A Dynamic Electrical Record of the Pathway of Human His Bundle Activation from Surface Mapping

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SUMMARY  Body surface potential maps of human His bundle activity have been difficult to produce for two reasons: (1) The peak surface potentials are often less than 5 μV, and (2) the simultaneous atrial repolarization potentials frequently exceed 100 μV. We have therefore amplified surface signals 25 times the standard gain of 1000, and then removed by cross-correlation the static pattern of atrial repolarization for serial 1-msec maps of the P-R segment in five normal men. A consistent finding emerged: a positive anterior chest peak appeared 40 msec before QRS onset, and then—within 10 msec—spread out into a long, low transverse mound before disappearing in 5 more msec. The map data were analytically converted to serial electrical sources: the center of electrical activity moved first slightly down, then directly forward, before retracing its path and disappearing. The retrace and accompanying surface spread-out strongly suggests diverging dipolar sources. Thus the data fit a simple heart source which moves anteriorly and then breaks into two (right and left)—as expected from activation of the bundle of His and its bifurcation into left and right bundle branches.

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BY direct recording from the exposed endocardial surface on the experimental animal, observers have demonstrated that, whereas the surface electrocardiographic P-R segment appeared relatively silent, several elements of myocardium were, nevertheless, electrically active in the experimental animal (Alanis et al., 1958; Hoffman et al., 1960). In 1973 and 1974, two groups of investigators independently reported recovery of signals in high-gain body surface electrocardiograms coincident in timing with the His bundle deflection recorded from intracardiac electrodes (Scherlag et al., 1968; Berbari et al., 1973, 1975; Flowers and Horan, 1973; Flowers et al., 1974). Pharmacological interventions designed to vary the timing of the His deflection with respect to the preceding atrial signal or the succeeding ventricular signal affected the putative surface deflection in exactly the same manner, thus strongly suggesting that the surface signal actually was caused by the activation of the bundle of His or its proximal branches.

This report describes aspects of the body surface potential distribution during the P-R segment of the human electrocardiogram. A stationary pattern attributed to atrial repolarization characterized most of the interval, but between 45 and 25 msec before the onset of ventricular activation a distinct but lower amplitude pattern appeared, then disappeared, prior to ventricular activation. Upon analytic reduction of this second, or superimposed, surface map pattern to serial equivalent dipole representation, we found a geometric path of the electrical heart center during the critical 10- to 15-msec period corresponding reasonably to the anatomic course of the common bundle of His and its proximal upper branches.

Methods

Five healthy men between the age of 15 and 35 years had been studied at the time of this writing. The method used—which records from 142 surface sites on the human body surface, averages and collates the data into serial body surface potential maps—was first described by Eddleman et al. in 1968. The present recording technique was modified only in that seven high-gain, low-noise Princeton Applied Research preamplifiers and accompanying isolation units were used to obtain amplification 25 times greater than that previously attained—or a total gain of 25,000. The bandwidth employed was between 0.1 and 3000 Hz.

Signal-averaging of 50 consecutive beats was performed with a constant eighth standard gain electrocardiographic lead (from an electrode in approximately the V5 position) as the source for a trigger signal. The QRS waveform after shaping and triggering produced a fiducial mark that varied less than 1.5 msec from beat to beat. We did not attempt to estimate the actual reduction of noise as compared to signal because part of the signal was off-scale. Using a sampling interval of 1 msec, we found that the maximum successive msec-to-msec varia-
tion in potential during the P-R segment shown in Figure 2 was 28.4 μV before averaging, and 1.6 μV after. The 20-msec segment immediately preceding the onset of the P-wave also was examined for noise reduction on the assumption that this represented a period of electrical silence. We made the assumption that the signal is zero. The rms estimate of noise before averaging was 7.4 μV and after was 1.7 μV.

The digital techniques of subtraction of one body surface distribution from another also have been well-described for the purpose of other analysis (Horan and Flowers, 1974; McLaughlin et al., 1974; Flowers et al., 1976). In this study, the purposes were both the basic one of establishing "zero" reference and that of removing interfering signal. Zero reference was designated as the mean potential pattern for the 20-msec interval just preceding the onset of the P-wave and thus completely after the U-wave. This approximates the period of cardiac electrical silence, and all the data were therefore reset to this reference (Spach et al., 1979) (i.e., from each potential value in the map of the 750 successive msec maps of the heart interval, we subtracted the respective mean potential value determined for "silence").

