Monophasic action potential mapping in human subjects with normal electrocardiograms: direct evidence for the genesis of the T wave

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ABSTRACT T wave concordance in the normal human electrocardiogram (ECG) generally is explained by assuming opposite directions of ventricular depolarization and repolarization; however, direct experimental evidence for this hypothesis is lacking. We used a contact electrode catheter to record monophasic action potentials (MAPs) from 54 left ventricular endocardial sites during cardiac catheterization (seven patients) and a new contact electrode probe to record MAPs from 23 epicardial sites during cardiac surgery (three patients). All patients had normal left ventricular funtion and ECGs with concordant T waves. MAP recordings during constant sinus rhythm or right atrial pacing were analyzed for (1) activation time (AT) = earliest QRS deflection to MAP upstroke, (2) action potential duration (APD) = MAP upstroke to 90% repolarization, and (3) repolarization time (RT) = AT plus APD. AT and APD varied by 32 and 64 msec, respectively, over the left ventricular endocardium and by 55 and 73 msec, respectively, over the left ventricular epicardium. On a regional basis, the diaphragmatic and apicoseptal endocardium had the shortest AT and the longest APD, and the anteroapical and posterolateral endocardium had the longest AT and the shortest APD ($p < .05$ to $< .0001$). RT was less heterogeneous than APD, and no significant transventricular gradients of RT were found. In percent of the simultaneously recorded QT interval, epicardial RT ranged from 70.8 to 87.4 (mean 80.7 ± 3.9) and endocardial RT ranged from 80 to 97.8 (mean 87.1 ± 4.4) ($p < .001$). Plotting of APD as a function of AT, independent of the recording site, revealed a close inverse relationship, such that progressively later activation was associated with progressively earlier repolarization . The linear regression slope of this relationship averaged from all 10 hearts was -1.32 ± 0.45 ($r = -.78 \pm .10$). These data suggest a transmural gradient of repolarization, with earlier repolarization occurring at the epicardium. The negative correlation between AT and APD, which was found at both the endocardial and epicardial surface and had an average slope of greater than unity, may further contribute to a positive ventricular gradient and T wave concordance.
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IN THE NORMAL electrocardiogram (ECG), the T wave has the same polarity as the QRS complex, although on a cellular level depolarization and repolarization cause deflections of opposite polarities. This paradox of the T wave concordance in the ECG has been explained by assuming that the repolarization wave travels, at least in some part of the ventricle, in a direction opposite to that of depolarization.[1] This hypothesis requires that some areas of early activation have longer action potentials than do areas excited later.

Direct experimental evidence supporting this hypothesis is scarce. Burgess et al.[2] determined the recovery of excitability at different ventricular sites as an indirect index of local repolarization; they found long functional refractory periods in the endocardium and the apex and short functional refractory periods in the epicardium and the base. Spach and Barr[3] used implanted electrode arrays in dogs to measure the potential distribution during depolarization and repolarization. They found a relative extracellular positivity on the epicardial surface, suggesting earlier repolarization, and a prolonged negativity at the apical free wall, suggesting delayed repolarization. Cohen et al.[4] and Watanabe et al.[5] recorded intracellular action poten-

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tials from small preparations excised from sheep and guinea pig ventricles, respectively. They did not, however, determine the local activation time at these sites before excision and therefore could not define local repolarization time (RT), which is the sum of activation time (AT) and action potential duration (APD). Autenrieth et al.[6] recorded monophasic action potentials (MAPs), using a suction electrode technique, from the epicardium of dog ventricles in situ and found a large dispersion of APD with a trend for later repolarization at the apex than at the base.

Corresponding data from the human ventricle are still lacking because it has not been possible to map the duration and configuration of transmembrane action potentials in the clinical setting. We have developed a new contact electrode technique for endocardial[7] and epicardial[8] mapping of MAPs in vivo and have demonstrated that these MAPs accurately indicate the time of activation and the entire repolarization time course of the transmembrane action potential.[9] In this study, we recorded MAPs and determined local AT, APD, and RT at multiple endocardial and epicardial sites in the human left ventricle. We detected an inverse correlation between AT and APD, which is compatible with a positive ventricular gradient and T wave concordance in the surface ECG.

