg (the first 20-30 msec) remained essentially unchanged at all cardiac cycles provided that there was no change in the QRS configuration in surface leads. This part represented activation of relatively normal myocardium. The later part of the IZeg showed characteristic changes on shortening of the cardiac cycle length. This part reflected delayed activation of the IZ. In the following text, only that part of the IZeg that reflected delayed activation of the IZ will be referred to as the IZ potential. It should be stressed that the IZ potential does not necessarily constitute the sole second portion of the IZeg but rather part of it. This means that certain areas of relatively normal myocardium may still be activated during the inscription of part of the IZ potential. Exact repetition of the same configuration of the IZeg in consecutive beats was taken to represent a 1:1 conduction pattern in the IZ. In all experiments, there was a critically short cycle length, that varied from one experiment to the other, at which a 2:1 conduction block of part or all of the IZ potential developed. This is illustrated in figure 2, panel B, which showed atrial pacing at a cycle length of 185 msec. The record shows that the later portion of the IZeg (the IZ potential) failed to be inscribed in every other beat. There was essentially no change in the initial portion of the IZeg, the NZeg, or the QRS configuration in surface leads.

When the heart rate was gradually decreased from the one that resulted in 2:1 block of the IZ potential, a critical rate was reached during which the conduction pattern changed to a Wenckebach-like structure with periodic changes in the IZ potential. This is illustrated in figure 2, panels C and D. Panel C shows that as a cycle length of 210 msec, there were alternating 2:1 and 3:2 conduction patterns in the IZ potential. During the second beat of a 3:2 pattern, the IZ potential was replaced by a slow deflection with superimposed multiple asynchronous spikes that extended for most, but not all, of the diastolic interval. During the third beat of a 3:2 pattern, most of the IZ potential failed to be inscribed. Meanwhile, the NZeg showed essentially no change. There was,

**Figure 3.** Recordings obtained from the same experiment shown in figure 2 utilizing different filter settings for both the infarction zone electrogram (IZeg) and the normal zone electrogram (NZeg). The preamplifier filters were set for frequencies of 40-200 cycles/sec in figure 3 compared to 12-200 cycles/sec in figure 2. Panel A was obtained during sinus rhythm while panels B to D were recorded during atrial pacing of varying rates. The higher cutoff filter showed more vividly the periodic fractionation of the IZ potential during certain beats of a Wenckebach-like conduction pattern (panels C and D). The continuous electrical activity in the IZ resulted in concealed re-entry in panel C (marked X) and a fusion beat in panel D (marked F). The figure also illustrates that the critical cycle length at which conduction in the IZ changes from a Wenckebach-like pattern to a 2:1 block (panel C) is shorter compared to the cycle length at which conduction changes in the opposite direction (panel D).
However, a small negative deflection at the end of the ventricular complex in the NZeg only in those beats showing a relatively synchronized IZ potential in the IZeg. This was also apparent in panel B during 2:1 block of the IZ potential. This would suggest that some events in the IZ may be reflected in recordings from the bordering NZ. Panel D shows that on further slowing of the heart rate to a cycle length of 245 msec, the alternating 2:1 and 3:2 pattern was converted to a regular 4:3 conduction pattern. The first beat of the 4:3 pattern (marked 2) showed a series of asynchronous relatively large amplitude spikes that extended for more than half the diastolic interval. The third beat of the 4:3 cycle (marked 3) showed a larger number of low amplitude spikes and slower deflections that extended for all the diastolic interval and ended with a relatively sharp spike that immediately preceded the next ventricular deflection (marked by an arrow). The fourth beat of the 4:3 cycle (marked 4) showed absence of a major portion of the IZ potential. However, during this beat, the NZeg showed a definite change in the configuration of the recorded ventricular deflection (marked X). This is a clear indication that the continuous electrical activity in the IZ during the third beat of the 4:3 cycle did, in fact, re-excite (re-enter) the bordering NZ resulting in change of its activation pattern.

The absence of a change of the QRS configuration in leads II and aV₆ may suggest that the area of the NZ re-excited by the delayed electrical activity in the IZ was relatively small and probably did not influence the basic depolarization pattern of the whole ventricle. This does not exclude, however, the fact that a more detailed recording of body surface electrocardiograms may have detected some QRS changes. Thus panel D clearly illustrates that a 4:3 Wenckebach-like pattern of the IZ potential did result in a concealed quadrigeminy. In the following text, the term Wenckebach-like conduction pattern will be used to describe characteristic changes in the IZ potential. The difference between this usage and the classical Wenckebach periodicity will be explained in the discussion.

Figure 3 illustrates tracings from the same experiment shown in figure 2 with both the IZeg and NZeg recorded with the preamplifier filters set for frequencies of 40-200 cycles/sec. Panels A and B were obtained during spontaneous sinus rhythm and atrial pacing at a cycle length of 285 msec respectively. Due to altered filter settings, the IZ potential was mainly represented by a relatively sharp spike, superimposed on the second half of the ventricular deflection in the IZeg (marked by an arrow in panel C). When the pacing cycle was shortened from 285 msec in panel B to 220 msec in the first half of panel C, the IZeg showed the periodic occurrence of a series of multiple asynchronous spikes that frequently extended for the entire diastolic interval and up to the next ventricular deflection. Critical analysis, however, reveals that these spikes represented periodic fractionation of the IZ potential in 3:2 and 4:3 Wenckebach-like patterns respectively, as was described in figure 2. The higher cutoff filter produced a recording that more vividly showed the continuous electrical activity originating from the IZ during certain beats of a Wenckebach-like pattern. The latter half of panel C shows that slight decrease of the pacing cycle from 215 to 210 msec was sufficient to change the Wenckebach-like periodicity to a 2:1 conduction pattern with absence of the IZ potential in alternate beats.

