Body Surface Mapping During Pacing at Multiple Sites in the Human Atrium

P-Wave Morphology of Ectopic Right Atrial Activation

Arne SippensGroenewegen, MD; Heidi A.P. Peeters, MD; Emile R. Jessurun, MD; Andre C. Linnenbank, PhD; Etienne O. Robles de Medina, MD; Michael D. Lesh, MD; Norbert M. van Hemel, MD

Background—The morphology and polarity of the P wave on 12-lead ECG are of limited clinical value in localizing ectopic atrial rhythms. It was the aim of this study to assess the spatial resolution of body surface P-wave integral mapping in identifying the site of origin of ectopic right atrial (RA) impulse formation in patients without structural atrial disease.

Methods and Results—Sixty-two–lead ECG recordings were obtained during RA pacing at 86 distinct endocardial sites in nine patients with normal biatrial anatomy. After P-wave integral maps were generated for each paced activation sequence, 17 groups with nearly identical map features were visually selected, and a mean P-wave integral map was computed for each group. Supportive statistical analysis to corroborate qualitative group selection was performed by assessment of (1) intragroup pattern uniformity by use of jackknife correlation coefficient analysis of the integral maps contained in each group and (2) intergroup pattern variability by use of the calculation of cross correlations between the 17 mean integral maps. The spatial resolution of paced P-wave body surface mapping in the right atrium was obtained by estimating the area size of endocardial segments with nearly identical P-wave integral maps by use of a biplane fluoroscopic method to compute the three-dimensional position of each pacing site. The latter approach yielded a mean endocardial segment size of 3.5±2.9 cm² (range, 0.79 to 10.75 cm²).

Conclusions—Use of the P-wave morphology on the 62-lead surface ECG in patients with normal biatrial anatomy allows separation of the origin of ectopic RA impulse formation into one of 17 different endocardial segments with an approximated area size of 3.5 cm². This database of paced P-wave integral maps provides a versatile clinical tool to perform detailed noninvasive localization of right-sided atrial tachycardia before radiofrequency catheter ablation. (Circulation. 1998;97:369-380.)

Key Words: mapping • morphogenesis • pacing

The feasibility of using the surface ECG to localize ectopic atrial rhythms has long been the subject of much debate. In early animal1 and human2–4 studies, the P-wave polarity and morphology on the 12-lead ECG and the P-wave loop on the vectorcardiogram were examined during RA and LA pacing primarily in an attempt to differentiate left-sided from right-sided ectopic foci. Although several authors2,4,5 proposed distinct but not universal ECG criteria for this latter purpose, their results could not be reproduced reliably by others.3,6,7 Moreover, application of multisite epicardial pace mapping with temporally implanted electrodes5 and more recently endocardial catheter pace mapping7 has demonstrated that the 12-lead ECG is of limited clinical value in identifying specific sites or regions of ectopic atrial excitation within the LA or RA. Alternatively, it has been suggested that the use of multichannel ECG recordings would offer improved resolution to localize ectopic atrial activity.10–13 Given the complex lead-by-lead scalar evaluation of the low-voltage P wave in conventional ECG, body surface mapping offers the advantage of a more comprehensive spatial evaluation of the P-wave potential distribution over the entire torso. Experimental use of this technique in two different canine models showed comparable surface map patterns when epicardial pacing was conducted at similar sites in either the lower RA or lower LA.10,12 Preliminary clinical data have demonstrated that endocardial
pacing at the lower RA or the high, middle, and lower LA generates four clearly different P-wave map patterns.\textsuperscript{13,14}

The present study was conducted to perform a systematic clinical evaluation of the resolution of body surface mapping in identifying ectopic RA impulse formation in terms of (1) the total number of distinct and segment-specific body surface P-wave map patterns that can be distinguished and (2) the dimension of the endocardial segments in which characteristic P-wave map patterns can be generated.