Methods

Patients. Seven patients referred to the Hospital of the Hannover Medical School underwent endocardial MAP mapping during normal sinus rhythm or during right atrial pacing at a constant rate. The clinical indication for cardiac catheterization was suspected coronary artery disease in five patients and evaluation of aortic valve disease and aortic coarctation, respectively, in the other two patients. Epicardial MAP recordings were obtained in an additional three patients who underwent cardiac surgery for coronary artery bypass grafting. The nine male and one female subjects had a mean age of 49.5 years (range 16 to 61). All had normal PR, QRS, and QT intervals and normal electrical axes with concordant T waves. Resting cardiac function, ventricular dimensions, and motility, as assessed by M mode and two-dimensional echocardiography or ventriculography, were normal; ejection fractions ranged from 55% to 79%. None of the patients received any cardioactive drug regimen in the days before or during cardiac catheterization or surgery. All patients gave written informed consent before the study, which had been approved by the University's Committee on Human Investigation.

Endocardial MAP mapping. Studies were performed with the patient in the nonsedated, postabsorptive state during sinus rhythm. If sinus rate varied by more then 5 beats/min, the heart was paced from the right atrium at the slowest rate required to overdrive the spontaneous rhythm. MAPs were recorded with a contact electrode catheter similar to that described previously.[7] This catheter has two nonpolarizable electrodes, one forming the catheter tip and the other located on the sidewalls 5 mm proximal to the tip. The MAP catheter was inserted percutaneously into the femoral artery and advanced to the left ventricle under fluoroscopic guidance. The left ventricular mapping

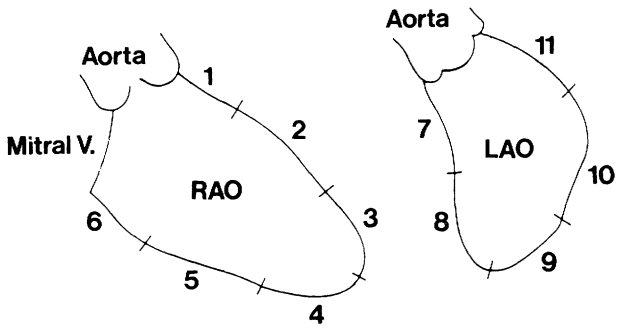

FIGURE 1. Endocardial mapping schema used to allocate MAP recordings to individual segments in the heart. RAO = right anterior oblique projection; LAO = left anterior oblique projection. There were 11 individual segments that were combined to six larger areas as follows: segments 2 and 3 = anteroapical; segment 4 = inferoapical; segment 5 = diaphragmatic; segments 6 and 7 = basoseptal; segment 8 = apicoseptal; segments 9 and 10 = posterolateral. Segments 1 and 11 situated just behind the aortic valve, were difficult to reach; only four endocardial recordings were obtained from these areas, which therefore were not included in the statistical analysis.

scheme used is shown in figure 1. The catheter sites were verified by multiple-plane fluoroscopy. All MAP signals were recorded with a high-impedance, direct-current coupled, differential preamplifier. The preamplified MAP and three standard ECG leads (usually lead II, III, and V_1) were displayed simultaneously on a multichannel recorder and recorded at paper speed of 100 or 250 mm/sec.

Epicardial MAP mapping. Epicardial MAP recordings were obtained during open-chest cardiac surgery just before initiation of cold cardioplegic heart-lung bypass. The device used to record epicardial MAPs is depicted schematically in figure 2. Two nonpolarizable silver—silver chloride electrodes are mounted on the distal end of a ribbonlike bar. The center electrode protrudes to contact the epicardial surface directly, whereas the peripheral (reference) electrode has electrical contact with the heart through a small piece of saline-soaked foam rubber. The ribbon is made from copper-steel alloy that allows it to be bent easily into the curvature required to reach the recording site while maintaining elasticity for stable "spring-loaded" contact of the center electrode with the epicardium. Because of the flatness and changeable curvature of the ribbon, the electrode head can be advanced between pericardium and epicardium to the posterior and inferior aspects of the left ventricle without dislodging the heart from its physiologic position.