Inspection of the serial maps from late P to early QRS made us consider the following assumptions (Fig. 1) upon which later data processing was based:

1. Surface maps during early PR segment probably were the result of both late atrial activation and early atrial repolarization;
2. Maps at the time of maximum rapid change probably were caused by the combined effect of common bundle firing and continued atrial repolarization;
3. Maps late in the P-R segment probably were the result of both the large steady pattern of atrial repolarization and the small, rapidly changing pattern of activation of distal bundle branch and Purkinje network. Therefore, as shown in Figure 2, we manually selected a segment in late P-R—after the period of acute change in pattern—usually beginning 30 or 35 msec before QRS onset and ending at least 5 msec prior to any ventricular activity. By displaying the rms value for each instantaneous map (defined as $\sqrt{\sum a^2/n}$ where a is the instantaneous potential value at each electrode site and n is the number of sites) in sequence, we could select a 10- to 30-msec time segment late in the P-R when there was very little serial change in the rms value. We averaged the map pattern during this segment of time. Thus the resulting mean Ta map was constructed from the mean potential at each electrode site during the selected interval. It was our expectation that the highly variable effect of activation of the distal branch and Purkinje network would be cancelled and the essential pattern of atrial repolarization would be preserved in the mean Ta map.

It was necessary to take into account the varying amplitude (rms value) of the serial P-R segment maps when we subtracted the Ta map pattern present. To find the amplitude or scale of the Ta map pattern imbedded in an instantaneous map, we determined the correlation between the observed map pattern and the mean Ta map pattern. Thus, if, for a given msec, the potential at each of the 142 electrode sites were b and the corresponding mean Ta potential were a, the correlation coefficient is $\Sigma ab/\sqrt{\Sigma a^2 \Sigma b^2}$. Taking into account the relative amplitudes, the gain or scaling factor $g = \Sigma ab/\Sigma a^2$. With this factor g, we multiplied each Ta map value by the corresponding map value b. This gave us a new calculated value for each electrode site according to the subtraction, $v = b - ga$. The resulting corrected maps were labeled "variance maps" or maps of instantaneous variation from the mean pattern of atrial repolarization. Figure 2 shows selected instants from the application of this process.

The estimation of dipole and quadripole components by numerical approximation of the surface integration (Gabor and Nelson, 1954) was performed by applying the dipole shift equations (Brody, 1954; Geselowitz, 1960; Brody et al., 1973; Horan et al., 1976) to the 142 electrode positions specified for an idealized average human torso (Horan et al., 1980). The equivalent dipole location for each serial map distribution was determined by solving the simultaneous quadripole equations (Gabor and Nelson, 1954; Brody, 1954; Geselowitz, 1960).
RESULTS

Figure 2 illustrates both the subtractive process and its result in a healthy 35-year-old man. The findings are representative of the group (see Table 1). The waveforms shown in Figure 2 are from a single electrode site near the manubrium. The top waveform resulted from digital averaging; data points are separated by 1-msec intervals. The vertical lines show the instant at which the maps were made for the successive sets A, B, and C. The bold line segment shown during late P-R represents the epoch for averaging for Ta effect (between 39 and 7 msec before QRS onset). The middle map in each set is the mean Ta pattern. Note that, while the pattern is constant, the gain or amplitude has been varied according to the result of the correlation calculation. The Ta maps of two subjects were strikingly similar in that the chest appeared divided into interdigitating vertical bands of negativity and positivity, as in Figure 2. For the other three subjects, the Ta maps were dipolar in pattern with the left hemithorax negative and the right positive. In the bottom trace and map, the Ta effect has been removed (by correlation and subtraction across the whole map pattern). The distinct deflection at instants A and B was interpreted by us in the raw
data as surface evidence of bundle or bundle branch activation, and remained after subtraction of the mean Ta combination. At many other electrode sites, the suspected His deflections were small, or not well seen, so that they did not form a coherent picture in the presence of the dominant atrial repolarization pattern.