Panel D that represents a consecutive recording shows that on gradual lengthening of the pacing cycle, the 2:1 conduction pattern reverted to a Wenckebach-like form with the reappearance of periodic fractionation of the IZ potential. As was noted in figure 2, when the fractionated IZ potential extended late in the diastolic interval, there was a chance for re-exiting the NZ. Panel C shows concealed re-entry that could be detected only by a slight change in the configuration of the NZeg (marked X). However, panel D shows that at a relatively longer pacing cycle, the delayed electrical activity in the IZ re-excited a relatively larger portion of the NZ myocardium that has recovered responsiveness. A detectable alteration of the QRS configuration in the ECG leads can be seen, giving rise to a ventricular fusion beat (marked F).

Panels C and D in figure 3 also illustrate another characteristic finding during gradual increase or decrease of the heart rate. It was commonly observed that the critical cycle length at which conduction in the IZ changes from 1:1 response to a Wenckebach-like pattern and the one at which a Wenckebach-like pattern changes to a 2:1 conduction are both relatively shorter (by 10-60 msec) compared to the cycle lengths at which conduction changes in the opposite direction. Thus, in panel C, a Wenckebach-like pattern changed to a 2:1 conduction at a cycle length of 210 msec. On the other hand, once a 2:1 conduction was established it was necessary to slow down to a cycle length of 235 msec before a Wenckebach-like pattern reappeared.

This point is re-emphasized in figure 4, obtained from a different experiment. Recordings in figure 4, panels A and B, are consecutive, with only few cycles omitted. The heart rate was gradually increased in panel A, then gradually decreased in panel B. At a cycle length of 325 msec, the IZ potential was a relatively sharp spike recorded at the end of the ventricular deflection in the IZeg (marked by an arrow). On gradual increase of the heart rate, the IZ potential showed a beat-to-beat change with gradual increase in duration, decrease in amplitude and fractionation into multiple asynchronous spikes before it finally blocked. This was followed by a 2:1 pattern during which the IZ potential returned as a large sharp spike in every other beat. The transition from a Wenckebach-like pattern to a 2:1 pattern took place at a critical cycle length of 260 msec.

Panel B shows that on gradual slowing of the heart rate, the 2:1 pattern was maintained up to a cycle length of 320 msec before it changed to a 3:2, 4:3, and 3:2 Wenckebach-like cycles respectively. The latter changed to a 1:1 pattern at a cycle length of 400 msec. Thus, a cycle length of 325 msec in panel A was associated with a 1:1 conduction pattern of the IZ potential while at the same cycle length in panel B, a Wenckebach-like pattern was still observed. In contrast to what was shown in figures 2 and 3 during a Wenckebach-like conduction pattern, the fractionated IZ potential did not extend far enough in diastole beyond the T wave of the surface ECG and there was no evidence of concealed or manifest re-entry.

In 40% of the experiments, a variable degree of conduction block was present in one or more parts of the IZ during
FIGURE 4. Recordings obtained from a different experiment during gradual increase of the heart rate (panel A) and gradual slowing of the rate (panel B). The IZ potential (marked by arrows) changes from a 1:1 conduction pattern to a Wenckebach-like arrangement followed by a 2:1 block in panel A. The reverse order of changes is seen in panel B. Note that the critical cycle length necessary for a change of one conduction pattern to the other was shorter in panel A compared to panel B.

spontaneous sinus rhythm (usually a sinus tachycardia of 120–170 beats/min in anesthetized dogs). The block was still tachycardia-dependent, meaning that at a critically slower rate, a 1:1 conduction pattern could be achieved. This is illustrated in figure 5. Panel A illustrates recordings obtained during spontaneous sinus rhythm at a cycle length of 380 msec. The IZeg showed a fractionated IZ potential in the form of multiple asynchronous spikes that extended in diastole to beyond the T wave of the surface leads but with no evidence of re-entry. Vagal-induced slowing of the heart rate at the end of panel A to a cycle length of 630 msec resulted in the appearance of a relatively sharp large

FIGURE 5. Recordings obtained from a different experiment showing a tachycardia-dependent paroxysmal conduction block to part of the infarction zone. The IZeg shows a fractionated IZ potential in the form of multiple asynchronous spikes. Note complete conduction block to the part of the IZ potential represented by the large amplitude spike (marked by arrows) during spontaneous sinus rhythm (first part of panel A). 2:1 block was present at slightly slower rate (panel B) and a 1:1 conduction pattern was achieved on further slowing of the rate (latter part of panel A and panel C).
amplitude spike at the end of the fractionated IZ potential (marked by an arrow). Panel B shows that a regular heart rate slightly slower than the spontaneous sinus rhythm in panel A was associated with a 2:1 inscription of the late spike. In panel C, sinus bradycardia at a cycle length of 840 msec resulted in a 1:1 pattern of the late spike which was also less delayed in diastole compared to panel B. Figure 5 thus illustrates a tachycardia-dependent paroxysmal conduction block to part of the IZ represented by the late spike during spontaneous sinus rhythm. Other areas of the IZ still revealed significant conduction delay as reflected by the delayed fractionated part of the IZ potential.