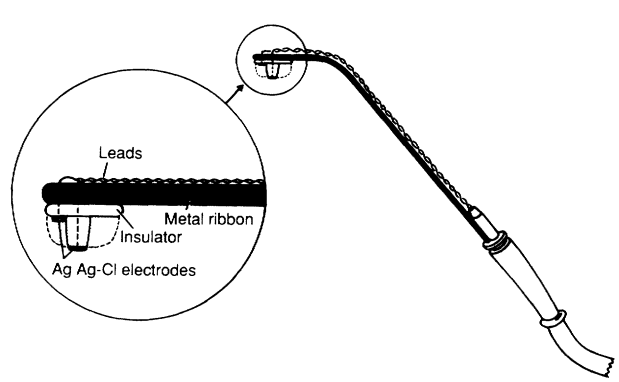

FIGURE 2. Schematic presentation of the contact electrode probe used to generate and record MAPs from the human epicardium during open-chest surgery. Further details in text and in ref. 8.

When the center electrode was pressed slightly against the epicardium, MAPs developed and stabilized within 2 to 6 beats. Recordings were made during stable sinus rhythm or during right atrial pacing at a constant rate. A detailed map of the left ventricular surface was used to identify the location from which each recording was made. MAPs were recorded only from the lateral, posterior, and inferior aspects of the left ventricle. These areas were covered by pericardium or lung tissue and not exposed to the cooling effect of room air. All patients appeared to be free from subepicardial ischemia at the recording sites at the time of study, as judged by previously identified indexes of ischemia in the MAP.[8]

Data analysis. Because of the sequential spread of excitation, activation at different left ventricular recording sites does not occur simultaneously but with varying delay. The delay from the earliest QRS deflection (in any lead) to the rapid upstroke of the MAP was defined as the AT. APD was the duration of the MAP from the upstroke to 90% repolarization.[7] RT was the time from the onset of the QRS complex to 90% repolarization at the recording site (AT + APD) (figure 3). The accuracy of the measured intervals was within 5 msec, as determined by repeated measurements made by two different observers. Only measurements made during regular sinus rhythm (± 5 beats/min) or during regular atrial pacing were analyzed. At least five consecutive MAP recordings were assessed at each site, and intervals at a single site were found reproducible with less than 1% variation. The maximum difference between all recordings in each patient, averaged for the patient group, was used as a measure of dispersion.[10] To examine the relationship between the intracardiac recordings and the body surface ECG, AT, APD, and RT were also evaluated in percent of the simultaneously recorded QRS and QT durations, respectively. Unpaired Student's t tests and Pearson's correlation coefficients were used to evaluate the significance of all results.

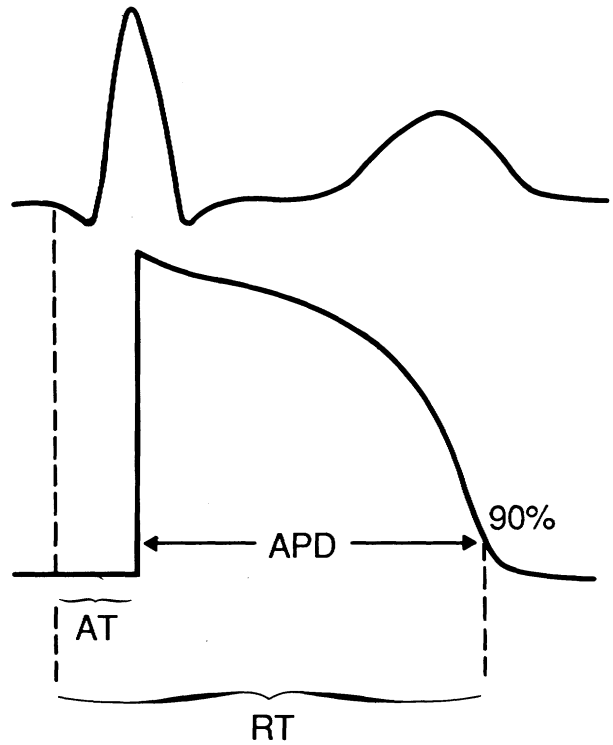

FIGURE 3. Method used to analyze local ventricular AT, APD, and RT. Details in text.

Results

In the seven patients undergoing cardiac catheterization, MAP recordings were obtained from five to 11 (mean 7.7 ± 1.8) different left ventricular endocardial sites and in one patient from an additional eight right ventricular endocardial sites. In the three patients undergoing cardiac surgery, MAPs were recorded from five to 10 different left ventricular sites. All MAPs had smooth configurations and stable amplitudes ranging from approximately 20 to 40 mV.