Methods

Study Subjects

The recruited patient cohort consisted of nine patients who underwent RA pace mapping before diagnostic electrophysiological study with or without subsequent radiofrequency catheter ablation of their supraventricular or ventricular arrhythmia (Table 1). Entry criteria included (1) normal P-wave morphology and axis on the 12-lead ECG during sinus rhythm; (2) normal RA and LA size and configuration assessed by two-dimensional and M-mode echocardiography; and (3) the ability to obtain beat-to-beat atrial capture at a slow pacing rate, thereby ensuring clear separation of the stimulus spike from the previous T-U wave. Discontinuation of antiarrhythmic drugs was performed with a 2-ms pulse duration and a current amplitude slightly above the threshold level. The pacing rate was selected to just supersede the rate during sinus rhythm with the requirement of volume respiration. On-line control of catheter stability was ensured by two video monitors on which additional marking of each stimulus site was carried out. Although frontal and lateral projections were initially favored for fluoroscopic display of the RA, the aforementioned slightly angled orthogonal projections were chosen because they allowed adequate radiographic image quality with both arms alongside the chest in the standard supine position. RA cineangiograms were obtained and recorded on videotape directly after each pace mapping procedure to obtain end-diastolic endocardial contours of the RA. Adequate filling of the RA cavity, including the appendage, was secured by injection of 40 mL of contrast dye in the proximal superior vena cava at a rate of 30 mL/s. Throughout the pace mapping procedure, three additional bipolar or quadripolar catheters that were introduced via the femoral route remained at stable locations in the RA appendage, coronary sinus, and right ventricular apex. These catheters served as anatomic reference markers for computation of the three-dimensional location of each stimulus site and facilitation of the visual translation of each stimulus site location on the biplane images to an anatomic representation of the RA endocardium. Off-line digitization of the end-diastolic biplane video images of each pacing sequence was subsequently carried out. After correction for fluoroscopic magnification and distortion, an improved version of a previously designed quantitative catheter localization technique\textsuperscript{16,17} was used to compute the three-dimensional stimulus site position. This method allowed for a fluoroscopic localization resolution of ±5 mm. After all pace mapping procedures were carried out, adequate global coverage of the entire RA, including the superior vena cava, was verified by visual comparison of the entire set of pacing sites relative to their individual biplane fluoroscopic locations; pacing sites at the inferior vena cava were not included because it was not possible to obtain capture at the latter venous structure. Fig 1 gives an example of the nine digitized pacing sites and end-diastolic RA contours in the 15° RAO and 75° LAO projections obtained in patient 1.

Biplane Fluoroscopic Assessment of Pacing Site Location

At each pacing site, biplane 15° RAO and 75° LAO fluoroscopic projections were recorded on U-matic videotape during resting tidal volume respiration. On-line control of catheter stability was ensured by two video monitors on which additional marking of each stimulus site was carried out. Although frontal and lateral projections were initially favored for fluoroscopic display of the RA, the aforementioned slightly angled orthogonal projections were chosen because they allowed adequate radiographic image quality with both arms alongside the chest in the standard supine position. RA cineangiograms were obtained and recorded on videotape directly after each pace mapping procedure to obtain end-diastolic endocardial contours of the RA. Adequate filling of the RA cavity, including the appendage, was secured by injection of 40 mL of contrast dye in the proximal superior vena cava at a rate of 30 mL/s. Throughout the pace mapping procedure, three additional bipolar or quadripolar catheters that were introduced via the femoral route remained at stable locations in the RA appendage, coronary sinus, and right ventricular apex. These catheters served as anatomic reference markers for computation of the three-dimensional location of each stimulus site and facilitation of the visual translation of each stimulus site location on the biplane images to an anatomic representation of the RA endocardium. Off-line digitization of the end-diastolic biplane video images of each pacing sequence was subsequently carried out. After correction for fluoroscopic magnification and distortion, an improved version of a previously designed quantitative catheter localization technique\textsuperscript{16,17} was used to compute the three-dimensional stimulus site position. This method allowed for a fluoroscopic localization resolution of ±5 mm. After all pace mapping procedures were carried out, adequate global coverage of the entire RA, including the superior vena cava, was verified by visual comparison of the entire set of pacing sites relative to their individual biplane fluoroscopic locations; pacing sites at the inferior vena cava were not included because it was not possible to obtain capture at the latter venous structure. Fig 1 gives an example of the nine digitized pacing sites and end-diastolic RA contours in the 15° RAO and 75° LAO projections obtained in patient 1.