**Functional Dissociation of Conduction in the IZ**

In over 50% of the experiments, evidence of functional dissociation of conduction in the IZ could be revealed by analysis of the composite electrode recording alone or in association with multiple close bipolar recordings. Figure 6 illustrates the presence of discordant conduction disorders in different portions of the IZ as reflected in the composite electrode recording. Figure 6, panel A, was recorded during spontaneous sinus rhythm and shows that the IZ potential consisted of a relatively sharp deflection (marked by a straight arrow) that immediately followed the portion of the IZeg that reflected electrical activity in relatively normal myocardium. This was followed by a series of low amplitude slow deflections superimposed on the local repolarization wave. Finally, there was another sharp deflection (marked by a curved arrow) that was inscribed late in diastole after the T wave of the surface ECG. The record reveals that the conduction patterns of the two distinct potentials were different. The early deflection marked by straight arrows showed a conduction pattern reminiscent of the so-called Mobitz II block. This was reflected in the IZeg by a few msec gradual separation of the deflection from the major ventricular potential prior to block. Following block, the deflection was inscribed much closer to the major ventricular potential. On the other hand, the second deflection, marked by curved arrows, showed at the same time a regular 2:1 conduction block.

Figure 6, panel B, illustrates that on marked slowing of the heart rate (through vagal-induced 2:1 A-V nodal block), there was a regular 1:1 conduction of both the early and late deflections. The later deflection occurred relatively closer to the major ventricular deflection. The low amplitude slow waves also became more evident and continued after the late sharp deflection was inscribed. Figure 6, panel C, shows that at a heart rate intermediate between those in panels A and B, the late sharp deflection showed a 3:2 Wenckebach-like pattern.

Figure 6 thus illustrates the presence of a low amplitude continuous electrical activity in the IZ that extended late in the diastole interval. In addition, there was evidence that

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**Figure 6.** Recordings obtained from a different experiment showing functional dissociation of conduction in the IZ. Panel A was obtained during sinus rhythm and illustrates discordant conduction patterns of two discrete portions of the IZeg (a Mobitz II conduction pattern of the deflection marked by straight arrows and a 2:1 block of the one marked by curved arrows). In addition, the IZeg also revealed continuous low amplitude deflections. Panels B and C illustrate changes in the conduction pattern of the discrete deflections at slower heart rates.
other discrete portions of the IZ simultaneously revealed variable degrees of conduction block. This reflects the highly desynchronized conduction pattern with complex functional dissociation of different portions of the IZ. In spite of the fact that both the low amplitude continuous electrical activity as well as the late sharp deflection extended well beyond the T wave of the standard ECG, there was no evidence that the electrical activity in the IZ did re-excite the normal zone.

Figure 7 obtained from the same experiment shows that re-entry did, in fact, occur and was consistently associated with a characteristic conduction pattern of the initial sharp deflection. Panels A and B, in figure 7, were obtained during spontaneous acceleration of the sinus rhythm. The late sharp deflection (marked by curved arrows) showed a 2:1 or 3:1 conduction pattern. The initial sharp deflection (marked by straight arrows) showed either a Mobitz II pattern with a few msec increment of conduction delay as shown in figure 6, panel A (first half of figure 7, panel A) or a 2:1 pattern (first half of figure 7, panel B). However, periodically the deflection revealed a 3:2 Wenckebach-like pattern with marked increment of conduction delay so that the deflection was inscribed very late in diastole. This pattern was consistently associated with evidence of either concealed re-entry that was revealed only by a change in the configuration of the NZeg (fig. 7, panel A, marked X) or manifest re-entry with change of the QRS configuration in surface leads (fig. 7, panel B).

Figure 7, panel C, illustrates the occurrence of high degree block of both the initial and late deflections on atrial pacing at a fast rate. On abrupt termination of atrial pacing, the two sharp IZ potentials were inscribed late in diastole and were also followed by a re-entrant ventricular beat.

Figure 8 illustrates the presence of discordant conduction disorders in the IZ revealed by simultaneous analysis of a composite and a close bipolar recording (IZeg [Comp.] and IZeg [Bip.] respectively). Panel A shows recordings obtained during spontaneous sinus rhythm at a cycle length of 345 msec. The IZeg (comp.) showed a 2:1 block of a portion of the IZ potential (marked by straight arrows). On the other hand, the IZeg (Bip.) revealed a 1:1 conduction pattern of the IZ potential (marked by curved arrows). Panel B was obtained during atrial pacing at a cycle length of 240 msec. The IZeg (Comp.) showed a 2:1 block of a larger portion of the IZ potential while the IZeg (Bip.) revealed a 3:2 Wenckebach-like conduction pattern of the IZ potential. During the second beat of the Wenckebach cycle, the IZ potential moved outwards in diastole and showed some increase in duration and decrease in amplitude. However, there was no evidence of a continuous electrical activity that bridged the interval between the major ventricular deflection and the delayed IZ potential.

Panel C was recorded at a slightly longer cycle length of 250 msec. This slight lengthening of the cycle length resulted in a change of the IZ potential in the IZeg (Comp.) from a 2:1 pattern (panel B) to a 2:1, 3:2, and 3:2 patterns in panel C respectively. During the second beat of a 3:2 Wenckebach-like cycle, the IZ potential was replaced by a series of multiple asynchronous spikes that extended for part or all of the diastolic interval. Simultaneously the IZ potential in the

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**Figure 7.** Recordings obtained from the same experiment shown in figure 6 illustrating ventricular re-entry during spontaneous sinus rhythm (panels A and B) and following abrupt termination of rapid atrial pacing (panel C) (marked by X). Re-entry was concealed in panel A and only detected by changes in the NZeg. The occurrence of re-entry was consistently related to delayed inscription of the deflection marked by straight arrows either during a 3:2 Wenckebach-like conduction pattern (panels A and B) or a higher degree block (panel C).
IZeg (Bip.) showed discordant 3:2, 2:1, and 3:2 patterns, respectively. Again, there was no evidence of continuous electrical activity between the major ventricular deflection and the delayed IZ potential. On the other hand, some of the delayed IZ potentials recorded by the IZeg (Bip.) were not depicted by the IZeg (Comp.).