Endocardial recordings. Data from an individual patient are shown in figure 4. Values for AT, APD, and RT showed a relatively large variability. Recordings at the apical region (segment 3 and 4) include both early and late activation and shorter and longer APD. Differences in AT and APD within these apical regions were nearly as large as those along the apicobasal axis. Despite this variability of AT and APD within the left ventricular endocardium, it was noted consistently that sites with early activation had longer APDs than sites activated later. Because of this inverse relationship of AT and APD, RT (the sum of AT and APD) was less heterogeneous than APD (figure 4). Figure 5 further exemplifies this finding by two sets of original MAP recordings, each comprising one with early and late AT.

Data from all seven patients who underwent catheterization are listed in tables 1 and 2. Table 1 lists the range of AT, APD, and RT for each individual patient and the average range (dispersion) of these indexes for the patient group as a whole. With respect to the simultaneously recorded surface ECG, left ventricular endocardial ATs ranged from 0 to 34.7% of the QRS duration and thus fell within the first third of global ventricular activation. AT varied by up to 32 msec in individual patients, with an average dispersion of 24.9 ± 6.1 msec. APD varied by up to 64 msec in individual patients, with an average dispersion of 41.4 ± 14.6 msec. Similar to the individual data presented in figure 4, endocardial RT in the entire group was less heterogenous than APD. The average dispersion of RT was 26.4 ± 12.0 msec. This was significantly less than the dispersion of APD ($p < .05$) (table 1).

Table 2 gives the comparative analysis of AT, APD, and RT for the six different left ventricular endocardial regions described in figure 1. The shortest endocardial ATs were measured at the diaphragmatic and apicoseptal region. Anteroapical and posterolateral regions had relatively late activation, and basoseptal and inferoapical regions had intermediate ATs. Because different patients had different heart rates, APDs and RTs

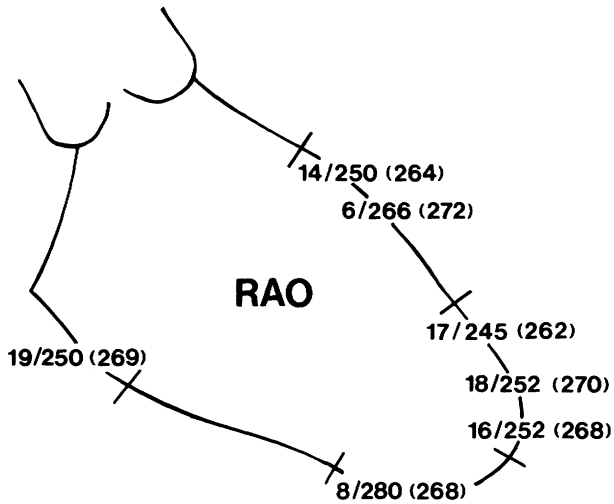

FIGURE 4. Numerical data from endocardial MAP recordings in an individual patient (No. 5). The left ventricular mapping scheme is the same as in figure 1. AT and APD separated by slash, RT in parentheses (all msec).

were expressed in percent of the longest value measured in each patient. Significant differences in average APD were found between the diaphragmatic and apicoseptal areas, which had the longest average APD, and the anteroapical and posterolateral areas, which had the shortest average APD. Between these areas, average AT was also significantly different, in a direction opposite to that of APD. RT did not demonstrate significant differences among the six left ventricular endocardial regions; there was a trend for later repolarization only in the diaphragmatic and apicoseptal regions as compared with the other regions (table 2). This is consistent with the findings that regions with shorter ATs have longer APDs and vice versa; the reciprocal relationship between AT and APD tends to synchronize repolarization in the ventricle. In one patient, recordings were obtained from both the left and right ventricles. Average ATs were longer and average APDs shorter in the right as compared with the left ventricle.

Regional APD and RT were also compared by expressing them in percent of the simultaneously recorded QT interval. The results from this type of normalization confirmed those described above.