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TABLE 1. Patient Information

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age, y</th>
<th>Cardiac Arrhythmia</th>
<th>Pacing Sites, n</th>
<th>Pacing Cycle Length, ms</th>
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</thead>
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<tr>
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<td>48</td>
<td>AVNRT</td>
<td>9</td>
<td>500</td>
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<td>M</td>
<td>64</td>
<td>AVNRT</td>
<td>6</td>
<td>600</td>
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<tr>
<td>3</td>
<td>M</td>
<td>32</td>
<td>AF+atyp AFI</td>
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<tr>
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<td>M</td>
<td>54</td>
<td>AVNRT</td>
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<tr>
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<tr>
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<td>41</td>
<td>IRVT</td>
<td>6</td>
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</tbody>
</table>

AVNRT indicates AV nodal reentrant tachycardia; AF, atrial fibrillation; atyp AFI, atypical atrial flutter; AT, atrial tachycardia; and IRVT, idiopathic right ventricular tachycardia.
box was used for signal amplification and digitization at a rate of 1000 Hz with a 14-bit AD converter. Amplifier specifications allowed for a peak-to-peak noise level of 2 µV. Recorded data were then transmitted optically from the preamplifier box to a 486 personal computer dedicated to on-line acquisition and storage of data. Special attention was paid to obtain high-quality single-beat ECG recordings in the range below 250 µV by eliminating all correctable causes of noise such as muscle tremor and suboptimal electrode contact and minimizing electromagnetic MAINS frequency interference predominantly generated by the biplane fluoroscopy system. The latter goal was achieved by use of advanced guarding techniques, optimal patient isolation, and positioning of the low-noise preamplifier unit directly next to the patient.

Data Processing

Data processing and graphic color display were performed on-line with an Amiga 1200 microcomputer (Commodore-Amiga, Ltd, with multitasking capabilities. This computer was directly linked by a parallel connection to the acquisition computer. The Amiga computer was also used to control the actual data acquisition by the personal computer and to constantly review incoming ECG signals. Storage, transportation, and backup of data on each of the two computers were secured by a 1080-MB hard disk and removable 3.5-in, 270-MB hard disk cartridges (SyQuest Technology, Inc). Manual editing was performed by choosing a distinct isoelectric time instant between the stimulus spike and the T-U wave; care was taken to check all individual ECG waveforms, thereby focusing on the left precordial area where the maximal U-wave voltage can be found during normal ventricular activation. Linear baseline drifting and interelectrode offset differences were then corrected by a linear interpolation algorithm. Lead recordings expressing nonlinear baseline drifting or otherwise unsatisfactory signal quality were deleted (mean, 2.5±1.6 per map) and substituted by computed values from neighboring leads. PTa wave potential maps were inspected visually on the Amiga computer at 2-ms intervals. P-wave onset and offset were defined as the time instant at which one of the extreme voltages progressed beyond ±30 µV and the time instant at which the earliest atrial recovery potentials could be noted during terminal atrial excitation, respectively. Subsequently, a P-wave integral map was computed for each paced sequence (Fig 2B). At least three consecutive beats were analyzed to verify that identical integral map patterns were obtained at every pacing site. All hard copies of the maps presented in this report were produced with a Sun Sparc Station 4 computer (Sun Microsystems, Inc).

Data Analysis

Protocol for Map Evaluation

Potential maps were inspected visually to assess P-wave duration and to document temporal changes in the potential distribution during ectopic atrial excitation. In particular, we assessed surface map features representative for complex intra-atrial conduction, including the presence of multiple simultaneous atrial wave fronts. These features included (1) a lack of temporal stability of the extreme positions, (2) the occurrence of multipolar map patterns clearly before the transition zone of terminal excitation and initial recovery; multipolarity of atrial excitation was defined as the simultaneous presence of three or more extremes with the additional requirement that two extremes of the same polarity are separated by an area of opposite polarity, (3) the presence of pseudopod extensions in the voltage distribution, and (4) the occurrence of sudden extreme movement from one stable position to another over a torso distance of at least three electrodes. The spatial configurations of P-wave and Ta-wave potential maps were also compared.

Rather than using an arbitrary preselected division of the RA to direct grouping of pacing sites and corresponding integral maps, we subdivided the maps visually on the basis of nearly identical P-wave morphology according to a method that was previously developed for the design of a database of characteristic body surface QRS integral maps obtained by endocardial pace mapping in the normal right or left ventricle and the infarcted left ventricle. Assessment of pattern correspondence was performed in a blinded fashion and included a comparison of the location and mutual orientation of the extremes and the zero-line contour. Descriptive statistics were used to validate qualitative group selection: (1) a jackknife procedure was conducted to establish intragroup pattern uniformity by comparing maps with the use of correlation coefficients; and (2) after mean integral maps were computed for each group, a cross correlation of all mean P-wave
integral maps was performed to document intergroup pattern variability. Finally, the pacing sites corresponding to each individual group were represented as segments on an anatomic representation of the RA\textsuperscript{23} based on the biplane fluoroscopic image information.