The fourth beat in panel D is a ventricular fusion beat (marked F). Analysis of the IZeg (Bip.) failed to show evidence that the IZ potential was markedly delayed prior to the occurrence of the fusion beat, a necessary prerequisite for a re-entrant etiology. In contrast, the IZeg (Comp.) clearly demonstrated continuous electrical activity originating from the IZ that bridged the interval between the third and fourth beats, a strong indication for re-entry. Panel D illustrates the difficulty that would be encountered when a close bipolar recording reflects electrical activity of a functionally dissociated portion of the IZ that does not actively participate in the re-entrant pathway.

Localized Ventricular Fibrillation

In figures 5 and 6, we have shown that electrical activity in the IZ can extend in diastole well beyond the T wave of the surface ECG without resulting in re-entry. In some experiments, low amplitude continuous electrical activity in the IZ was shown to overlap consecutive cardiac cycles during spontaneous sinus rhythm. This electrical activity, that closely simulated localized ventricular fibrillation, never showed evidence of being able to re-excite the NZ and give rise to re-entry (fig. 9). Panel A was recorded during atrial pacing at a cycle length of 210 msec. The IZ potential showed gross fractionation. At least two distinct IZ deflections could be identified (marked by straight and curved arrows). The deflection marked by curved arrows showed a 2:1 conduction block while the one marked by straight arrows revealed a 4:1 conduction pattern. Slowing of the heart rate in panel B to a cycle length of 380 msec resulted in 1:1 conduction of the deflection marked by curved arrows and 2:1 block of the deflection marked by straight arrows. However, in addition, it became apparent that multiple asynchronous low amplitude slow deflections were continuously inscribed during the rest of the diastolic interval and up to the next major ventricular deflection. Further slowing of the heart rate was achieved through vagally-induced sinus bradycardia and A-V nodal block (the last part of panel B and panel C; both are parts of a consecutive recording). One-to-one conduction of the distinct IZ deflection (marked by straight arrows) was achieved but the asynchronous low amplitude deflections continued to occupy all the diastolic interval up to a cycle length of 985 msec. On lengthening of the cycle length to 1325 msec, the low amplitude deflections seemed to end after an interval of 1025 msec and the rest of the diastolic interval showed an apparently isoelectric baseline. It should be emphasized that the NZeg (trace below) that was recorded close to the border.

**Figure 8.** Recordings obtained from another experiment showing functional dissociation of conduction in the infarction zone revealed by simultaneous analysis of a composite and a close bipolar electrogram (IZeg [Comp.] and IZeg [Bip.], respectively). Note varying discordant conduction patterns of the IZ potential in both electrograms at different heart rates (marked by straight and curved arrows). The re-entrant fusion beat in panel D (marked F) was related to the periodic fractionation of the IZ potential in the IZeg (Comp.) during a Wenckebach-like conduction pattern. The IZeg (Bip.) reflected electrical activity of a functionally dissociated portion of the infarction zone that did not participate in the re-entrant activity in panel D.
of the IZ showed a perfectly isoelectric line in diastole apart from the smooth local repolarization wave during the early part of diastole.

Re-entrant Beats with Fixed and Variable Coupling, Uniform, Multiform, and Bidirectional QRS Configuration

Re-entrant ventricular beats with similar QRS configuration in ECG leads can have variable coupling intervals due to variation in the pathway of re-entry in the IZ. On the other hand, under relatively constant electrophysiologic conditions, the cardiac impulse can precisely retrace the same re-entrant pathway resulting in constant coupling of re-entrant beats. This is illustrated in figure 10 in which re-entry was induced by atrial premature beats applied during a slow junctional rhythm in panel A and sinus bradycardia in panel B. All four atrial premature beats resulted in complex fractionation of the IZ potential that consistently extended beyond the T wave of the surface ECG resulting in a re-entrant ventricular beat. The re-entrant ventricular beats showed a remarkably similar QRS configuration in the surface ECG denoting an overall similar ventricular activation pattern. However, there was significant variation in the pathway of re-entry in the IZ. The coupling intervals of the re-entrant beat compared to the preceding supraventricular impulse as well as the changed configuration of the fractionated IZ potential recorded by the composite electrode reflect this variation. Thus, the first atrial premature beat in panel A is followed by two series of asynchronous spikes that occupied the first and last third of the diastolic interval, with an apparent isoelectric interval in the middle third. This was different from the pattern of the fractionated IZ potential that followed the second atrial premature beat in panel A and the two premature beats in panel B. On the other hand, both atrial premature beats in panel B that had similar coupling intervals were followed by an almost identical series of multiple asynchronous spikes that extended through the entire diastolic interval and up to the re-entrant ventricular beats. The latter had exactly the same coupling intervals.

Figure 11 was taken from the same experiment shown in figure 10. The record shows that alternation of the coupling intervals of the atrial premature beats resulted in re-entrant ventricular beats with bidirectional QRS configuration in standard leads (panel A). There were variations in the coupling intervals of re-entrant beats and/or the configuration of the fractionated IZ potential even between re-entrant beats with similar QRS configuration. Panel B illustrated two consecutive re-entrant beats with bidirectional QRS configuration. Perpetuation of this pattern would result in bi-

![Figure 9](http://circ.ahajournals.org/)

**FIGURE 9.** Recordings obtained from a different experiment showing evidence of continuous electrical activity in the infarction zone that overlaps consecutive cardiac cycles during spontaneous sinus rhythm (first part of panel B) simulating localized ventricular fibrillation. The IZeg in panel C was obtained during vagal-induced marked cardiac slowing and illustrates continuous low amplitude asynchronous deflections that extend for at least 1025 msec in diastole. Panels A and B also illustrate tachycardia-dependent block of varying degrees in other discrete portions of the IZ potential (marked by straight and curved arrows).
directional ventricular tachycardia that was occasionally observed in some experiments. Vagal stimulation in panel C revealed an underlying slow escape rhythm with a QRS configuration similar to one of the re-entrant beats. Figure 11 illustrates that re-entrant beats arising from the same IZ can follow different re-entrant pathways with different exit points to the NZ, resulting in varying ventricular activation patterns. Regular alternation of two of these patterns may give rise to a bidirectional ventricular tachycardia in the surface ECG.