Epicardial recordings. ATs of left ventricular epicardial recordings in three patients ranged from 25 to 80 msec (table 1) or from 26.3% to 64.8% of the simultaneous QRS duration. The degree of heterogeneity of epicardial APD was similar to that of endocardial ATs, with a maximum difference of 73 msec between the shortest and longest APD in one patient (table 1). Because of the limited sample size of epicardial recordings, a statistical comparison of different epicardial regions was not performed.

To compare epicardial and endocardial RT, measurements from the three surgical patients and the seven patients undergoing cardiac catheterization were expressed in percent of the simultaneously recorded QT interval. Epicardial RTs ranged from 70.8% to 87.4% (mean 80.7 ± 3.9%) of the QT interval, which was markedly shorter than endocardial RTs, ranging from 80% to 97.8% (mean 87.1 ± 4.4%) of the QT interval ($p < .001$). Thus, based on this global comparison, the epicardium had later activation but repolarized earlier than the endocardium.

Relation between AT and APD. To examine the relation between AT and APD independently of the area, we plotted all APD values as a function of AT, regardless of the site from which the recordings were obtained. Linear regression analysis of these data showed a significant inverse correlation between AT and APD, such that progressively later activation was associated with progressively shorter APD (figure 6 and table 3). The average slope of the regression lines, derived from the seven endocardial and three epicardial data sets, was −1.32. This slope, which is greater than negative unity, indicates that the increase in AT along the activation pathway was more than compensated by a shortening of the action potential.

Discussion

In this study, we recorded MAPs from multiple endocardial and epicardial sites in the human ventricle in situ by means of the contact electrode technique.[7, 8] The contact electrode has a tip diameter of 1 mm and

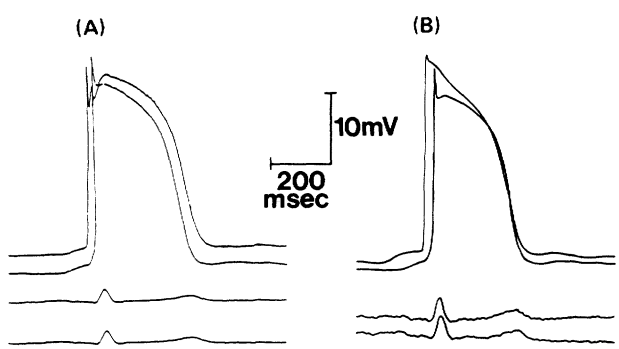

FIGURE 5. Original MAP recordings from left ventricular endocardium exemplifying the relation between AT and APD. Two sets of recordings (each set from a different patient) were superimposed so that the concomitant QRS complexes align. *A*, One MAP (recorded from the left ventricular mid septum) was activated 34 msec before the other (recorded from the anterior wall), yet repolarized after the MAP with later activation; *B*, One MAP (apex) was activated 42 msec before the other (posterolateral), yet repolarized at nearly the same time.

TABLE 1
Range of left ventricular AT, APD, and RT in 10 patients

Patient	n	AT (msec)	APD (msec)	RT (msec)	HR (beats/min)
Endocardial					
1	7	3–34	271–311	300–315	85
2	7	12–42	286–347	318–362	76
3	8	0–22	277–317	298–318	95
3 RV[A]	8	10–39	262–286	282–309	95
4	5	0–25	306–336	306–330	72
5	7	6–19	245–266	262–272	99
6	9	0–32	239–273	252–275	101
7	11	7–28	284–348	312–358	64
Mean ± SD[B]		24.9 ± 6.1	41.4 ± 14.6	26.4 ± 12.0	
Epicardial					
8	5	25–49	247–320	296–354	97
9	8	37–68	261–306	322–355	76
10	10	50–80	270–330	348–380	81
Mean ± SD		28.4 ± 3.8	59.3 ± 11.4	41.0 ± 12.0	

HR = heart rate during the recording period.

[A]Patient 3 had an additional eight recordings from right ventricular (RV) endocardium (not included in mean values).

[B]The average of the range of values for each patient in the group, a measure of dispersion.

thus samples the electrical activity of probably several hundred cells. Despite this local averaging effect, the contact electrode MAP reproduces the AT and the APD of adjacent transmembrane potentials with high accuracy.[9] In contrast to the intracellular microelectrode, the contact electrode technique produces stable recordings in the beating heart and is safely employed in the clinical setting.[7] These features combined make the contact electrode MAP a unique tool for measuring both the AT and the APD at various sites in the human ventricle. The sum of AT and APD at an individual site yields the local RT, which can be used to map the sequence of ventricular repolarization with respect to ventricular activation. We will first discuss our results individually for each index and then relate them to the electrocardiographic T wave.