**Assessment of Spatial Resolution**

The spatial resolution of body surface mapping in localizing ectopic RA activation was obtained by estimating the size of the endocardial segments at which nearly identical P-wave integral maps were produced.\textsuperscript{15,22} The distances between pairs of disparate pacing sites with nearly identical P-wave integral maps were computed in individual patients. Nearly identical maps produced at two given pacing sites were compared only if these catheter positions had been obtained at different parts of the mapping procedure. Three-dimensional coordinates of each stimulus site location were provided by the quantitative fluoroscopic catheter localization technique.\textsuperscript{14,23} An approximation of the corresponding endocardial segment size was obtained by calculating the circular area between a pair of sites. The largest area was selected whenever two or more pairs of disparate sites were found in a given segment.

**Additional Statistics**

All data are reported as mean ± SD. An unpaired two-tailed Student's \( t \) test was carried out whenever appropriate. A value of \( P < .05 \) was considered statistically significant.

**Results**

**P-Wave Potential Maps**

Paced PtA wave body surface maps were produced in nine patients at a total of 86 RA endocardial sites (mean, 9.6 ± 4.1 per patient) (Table 1). All PtA-wave potential maps displayed dipolar map patterns. Pattern instability during the early or late or both phases of RA excitation was noted in 88% of the body surface maps. There was a higher incidence of initial (71%) versus late (31%) pattern instability occurring during the first 27 ± 13 ms (range, 6 to 52 ms) and the last 31 ± 14 ms (range, 16 to 64 ms) of the P wave, respectively. Pseudopod extensions (81%) and sudden extreme movement (49%) were both frequently observed. There appeared to be no relation between a certain region of ectopic impulse movement and the occurrence of pattern instability, pseudopod extensions, or extreme movement. We did not observe any multipolarity of the map patterns during atrial excitation. All potential maps showed a clear transition between atrial excitation and recovery (atrial equivalent of J point) with marked pattern reversal resulting in an overall mirror image potential distribution during the Ta wave compared with the predominant map pattern during the P wave. A set of potential maps produced during pacing at the lower posterior RA is shown in Fig 3. Globally, the P wave demonstrates stable locations of the maximum and minimum at the right axilla and left upper anterior chest, respectively. However, there is pattern instability of the low-level positive potentials at the beginning (first 24 ms) and end (last 16 ms, from 80 to 96 ms) of atrial excitation. The terminal 16 ms of atrial excitation also feature a sudden superior shift of the maximum to the left upper axilla while the minimum gradually moves to a more superior and anterior location at the upper right frontal chest (90 ms). Maps obtained during the Ta wave (120 ms) displayed a similar spatial voltage distribution as the P-wave maps, albeit with opposed polarity of the extremes. Fig 4 features a sequence of potential maps obtained during pacing at the inferior wall of the RA near the inferior vena cava. At the onset of atrial excitation (4 ms), a maximum and minimum can be observed at the lower left and right anterior chest, respectively. One may also observe that the positive potentials display a typical pseudopod extension. Subsequently, the maximum suddenly moves to the top of the sternum while the minimum remains at the same location. The following part of the P wave (beyond 8 ms) is characterized by a stable potential distribution. Evidence for the onset of atrial recovery, reflected by positive potentials at the left upper anterior torso, may be noted at the last 2 ms of atrial excitation (106 ms) (atrial equivalent of J point).

**P-Wave Integral Maps**

A total of 17 groups with nearly identical P-wave integral map patterns were visually selected from the entire set of 86 paced atrial activation sequences. Two representative groups are represented in Figs 5 and 6. Group 10 contains five P-wave integral maps and was produced during pacing at the lower posterior RA (Fig 5). All maps highlight a characteristic zero-line morphology and a comparable location of the positive and negative extremes at the right axilla or right anterior chest and the left anterior chest or left axilla, respectively. The integral map of site A was produced at the same stimulus site as the potential maps demonstrated in Fig 3. It may be appreciated that the integral map resembles the potential distribution during the peak of the P wave (30 to 60 ms). The five integral maps shown in Fig 6 (group 12) were all produced at the inferior wall of the RA close to the inferior vena cava. Highly comparable map patterns can be recognized with a maximum and minimum at the upper sternum or the high left anterior chest and the lower right anterior chest, respectively. Pacing at site E also generated the potential maps displayed in Fig 4. Again, the integral map compares closely with the peak P-wave voltage distribution (50 to 70 ms).