The Composite Versus Close Bipolar Recordings

In this study, the composite electrode recording was able to depict the electrical activity of the entire re-entrant pathway in the form of a continuous series of multiple asynchronoous spikes in 75% of the re-entrant beats. In the remaining beats, only part of the electrical activity of the re-entrant pathway was recorded. On the other hand, two to five close bipolar electrodes were unable to record the entire electrical activity of the re-entrant pathway. A larger number of
close bipolar recordings might have allowed recording the entire pathway. The main objective of the limited epicardial mapping in this study was to provide evidence that the composite electrode depicts an averaged recording of multiple close bipolar sites (fig. 12).

Figure 12 shows simultaneous recordings of a composite electrode and three close bipolar electrodes that were threaded through the frame of the composite electrode. The schematic diagram at the bottom of the figure shows the position of the composite and close bipolar recordings in relationship to the epicardial surface of the IZ that was roughly determined by postmortem naked eye examination. Panels A to C illustrate three atrial premature beats that resulted in a limited degree of fractionation of the IZ potential in A, a single re-entrant beat in B, and a short run of multiform ventricular tachycardia in C. Panels A and B suggest that the two atrial premature beats pursued an almost identical course in the IZ, as judged by the similar configuration and timing of the multiple IZ recordings. However, the atrial premature beat in panel A failed to complete the entire re-entrant circuit, probably because of refractoriness of the terminal part of the re-entrant pathway. In panel C both the configuration and timing of the IZ recordings during the three re-entrant beats suggest different degrees of variation of the re-entrant pathways in the IZ. During the four re-entrant beats in panels B and C, the composite electrode recording depicted the electrical activity of the entire re-entrant pathway in the form of a continuous series of multiple asynchronous spikes. On the other hand, each of the close bipolar recordings depicted only part of the electrical activity of the re-entrant pathway. The rest of the diastolic interval showed an apparent isoelectric interval. During the re-entrant beat in panel B, one of the close bipolar electrodes (Bip 3) failed to record evidence of the re-entrant activity. In panel C, the same electrode depicted the terminal part of the re-entrant wavefront as a sharp spike (marked by an arrow) during re-entrant beats. Because of the different degrees of variation of the re-entrant pathways in the IZ, the schematic diagram only roughly outlines part of the re-entrant pathway of the beat marked X in panel C. The re-entrant wavefront was sequentially depicted by the close bipolar electrodes 1, 2, and 3 in that order. The diagram shows the arrival time of the re-entrant wavefront to the different bipolar sites in msec measured from the onset of the ventricular deflection of the atrial premature beat. The exact site of entrance and exit of the re-entrant pathway from the NZ to the IZ and vice versa could not be delineated, however, by this limited form of mapping.

**Discussion**

In this study, the demonstration of continuous electrical activity that regularly and predictably bridged the entire diastolic interval between the initiating and re-entrant beats, as well as between consecutive re-entrant beats, constitutes the necessary missing link long sought to document re-entry. The composite electrode with its multiple bipolar contact points covering a large portion of the IZ seems to function as multiple close bipolar electrodes connected in series. Each contact point will be influenced by the activation wavefront
as it approaches its site. The presence of continuous electrical activity in the IZ representing the entire re-entrant pathway will be usually depicted by the composite electrode as a continuous series of multiple spikes. The composite electrode recording would provide reliable information on the degree of conduction delay in the IZ of one or a series of beats as reflected by the duration of the fractionated electrogram. However, a note of caution should be expressed in relation to analysis of the waveform recorded by the composite electrode. In contrast to a unipolar or a close bipolar recording, in a composite electrode recording it is almost impossible to assign certain portions of the recorded deflections to electrical activity originating from specific areas in the IZ. However, an exact repetition of a certain configuration (e.g., figure 10, panel B) would suggest that the cardiac impulse may have pursued an almost identical pathway in the IZ. Still, this will not exclude the possibility of minor variation in the pathway.

The construction of the composite electrode in regard to recording from both the IZ and the NZ offered two obvious advantages. First, it made it highly improbable that the characteristic and consistently reproducible changes in the IZeg could have been partly tainted with artifacts at times at which the NZeg showed a perfectly clear isoelectric baseline. Second, by recording of the NZeg from an area closely bordering the IZ, it was frequently possible to detect early breakthrough of the re-entrant wavefront in the NZ, thus offering the most genuine illustration of concealed re-entry. However, it should be emphasized that it was not possible, with this electrode arrangement, to exactly delineate the so-called border zone from other areas of the IZ.

Although composite electrode recording coupled with a limited number of close bipolar recordings provided a relatively simple and adequate means of analyzing the electrical activity in the IZ, further studies utilizing extensive epicardial and possibly subepicardial mapping by close bipolar electrodes are probably needed for further elaboration. Mapping will be necessary for precise delineation of the re-entrant pathways. Although mapping is not crucial to the proof of re-entry, coupled with detailed histochemical studies, it may provide valuable electrophysiologic-anatomic correlations. Mapping will also be necessary to analyze the re-entrant pathway length and conduction velocity. It can provide better insight into the presence and role of functionally dissociated areas in the IZ, the presence and sites of unidirectional block, and the possible contribution of inhibition and summation of activation wavefronts in the IZ to re-entry.