AT. Earliest endocardial activation occurred in the diaphragmatic, apicoseptal, and basoseptal regions. This agrees well with data previously obtained in resuscitated perfused isolated human hearts[11] and, more recently, in normal human hearts in situ.[12] Durrer et al.[11] noticed the latest activation (above 30 msec) of the left ventricular endocardium in the posterobasal region, and we also measured only relatively long ATs

TABLE 2
Average AT, APD, and RT in six left ventricular endocardial regions and the right ventricle[A]

Region	n	AT (msec)	Signif. diff. from region	APD (%)	Signif. diff. from region	RT (%)
D	7	6.4 ± 5.0	AAp[B],PL[B]	96.3 ± 3.1	AAp[D],PL[D]	96.8 ± 2.6
ApS	10	8.2 ± 8.4	AAp[C],PL[C]	95.7 ± 4.8	AAp[D],PL[D]	97.1 ± 3.4
BS	8	10.5 ± 3.7	AAp[C],PL[C]	95.0 ± 2.8	—	95.8 ± 3.0
IAp	11	11.9 ± 8.2	AAp[D],PL[D]	93.9 ± 4.1	—	95.9 ± 2.4
AAp	17	19.9 ± 8.0	D[B],ApS[C]	91.3 ± 5.3	D[D],ApS[D]	95.6 ± 4.0
PL	19	20.4 ± 8.4	D[B],ApS[C]	91.8 ± 5.5	D[D],ApS[D]	95.1 ± 4.3
RV	8	25.9 ± 9.8	n/a	86.5 ± 2.4	n/a	94.3 ± 2.9

Data expressed as mean ± SD.

D = diaphragmatic; ApS = apicoseptal; BS = basoseptal; IAp = inferoapical; AAp = anteroapical; PL = posterolateral; RV = right ventricular.

[A]Data are summarized from all seven patients with endocardial recordings. To eliminate the effect of heart rate, APD and RT are expressed as percent of the maximal value in a given patient.

[B]$p < .0001$; [C]$p < .005$; [D]$p < .05$. There were no significant differences in average RT among any of the six left ventricular regions.

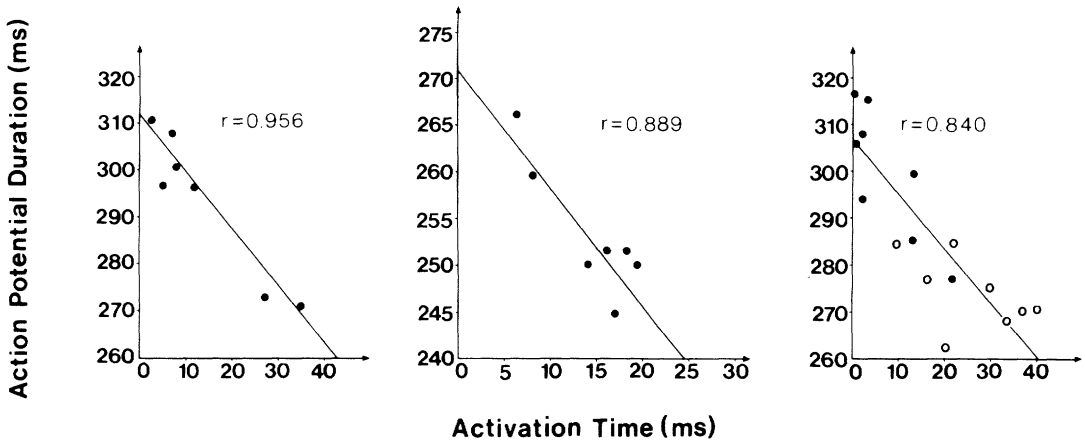

FIGURE 6. Relationship between AT and APD demonstrated by linear regression analysis of data from three representative patients. Open circles in right panel denote right ventricular data.

(above 20 msec) in the posterolateral endocardium.