Figure 3 presents four isometric map projections of body surface potential in a 24-year-old man. The lower plane is zero-baseline and the upper plane represents a positive 5-μV deflection. The upper border of each map represents the potential around the upper chest at the manubrial level; the vertical midline of the map indicates the sternum; the respective right and left midaxillary lines are labeled in the fourth panel. The upper left hand map represents the average Ta map effect. Then successive maps of potential distribution after extraction of the Ta pattern are illustrated for instants, respectively, 40, 30, and 20 msec before QRS onset. Note that in the earliest pattern (~40 msec), one peak dominated, but 10 msec later, the region of positivity was pulled into a long left-to-right-oriented mound. At ~20 msec, only minor departure from the extracted basic Ta remained.

Figure 4 shows the result of reducing the successive map patterns during the P-R segment into equivalent dipole format. Serial dipole location is shown for right sagittal and frontal plane projections. The example shown here was typical for the group. The patterns in the right sagittal plane were consistent: in each instance, a serial path was found that ran downward from “late atrial” sites, then forward, and finally backward before disappearing. The “back track” for each was slightly more superior anatomically than the forward movement. Variance maps during early P-R for the group were remarkably similar: during the time of forward dipole movement, there was an anterior peak of positivity; during the back track, a spreading mound—usually elongated horizontally—but in one subject the elongation was almost vertical.

### Discussion

The assumptions underlying the technique of forming the variance map by subtracting out whatever correlates mathematically with the mean atrial repolarization pattern constitutes an important set of limitations. First, is the atrial repolarization pattern stable or stationary? The theoretically desirable and appropriate electrical heart sources with which to predict body surface potentials are the internal ion flows across gap junctions (Horan and Flowers, 1980), but direct experimental determination of these sources on a large scale is impractical and the experimenter instead must obtain the more indirect measurement of the return current outside the cells (Spach et al., 1969). However, inspection of serial maps in late P-R consistently showed very little change in amplitude and even less in pattern. Second, is the pattern contaminated by other information or noise? Because of this question, we avoided including early P-R maps that we felt were likely to include effects from the very last bits of atrial activation, and we averaged to reduce noise in the 10 to 20 maps available in the late “clear” period. However, this period contains the effects of the activation of the distal His-Purkinje network and, indeed, it has been suggested that the latter may generate a highly distinctive ramp-like signal which begins at about 40 msec before QRS and which crescendos into the ensuing QRS complex.

### Table 1: Serial P-R Map Measurements in Five Men

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>P-R segment Duration (msec)</th>
<th>Averaging interval Duration (msec)</th>
<th>Averaging interval Onset/offset (msec)</th>
<th>g range</th>
<th>Ta map, spatial rms (μV)</th>
<th>Distinct variance pattern sequence Duration (msec)</th>
<th>Distinct variance pattern sequence Onset/offset (msec)</th>
<th>Distinct variance pattern sequence g range</th>
<th>Distinct variance pattern sequence Peak spatial rms (μV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>0.01 to 1.12</td>
<td>33</td>
<td>−39/−7</td>
<td>0.72 to 1.12</td>
<td>21</td>
<td>−45/−25</td>
<td>0.25</td>
<td>0.42</td>
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<tr>
<td>2</td>
<td>70</td>
<td>0.80 to 6.46</td>
<td>25</td>
<td>−30/−6</td>
<td>0.81 to 1.40</td>
<td>19</td>
<td>−45/−27</td>
<td>0.52</td>
<td>0.79</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>0.04 to 9.24</td>
<td>20</td>
<td>−24/−5</td>
<td>0.78 to 1.37</td>
<td>17</td>
<td>−51/−35</td>
<td>0.54</td>
<td>0.32</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>0.00 to 3.44</td>
<td>29</td>
<td>−35/−8</td>
<td>0.39 to 2.40</td>
<td>18</td>
<td>−66/−49</td>
<td>0.23</td>
<td>0.61</td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>0.05 to 1.55</td>
<td>24</td>
<td>−28/−5</td>
<td>0.50 to 1.55</td>
<td>21</td>
<td>−51/−30</td>
<td>0.52</td>
<td>1.17</td>
</tr>
</tbody>
</table>
FIGURE 3  A: Sample isometric projection map patterns found during the P-R interval in a normal 24-year-old man. The first pattern (upper left) represents the basic mean derived by averaging maps during the 11-msec interval beginning at 26 msec before onset of QRS. The mean Ta pattern has been subtracted from the raw data to reveal the three succeeding patterns. The second map (upper right) shows a prominent high left anterior peak of positivity at the expected time of early His bundle activation; the second pattern (lower left) later when the positivity has pulled out into a long left-to-right mound suggesting separate firing of right and left branches; the third pattern (lower right) late in the PR interval showing little residual after removal of the Ta pattern. Vertical chest lines are labeled in the lower right map; VL for vertebral, R for right axillary, S for sternal, and L for left axillary.