Re-entry and Conduction Disorder in the IZ

A schematic representation of the conduction disorder in the IZ leading to re-entry is shown in figure 13. The schematic figure is consonant with our electrophysiologic observations. It is also corroborated by the known anatomic characteristics of the IZ which may show islands of relatively viable muscle alternating with areas of infarction. In the figure, the area of straight lines represents normal myocardium. The IZ consists of multiple irregular islands of severely depressed, unexcitable myocardium (the white areas) and intervening portions of less severely depressed myocardium that allows slow conduction of the cardiac impulse (stippled areas). The figure illustrates the area covered by the composite electrode as well as the three close bipolar electrodes. Tracings from top to bottom represent a standard ECG lead, a composite electrode recording, IZeg (Comp.), and three close bipolar recordings, IZeg (Bip.), 1–3. The figure depicts the activation wavefront in the NZ invading the IZ at multiple sites (black arrows) while failing to conduct at other sites (white arrows) creating areas of unidirectional conduction block. The IZ shows more than one pathway. Impulses propagate from opposite directions in the pathway in the upper part of the IZ where they collide and die out. On the other hand, the cardiac impulse enters a potentially re-entrant pathway at the lower left side of the IZ and conducts slowly in a highly circuitous pathway. The diagram shows that the impulse reaches the lower part of the IZ but fails to re-excite the NZ, which is still refractory (the white arrow at the bottom of the IZ). The impulse continues propagation to the right border of the IZ; there it succeeds in re-exciting the NZ because of recovery of excitability of the tissues proximal to the unidirectional block, resulting in a re-entrant beat.

The schematic diagram illustrates the two prerequisites long considered necessary for re-entry:12 1) unidirectional block of conduction at certain sites; 2) conduction over alternate route(s) at a velocity slow enough to allow recovery of excitability of tissues beyond the block. The composite electrode which covers the entire re-entrant pathway in panel A of figure 13 records a continuous series of multiple asynchronous spikes that bridge the total diastolic interval between the initiating and re-entrant beats. On the other hand, the close bipolar electrodes depict the arrival of the slow activation wavefront as it passes close by. This is reflected in the bipolar electrograms as one or more potentials that only cover part of the diastolic interval.

In this study, the composite bipolar recording occasionally failed to depict the electrical activity of the entire re-entrant pathway. Figure 13, panel B, illustrates one possible explanation for this observation. The diagram shows that the composite electrode does not cover the entire re-entrant pathway. Two series of spikes reflect the initial and terminal parts of the re-entrant circuit while activity in between is represented by an apparently isoelectric line. This is explained by the fact that part of the slow activation front was located far from the closest contact points of the composite electrode. Previous studies have shown significant reduction in the amplitude of recorded deflection the greater the distance between the close bipolar electrode and the activation wavefront.15

The diagram shows that the part of the re-entrant circuit not depicted by the composite electrode still takes place on the epicardial surface not in close contact with the electrode. The same recording would be obtained if part of the re-entrant pathway is located deep in the subepicardial muscle zone. Since 75% of the re-entrant circuits were depicted by a composite electrode in contact with the epicardial surface, most re-entrant activity is probably taking place in or close to the epicardial layer of muscle.

Complex as the schematic illustration of the re-entrant pathway in figure 13 is, our observations show that this is an oversimplified version of the highly complex pattern of conduction in the IZ. Three of these complex patterns deserve...
emphasis. First is our repeated demonstrations of the presence of multiple potentially re-entrant pathways in the IZ. Second is the common observation of functionally dissociated areas with either concordant and discordant patterns of conduction delay that may not participate in the re-entrant pathway. These areas resemble the dead-end pathways described in the A-V node. Third is the presence of low amplitude continuous electrical activity that overlaps consecutive cardiac cycles. This continuous electrical activity corresponds in part to the localized ventricular fibrillation first demonstrated by Moe et al. during the onset of induced generalized ventricular fibrillation. On the other hand, Waldo and Kaiser demonstrated continuous electrical activity following acute ligation of the anterior descending artery which was not always associated with ventricular arrhythmias. This observation probably reflected periodic fractionation of the IZ potential during Wenckebach-like conduction pattern as was shown in this study. These authors also emphasized the fact that in a markedly fractionated IZ potential, no clear distinction can be made between deflections that reflect local depolarization and repolarization. They suggested that the multiple asynchronous deflections probably reflect more than one local depolarization.

The different types of dissociated electrical activity in the IZ shown in this study clearly demonstrate that the mere presence of delayed activation in the IZ does not necessarily result in re-entry. Re-entry appears to require a certain level of electrical density (strength) of the activation wavefront necessary to excite the NZ. It is reasonable to assume that the fractionated activation wavefront during re-entry represents a weak dissociated and partly decremental electrical activity that can gradually become incremental once it reaches relatively normal myocardium. The complex conduction pattern in the IZ is a most fertile soil for summation and cancellation of electrical wavefronts; the feasibility of both phenomena have been elegantly demonstrated in micro-electrode studies of depressed Purkinje fibers. However, the contribution to re-entry of summation and cancellation of activation wavefronts in the IZ requires further study.