Epicardial ATs, measured in three patients' left ventricles, ranged from 25 to 80 msec, which was considerably greater than the range of endocardial ATs. This agrees with measurements in isolated human hearts[11] in which epicardial ATs ranged from 40 to 70 msec with early breakthrough points at 20 to 25 msec.

APD. Previous animal studies have suggested several partly conflicting geographic gradients of APD. Cohen et al.[4] using microelectrode records from excised tissue of sheep ventricle, suggested a shortening of APD from the base to the apex. Autenrieth et al.,[6] who used epicardial suction-electrode recordings in intact dog ventricles, and Watanabe et al.,[5] who recorded intracellular potentials in partially dissected guinea pig ventricles, reported action potential shortening from the apex to the base. Watanabe et al.[5] found a significantly shorter average APD at the lateral free wall as compared with the septum and papillary muscles.

Our data do not verify these gradients for the human left ventricular endocardium. Although our sample size was limited, a uniform gradient in, for instance, an apicobasal direction, should not have gone undetected. We instead noted that APDs were markedly disparate, even within a given region. This agrees with results of previous animal investigations, which indicated that inhomogeneities of APD or refractory periods occur within very small distances over the entire surface of the ventricle.[2, 5, 6, 13, 14] In our study, the longest average APD was measured in the septal and diaphragmatic area and the shortest at anteroapical and posterolateral sites. There are no endocardial data from a large mammalian species with which to compare this gradient.

RT. The T wave is a reflection of regional differences in RT, not APD. Ventricular repolarization gradients deduced from regional differences in APD[4, 5, 10] may be invalid because they ignore the varying delay with which different sites are activated in the whole ventricle. In this study, the RT, i.e., the interval with which a given ventricular site repolarizes after the earliest deflection of the QRS complex, was obtained by adding the APD to the corresponding AT. RT was found to be more evenly distributed over the left ventricular endocardium than APD; the average dispersion of repolarization, estimated from the RT range in all patients, was significantly smaller than the average dispersion of APD. In contrast to APD, we could not detect statistically significant differences in mean RT among the six endocardial regions; there was only a trend of longer RTs in the diaphragmatic and apicoseptal regions as compared with the other regions.

Endocardial and epicardial RT, expressed in percent

TABLE 3
Data from linear regression analysis for the relationship between AT and APD in all patients

Patient	s slope	r	p value
1	−1.27	−.96	<.0001
2	−1.48	−.76	<.01
3	−1.16	−.84	<.0001
4	−0.83	−.66	<.05
5	−1.24	−.89	<.0001
6	−0.82	−.73	<.005
7	−2.11	−.79	<.0001
8[A]	−2.00	−.67	NS
9[A]	−0.90	−.65	<.05
10[A]	−1.43	−.83	<.005
Mean	−1.32	−0.78	
± SD	0.45	0.10	

[A]MAP recordings taken from the left ventricular epicardium; all others from left ventricular endocardium and patient 3 also from right ventricular endocardium.

of the simultaneously recorded QT interval, showed that in the sampled areas average epicardial RTs were significantly shorter than endocardial RTs. This agrees with measurements of refractory periods[14, 15] and extracellular field potentials[3] in canine hearts and supports the concept of a transmural gradient of repolarization that may contribute to the T wave genesis.

Watanabe et al.[5] found endocardial and epicardial APDs in guinea pig ventricles too short to account for the entire T wave duration and postulated longer APDs in the intramural myocardium. In our study, the longest endocardial RTs were nearly as long (97.8%) as the simultaneously recorded QT interval. Thus, in keeping with previous canine data,[6] there is no need to assume longer action potentials in the intramural myocardium than on either its endocardial or epicardial surface.

Relation between AT and APD. We found a close negative correlation between AT and APD, such that sites activated early had longer action potentials than did sites activated late. The dependence of APD on AT appeared independent of the location in the heart from which the measurements were obtained. This raises the intriguing question of whether regional differences in APD are caused by intrinsic electrophysiologic differences between myocardial cells or whether they are secondary to the sequence of activation. Does a myocardial cell "know" when to repolarize, just because of its site within the ventricle, or does an overriding mechanism "tell" the cell when to repolarize?