**RA Database of Mean P-Wave Integral Maps**

A mean integral map was computed for each of the 17 groups of paced integral maps (Fig 7). For each group, the corresponding pacing site locations were represented in an anatomic diagram of the RA. It may be noted that there are striking differences between paced map patterns generated at anatomically opposed superior or inferior segments in the RA. Pacing at the superior vena cava (segments 2 and 3), high lateral RA (segment 4), and RA appendage (segment 5) show complete reversal of the extreme locations compared with pacing at the inferior (segment 13) and inferoseptal wall (segment 14) near the os of the coronary sinus and the lower septum (segment 15). Similarly, the map patterns of segments 1 (high septum) and 12 (inferior wall near the inferior vena cava) contain opposite directions of the atrial electromotive forces. However, a more discrete level of pattern analysis is mandatory to discriminate maps produced at adjacent segments. The maps obtained during pacing at segments 13 and 14 (inferior and inferoseptal wall near the coronary sinus os) show an identical position of the maximum as well as a comparable zero-line morphology. Pattern separation of the latter two maps can be obtained only on account of the difference in the position of the minimum. Also, differentiation of the maps produced during pacing at the medial (segment 2) or lateral superior vena cava (segment 3) can be achieved only on the basis of subtle
differences in the position of the zero line on the middle right half of the chest.

Mean positive and negative integral amplitudes of the paced P waves vary considerably, mainly because of the thoracic location of the extreme and its proximity to the underlying cardiac source (Table 2). Thus, high positive and negative extreme values can be noted with a position of the maximum or minimum around the precordium or the middle anterior thorax, eg, with pacing at the superior vena cava (segments 2 and 3) or the inferior and inferoseptal wall near the inferior vena cava (segments 13 and 14), respectively. It is interesting to note that pacing at the RA septum (segments 1, 15, and 16) produces both the lowest positive and negative extreme voltages. This observation may be explained by cancellation effects caused by synchronous activation of both atria as a result of propagation of the ectopic wave front from the septal origin in opposed rightward and leftward directions. The mean P-wave durations of the 17 different groups are also featured in Table 2. A separation in three larger areas with comparable P-wave duration can be performed: (A) superior vena cava, septum, and the region around the os of the coronary sinus (segments 1 through 3 and 13 through 16), 75±11 ms; (B) midanterior wall, RA appendage, high-middle and middle-low lateral wall, and low posterior wall (segments 4 through 10), 94±16 ms; and (C) inferior and low lateral wall (segments 11 and 12), 110±16 ms (P<.0001 and P<.002 for A versus B and B versus C, respectively).

Quantitative Validation of Database Formation
Mathematical assessment of pattern uniformity within each of the 17 groups is shown in Table 2. A high versus low level of intragroup map pattern correspondence translates into a high correlation coefficient with a low SD versus a low correlation coefficient with a high SD. Of the 17 groups, 15 appeared to contain a high degree of quantitative pattern uniformity with values of $r=0.90$ or higher and SDs ranging from 0.01 to 0.07, whereas the two remaining groups expressed a slightly lower pattern correspondence with $r=.79$ (segment 15) and $r=.89±.10$ (segment 7). Intergroup pattern variability was determined by performing 136 possible cross correlations between the 17 mean P-wave integral maps. Correlations ranged from high negative correlations between map pairs with
opposed positive and negative voltage distributions caused by mutually remote sites of ectopic impulse formation (eg, \( r = -.92 \) with segments 2 and 14) to high positive correlations between map pairs with less dominant spatial differences as a result of adjacent stimulation sites (eg, \( r = -.92 \) with segments 5 and 6). Intergroup pattern variability was also examined relative to the intragroup pattern uniformity. It appeared that 127 of the 136 cross correlations (93%) yielded lower correlation (\( r \)) values than the coefficients obtained with the corresponding intragroup map correlations. With 7 cross correlations, the coefficients were either the same (eg, \( r = .91 \) with segments 13 and 14) or marginally higher (eg, \( r = .82 \) with segments 14 and 15) than the intragroup map correlations displayed in Table 2. All 7 latter cross correlations, however, were pairs of mean integral maps generated at segments that were either adjacent (six pairs) or one segment apart (three pairs).