The diagrammatic representation of re-entry in the IZ shown in figure 13 is similar to the one suggested by Boineau and Cox based on both electrophysiologic and histopathological studies in acute myocardial infarction. These authors described patterns of either slight or marked inhomogeneity in the IZ. These two different anatomic patterns were aligned with two corresponding electrical recordings showing a lesser and a greater degree of fractionation of the IZ potential. These authors failed, however, to consider the essential tachycardia-dependent characteristics of conduction in ischemic myocardium. This means that the same IZ potential can vary between a lesser or greater degree of fractionation depending on slight changes of rate or even from beat-to-beat, and without any change of rate during a Wenckebach-like conduction pattern. In our study, such an anatomic-electrophysiologic correlation seems spurious since the alteration in IZ potential was significantly dependent on functional changes.

**Conduction Characteristics of Ischemic Myocardium**

The present study confirms previously-reported observations following acute ligation of the anterior septal artery in the dog: conduction disorder of ischemic myocardium
closely simulates the patterns of conduction disorder in ischemic and depressed His-Purkinje system. These include delayed conduction equivalent to a block (fig. 2, panel A), a block with a few msec increment of conduction delay simulating the so-called Mobitz type II block (fig. 6, panel A), a block with marked increment of conduction delay reminiscent of the Wenckebach type of conduction, (figs. 2, 3, 4, 6, 7, and 8), high degree block (2:1, 3:1, etc., figs. 2-9) and paroxysmal complete block (fig. 5, panel A). In contrast to normal muscle cells, ischemic myocardium shows varying degrees of tachycardia-dependent conduction block at relatively long cycle lengths. Our preliminary in vitro studies show that, similar to ischemic His-Purkinje cells, ischemic muscle cells have time-dependent refractoriness with full recovery of responsiveness far outlasting the action potential duration. These studies also revealed marked heterogeneity of conduction in ischemic myocardium with irregular wavefronts.

In this study, the spontaneous onset of re-entrant ventricular beats was specifically associated with the Wenckebach-like pattern of conduction delay. Figure 14 illustrates that there is more than a subtle difference between the Wenckebach type of conduction in an insulated single pathway (e.g., the proximal His-Purkinje system) and the Wenckebach-like pattern in ischemic myocardium associated with the onset of ventricular re-entry. Thus, in the former situation, a Wenckebach type of conduction reflects a beat-to-beat change (increment) of refractoriness of a group of Purkinje cells critically situated within the pathway resulting in slower and slower conduction of the activation wavefront before it finally blocks. This is usually followed by return of refractoriness to a relatively normal level associated with better conduction. Electrographic monitoring of the Wenckebach cycle by recording of two electrograms proximal and distal to the site of maximum conduction delay will manifest as a beat-to-beat gradual delay of the distal deflection in relation to the proximal one before it finally fails to be inscribed.

Figure 14 illustrates a relatively more complex sequence of events during a Wenckebach-like conduction pattern in ischemic myocardium. Diagrams A to C represent three consecutive cycles of a Wenckebach-like conduction pattern in the IZ. The schematic illustration of conduction in IZ is essentially similar to the one utilized in figure 13. The three tracings represent from top to bottom: a surface ECG lead, recording of a composite electrode that reflects the entire IZ (IZeg [Comp.]), and a close bipolar recording from a localized portion of the IZ (IZeg [Bip.]). Diagram A shows that during the first beat of a Wenckebach-like cycle, conduction in the IZ is represented by several islands of severely depressed unexcitable myocardium (white areas) with intervening relatively wide pathways of less severely depressed myocardium (stippled areas). The activation wavefront in the NZ invades the IZ at multiple sites (black arrows) with the impulses that propagate from opposite directions collide, and die out. Both the composite and the close bipolar electrograms record an initial multiphasic deflection that represents activation of relatively normal myocardium and a late deflection (marked by arrows) reflecting a delayed but relatively synchronous conduction in the pathway at the lower part of the IZ (the IZ potential).

Diagram B illustrates the changes in conduction in the IZ during the second beat of the Wenckebach-like cycle. One or more groups of cells in the lower pathway that was showing a slow but synchronized conduction during the first beat develop different degrees of increment of refractoriness resulting in either relatively slower conduction or block of the activation wavefront advancing from the NZ. This is represented by several small white islands in the pathway that was first represented by a homogeneous stippled area in diagram A. Since the myocardium is a free syncytium, the irregular change in refractoriness will force the activation wavefront to take a circuitous and much longer pathway in the IZ.

The conduction pattern in the IZ is reflected in the composite electrogram as a series of highly complex spikes and low amplitude slower deflections that replace the initial relatively simple IZ potential and extends for a variable distance in diastole. On the other hand, the close bipolar electrode which is positioned relatively distal to the maximum zone of conduction delay will only depict the arrival of the activation wavefront as it passes close by. This is reflected in the bipolar electrogram as a marked delay in the inscription of the IZ potential relative to the initial ventricular deflection as well as a varying degree of decrease in amplitude and
increase in duration of the potential. An apparently iso-electric interval separates the IZ potential from the rest of the ventricular deflection.

During the third beat of a 3:2 Wenckebach-like cycle (diagram C), there is further increment of refractoriness in most of the groups of cells that formed the circuitous pathway in diagram B. This is represented by a significant increase in the portion of the IZ occupied by the white islands which are unable to conduct the cardiac impulse. This will result in complete failure of conduction of the activation wavefront advancing from the NZ through the IZ pathway that was originally conducting slowly in diagram A. Both the composite and the close bipolar electrograms show failure of inscription of the IZ potential. For re-entry to take place following the second beat of a 3:2 Wenckebach-like cycle, two requirements are necessary. These are 1) unidirectional block of conduction at certain sites(s), (white arrow), and 2) sufficient conduction delay of the impulse propagating in the lower pathway to allow recovery of excitability of tissues beyond the block. The re-entrant beat will replace the third beat of a 3:2 Wenckebach-like cycle that did not result in re-entry. The first re-entrant beat can change the refractoriness in several portions of the IZ. This may result in either one or more re-entrant beats or change the pathway in the IZ of the next sinus beat.