(Berbari et al., 1979). Again, little detectable serial change suggested to us that the distal network effect probably was diffuse and therefore producing a rapidly changing higher-order-than-dipolar surface pattern of low amplitude indistinguishable from noise. (Any stationary pattern would have included with the mean Ta pattern and also extracted.) Finally, are the “real” His bundle surface patterns orthogonal to the mean Ta pattern? We do not know. The variance map, we believe, represents that portion of the electrical activity during the time of bundle activation which is orthogonal to the mean Ta wave. However, we cannot be certain what amount of the original was that fortuitously produced a similar (correlated) potential pattern and therefore was removed by the extraction process.

We believe that the pattern of anterior movement of the electrical heart center followed by progressive “back tracking” during the P-R segment is consistent both with the anatomy of the bundle and its branches and with dipole theory (Horan and Flowers, 1972). When the physiological source is dipole-like in compactness, the surface integration identifies moment and location rather closely. However, when the source is two separate and divergent dipoles, as in the case of the diverging left and right bundle branch, the equivalent dipole is identified as one with an orientation intermediate between the two and with a location deeper into the interior of the conducting medium than the actual sources. Thus, it should be expected that a dipolar source traveling down the common bundle would be localized accurately, but when the sources “split” to follow the right and left branches, the equivalent dipole would be represented as still oriented along the “axis” of the common bundle but now “backing away” from the surface and into the interior—thus appearing almost to back up along the common bundle pathway (compare Figs. 4 and 5).

The backing-up phenomenon can be predicted directly from known dipolar sources by the dipole shift equations (Brody, 1954; Gabor and Nelson, 1954; Geselowitz, 1960; Brody et al., 1973; Horan et al., 1976), or indirectly by calculating the surface effect on a surrounding surface (sphere or torso) from the dipole sources and then reducing the surface potential pattern to equivalent dipole location or moment. In either event, the result is the same. This effect may be appreciated intuitively by examining Figure 5 (for which we utilized the direct calculation). When the two input dipoles are nearly
identical (instant 1) in location and moment, they add, and the effect is that of a simple 2-pole surface pattern potential positive in front of the dipole and negative behind the source, with the surface clue to location expressed as a peaking or relative concentration on the nearer side. When the two input dipoles diverge (instant 8), the positivities in front of each become separated on the surface so that a mean positive value running through the peaks is relatively low in amplitude. However, the combined effect of the dipole tails is a concentration of negativity on the opposite boundary wall suggesting greater "nearness" of the single equivalent dipole to the opposite wall than the two separate sources dipoles actually possess. When the calculation for a single equivalent dipole is made, the positive mounds are averaged down and the negative concentration is credited to the relatively posterior equivalent dipole.

Although there is rough correspondence between the length of the initial limb (Fig. 4) and the length of the common bundle (Fig. 6), the serial location of the moving equivalent dipole is, of course, not the literal bundle pathway. It is more suggestive or representative in nature than that, because certain obvious simplifications have taken place in the inverse process: the calculation approximates integration by summing over a simple 142-element surface and assumes a homogeneous medium. This simplicity contrasts with the complexity which, in life, formed the surface potential pattern; however, if we could actually follow the firing of the bundle of His along its precise coordinates and take into account the multiple inhomogeneities through which the electrical signal must pass and—finally—specify the boundaries with far greater detail, we could predict the surface pattern with exactness. The reverse calculation based on a limited surface sample (i.e., an idealized stylized surface and an uncomplicated medium) does not reproduce the original anatomic pathway, but the results that we have obtained show a configuration consistent with a tiny electrical source following a short anteriorly directed course and then bifurcating to the left and right.