One mechanism that could relate APD to activation sequence is electrotonic interaction. Studies in isolated ventricular muscle and Purkinje fiber preparations have shown that repolarizing (anodal) currents applied during repolarization shorten the action potential[16–18] and that depolarizing (cathodal) currents applied during repolarization prolong the action potential.[17] As Hoffman[19] suggested, "During the cycle of ventricular depolarization and repolarization, electrotonic current from the area to be excited last may retard repolarization of areas excited earlier in the activation sequence, and current from the first area to repolarize may speed repolarization in areas not yet repolarized." Evidence for electrotonic interaction in the canine heart in situ was obtained by Toyoshima and Burgess,[20] who found that recovery of excitability was delayed when activation was initiated at or near the site at which it was measured, as compared with stimulation at a distant site. Autenrieth et al.[6] and Toyoshima et al.[21] recorded MAPs with suction electrodes from the canine epicardium and also noticed that action potentials activated earlier had longer durations than did those activated later.

Several limitations apply to this clinical study. (1) Because of T wave results from many simultaneous voltage gradients during repolarizaiton, even a relatively small net gradient in a predominant direction may determine the polarity of the T wave.[1] It is possible that a larger sample size would have revealed further endocardial or epicardial repolarization gradients. Also, endocardial areas located near the aortic valve were difficult to reach and are underrepresented in this study. (2) We pooled data from different patients with different heart rates by expressing APD and RT as a percentage of the longest APD sampled in each patient. Although the range of APDs recorded per patient was large, we may have missed the longest APD present in a given patient. Also, it cannot be excluded that heart rate alters APD nonuniformly over the heart. These factors may have increased the variability of APD and RT in our analysis of the patient group as a whole but not the dispersion found in an individual patient. We tested our method of normalization by expressing all data also as a percentage of the simultaneously recorded QT interval and obtained essentially identical results. (3) Local AT was determined as the interval between the onset of QRS and the MAP upstroke. Because of the limited number of ECG leads recorded, it is possible that we have missed the very earliest beginning of ventricular activation. However, because all measurements were referenced to the earliest QRS deflection in the same lead, the relationship between AT and APD or RT, respectively, should not be affected. (4) We do not know to what extent the different conditions in patients undergoing cardiac catheterization and open-chest surgery influence the quantitative comparison of endocardial and epicardial measurements. By recording epicardial MAPs only from areas covered by pericardium or lung tissue, we attempted to minimize the effect of cooling on the APD. If cooling did occur, it should have resulted in an underestimation of the transmural repolarization gradient found in this study.

T wave concordance. A model often used to explain the T wave concordance of the normal ECG is based on two assumptions: (1) activation and repolarization of the ventricle both have relatively uniform and closed wavefronts, and (2) both wavefronts propagate in opposite directions. Our data from endocardial and epicardial measurements, although obtained in different patients, strongly support for the human heart the concept of a transmural gradient of repolarization with a direction opposite to that of depolarization. A transventricular gradient of repolarization was not detected in this study. This may have been a result of the limited

sample size or of nonuniformity of the repolarization wavefront. In the canine heart, the *activation* wavefront has been shown to follow a very complex, nonuniform pattern.[22] Because of the close (inverse) coupling of repolarization and activation, one might expect a similarly complex *repolarization* wavefront. The relatively large variability of RT within and among different ventricular regions in previous animal experiments[5, 6, 14] and our human study is consistent with this hypothesis. Electric field mapping in the canine heart demonstrated that transmural gradients are the probable cause of T waves during sinus rhythm but transventricular gradients are responsible during ectopic stimulation.[23] Regional gradients may therefore be expected to be either absent or less important during sinus rhythm. The inverse correlation between AT and APD, noticed at both the endocardial and epicardial surface independent of the area, still supports the concept of opposite directions of depolarization and repolarization. The linear regression between AT and APD had an average slope of greater than -1, and this may contribute to a net ventricular gradient and T wave concordance even in the absence of continuous depolarization and repolarization wavefronts.

The inverse correlation between AT and APD not only helps to explain the genesis of the concordant T wave, but also has implications for arrhythmogenesis. Dispersion of ventricular repolarization predisposes to reentrant excitations.[10] Progressive action potential shortening with progressively later activation, previously recognized in the canine heart[2, 24] and corroborated in this human study, tends to synchronize ventricular repolarization. This may be an important physiologic mechanism in the prevention of ventricular reentrant arrhythmias.

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