Similarity could be drawn between the Wenckebach type of conduction in the A-V node associated with A-V nodal re-entry and the Wenckebach-like conduction pattern in the IZ resulting in ventricular re-entry. Thus, the close bipolar recording in figure 14 will closely simulate the His bundle recording during A-V nodal re-entry. However, a recording similar to the composite electrogram during ventricular re-entry that reflects the circuitous pathway of re-entry in the A-V node has not so far been obtained.

Experimental Models for Ventricular Re-entry

The significance of the present experimental model for ventricular re-entry can be appreciated by comparing it to some of the previous models that were used to study re-entry. One of the first significant models for re-entry was that of Schmitt and Erlanger who utilized strips of turtle ventricles depressed by pressure, exposure to cold or to elevated potassium to create slow conduction, one way conduction, and re-entry. As late as 1972, Wit et al., using a modification of the original Schmitt and Erlanger model, depressed conduction in unbranched bundles and closed loops of canine Purkinje fibers by high extracellular K+ and demonstrated the possibility for re-entry. As, WALLACE and Mignone utilized cooling of a discrete area of the canine left ventricle to produce conduction delay and re-entry. On the other hand, Sasyniuk and Mendez utilized two premature beats in close succession to create re-entry in isolated canine papillary muscle — false tendon preparations, presumably by inducing nonuniform shortening of refractoriness.

These models failed to demonstrate the central occurrence in re-entry, the presence of continuous electrical activity that regularly and predictably bridge the entire diastolic interval between the initiating and re-entrant beats as well as between consecutive re-entrant beats. These studies, however, did establish the theoretical basis for re-entry in the form of unidirectional block coupled with critically slow conduction in alternate routes.

The artificial nature of all of these models limits the direct extrapolation of their results to the clinical situation. Furthermore, models of re-entry based on His-Purkinje preparations or Purkinje fiber muscle junctions seem to be conceptually different from the situation of re-entry in ischemic myocardium. These models supposedly create a single re-entrant pathway with a relatively simple geometric outline. Such a situation differs significantly from the pattern of conduction in the IZ with complex functional dissociation of conduction and multiple potentially re-entrant pathways. The latter pattern is probably more akin to re-entry in the A-V node.

In summary, both the experimental model for ventricular re-entrant arrhythmias and the recording technique described in this report offer the most direct expression of re-entry in the intact heart and put this mechanism of abnormal rhythm formation, for the first time, within the reach of systematic electrophysiologic and pharmacologic studies. Some of these studies will be reported in part 2 of this presentation.

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Re-entrant Ventricular Arrhythmias in the Late Myocardial Infarction Period

2. Patterns of Initiation and Termination of Re-entry

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SUMMARY The electrophysiologic mechanisms for the initiation and termination of re-entrant ventricular arrhythmias (RVA) were critically analyzed in dogs 3–7 days following ligation of the anterior descending coronary artery, utilizing direct recordings of the re-entrant pathway (RP) from the epicardial surface of the infarction zone. Re-entry could occur during a regular cardiac rhythm if the heart rate is within the narrow critical range during which conduction in a potentially RP exhibits a Wenckebach-like (W) pattern with a beat-to-beat increment of conduction delay until the activation wavefront is sufficiently delayed to re-excite normal myocardium. If a regular cardiac rhythm is associated with limited conduction delay in a potentially RP, premature beats within a critical range of coupling intervals could result in sufficient conduction delay to induce re-entry. Re-entrant ventricular arrhythmias may be unmasked on abrupt termination of a critical fast rate of cardiac pacing only if pacing was terminated during those beats of a W pattern associated with marked conduction delay in a RP. RVA could be ended by one or more properly timed premature beats that would pre-excite part of the RP. An electrophysiologic mechanism for R-on-T and its relationship to onset of ventricular fibrillation was shown, based on markedly delayed RP conduction of the beat prior to the one apparently coupled to the premature beat.

MOST EXPERIMENTAL MODELS OF VENTRICULAR RE-ENTRY had relatively simple designs.1–4 Clinical studies of ventricular re-entry depend on deductive analysis of clinical records. Even in those clinical studies in which the initiation and termination of ventricular arrhythmias were induced by premature beats with critical coupling intervals,4 re-entry was no more than a speculative etiology. Myocardial infarction represents a highly likely source of re-entrant ventricular arrhythmias. Although most studies of the early phase of ventricular arrhythmias that follow acute ligation of a major coronary artery in the dog have shown some of the basic prerequisites for re-entry in the form of desynchronized slow conduction in ischemic myocardium,5–8 they all fall short of actually documenting the presence of re-entry. This was due, we believe, to the highly dynamic situation following acute ligation of a major coronary artery with constantly changing electrophysiological properties in the ischemic zone. Thus, it is difficult to conduct systematic electrophysiologic studies of the possible re-entrant mechanism under such dynamic conditions. In addition, the recording techniques usually failed to demonstrate the one unequivocal evidence for re-entry, viz: the presence of continuous electrical activity originating from the infarction zone that regularly and predictably bridge the diastolic interval between the re-entrant beat and the preceding impulses, as well as between consecutive re-entrant beats.17

We have recently shown that dogs, three to seven days following ligation of the left anterior descending artery, represent a remarkably stable model for re-entrant ventricular arrhythmias and one in which systematic electro-
Re-entrant ventricular arrhythmias in the late myocardial infarction period. 1. Conduction characteristics in the infarction zone.
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