It may be reasonably argued that, even within the first centimeter after bifurcation, the division between right and left bundle is not equal in tissue mass and the effect should be dominated by the left-sided activation. However, the diagram in Figure 6 (following the careful histological study of James, 1961) suggests that a "double divergence" may be at work: the left bundle branch itself quickly diverges into a diffuse radiation in a plane diverging from the single strand of the right bundle branch. The net effect of the many dipoles of the left bundle branch fan may be considered a single equivalent dipole, reduced in amplitude by the divergence effect toward a magnitude more nearly equal to that of the simultaneous single right branch dipole. Then the total effect or final equivalent dipole would be
FIGURE 6  Diagram of the path of the moving dipole superimposed on a similarly scaled drawing of the anatomy of the AV node, common bundle of His, and initial branching, modified from James’ diagram (James, 1961). Note the common dimensionality, as represented by the three-dimensional reference frame in millimeters of the dipole path. The initial limb of the putative dipole path (between –40 and –34 msec) has been superimposed on the common bundle which also harbors the “back track” believed to be generated by the immediately adjacent right and left branches.

Our technique for extracting the average potential pattern of the selected segment in the form of the variance map could be expected to distort (i.e., suppress) electrical expressions within the time of that segment, unless distinctly uncorrelated with the basic Ta pattern. We believe that the “other” signal operating in the last 25 msec or so before QRS onset derives largely from the distal conduction network. If the distal network effects were imperfectly “averaged out” of the mean Ta pattern, their serial expression would not be revealed by the subtraction process—merely distorted. However, the surface pattern in late P-R fell within the noise level and led to no systematic dipole reduction. This suggests to us that the intense ramification beyond the upper centimeter or so of the branch system yields, upon activation, electrical sources so geometrically diffuse and divergent that cancellation effects predominate, and surface signal quickly reduces to the noise level.

The fact that the pattern we have called Ta is found as quantitively extractable from the early P-R (before His-Purkinje activation) suggests that it really does relate to atrial repolarization. Should atrial repolarization prove to be an unstable process (i.e., variable in space and in its contribution to the chest surface pattern), the alternative explanation would have to be that the late P-R pattern is an unexpectedly stable expression of His-Purkinje activation which only coincidentally is mathematically correlated with much of the P-R pattern found before the conduction system depolarizes.

The full validation of extracting the moving dipole representation of His bundle activation awaits repeated demonstration of a spatial pathway similar to the anatomical course, instances of retrograde conduction separable from the far stronger ventricular signal, and pharmacological verification that the identified spatial His pattern behaves under intervention just as His bundle conduction should. Technically, further accumulation of data should be facilitated by simultaneous signals from 24 to 35 electrodes from which both full maps and equivalent moving dipole reduction can be obtained on a beat-to-beat basis (Lux et al., 1978, 1979; Horan et al., 1980). This would allow decisive comparison in instances of variable heart block, echoes, and retrograde conduction, all of which should illustrate the character of surface signal from bundle activation.

Whereas we are convinced that rational extraction of conflicting signal (i.e., removal of the simultaneous atrial repolarization signal) permitted detection of the His bundle signals, it might be argued that arbitrary manipulation of the body surface potential pattern permitted an interesting but also arbitrary result which only coincidentally resembled that expected from His bundle activation with a limited number of samples. This consideration must be addressed, but the consistent and repeated pathway we have illustrated from our subjects, as well as the serial map pattern consistent with the rational division of one source into two, strongly suggest that we have identified the electrical trail down the common bundle and its branches. With responses to the intervention as just mentioned, this objection should disappear.

In brief, we believe we have shown that there is an organized, detectable deviation from the mean potential surface pattern of the normal human P-R interval and that this distinctive signal lasts about
20 msec and occurs before 25 msec prior to QRS onset. Further, we believe that the remainder of the body of electrophysiological understanding makes it probable that this signal derives from activation of the bundle of His and its upper branching, and that serial reduction of the surface pattern to equivalent dipole representation inscribes a path in space very like that expected from the anatomical pathway.

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