**Spatial Resolution of Paced Body Surface Mapping in the RA**

An approximation of the area size of each individual segment with a characteristic paced P-wave morphology was feasible in 12 of 17 segments (71%). Segment sizes varied between 0.79 (segments 1, 7, 10, and 16) and 10.75 cm\(^2\) (segment 11) (mean, 3.5±2.9 cm\(^2\)). Specific regions with a high or low spatial resolution of paced body surface mapping (small versus large segment size) could not be discriminated on the basis of the approximated segment size. However, given the fact that the total set of 86 pacing sites provided global coverage of the entire RA, it may be appreciated from the segmental distribution in Fig 7A that pacing at the superior caval vein appears to result in a lower spatial resolution compared with the body of the RA.

**Discussion**

**Use of Paced P-Wave Mapping to Discriminate Ectopic Right Atrial Foci**

**Current Report**

This study presents the first systematic attempt to gain insight into the clinical value of using the multiple-lead surface ECG to estimate the endocardial origin of ectopic RA activation. After 62-lead body surface P-wave maps in 9 patients without structural atrial disease at 86 distinct RA endocardial pacing
sites were accumulated, a total of 17 characteristic mean P-wave integral map patterns were identified. Each of the mean P-wave integral maps contained a spatial configuration specific to a particular segment of ectopic RA impulse formation. These RA segments were discrete in dimension, given an estimated mean area size of $3.5 \pm 2.9 \text{ cm}^2$. It was remarkable to find that body surface mapping is capable of attaining such a high spatial resolution in discriminating ectopic RA excitation, given the expected low amount of electromotive force generated by the relatively thin walled atria. In view of this latter consideration, it is even more striking to realize that paced body surface mapping allows differentiation of ectopic RA activity at a considerably higher spatial resolution compared with ectopic right ventricular activity; in a previous right ventricular pace mapping study, we were able to discriminate only 13 characteristic mean QRS integral map patterns with a considerably larger mean segment size of $6.7 \pm 2.9 \text{ cm}^2$ in patients without structural cardiac disease. We believe that the complex geometric outlay and architecture of the RA, together with the various orifices of penetrating vessels, provide a unique ensemble of conductive properties that not only outweigh the disadvantage of the low electromotive force generated by the thin atrial walls but in fact constitute the key factors for obtaining a high ECG resolution in the localization of ectopic RA foci.

**Previous Reports**
Examination of the P-wave morphology on the 12-lead ECG has been conducted by Maclean et al during bipolar pacing at 12 predefined RA and LA sites using temporarily implanted epicardial electrodes after open-heart surgery in patients with organic heart disease of various origins. The only site-specific ECG criteria that could be developed included the presence of a negative P wave in lead I with paced rhythms of the LA near the pulmonary veins and a positive or bifid P wave in V1 with LA pacing at the inferior pulmonary veins or coronary sinus. Recently, Man et al studied the P-wave morphology, amplitude, and duration on the 12-lead ECG during unipolar endocardial pacing from each electrode of a quadripolar catheter positioned at the lateral RA or in the coronary sinus in patients without structural heart disease. It was shown that pacing at sites separated by 1.7 cm in the RA and 3.2 cm in the coronary sinus did not result in visually apparent changes of the P wave. Thus, both of the aforementioned reports concluded that the 12-lead ECG was of limited clinical value in localizing ectopic atrial foci.

Body surface mapping has been used to identify the origin of ectopic atrial activity both experimentally and clinically. King et al used a canine model to simultaneously study the potential distribution on the body surface and epicardium during pacing at the lower RA and LA. Apart from demon-
strating characteristic P-wave surface map patterns at these two pacing sites, it was also reported that a 1- to 2-cm shift of the RA or LA pacing site produced clear surface map changes, whereas many of the 150 scalar ECG waveforms used to generate the maps did not exhibit apparent differences in P-wave polarity or morphology. A similar experimental setup was adopted by Kawano et al, who demonstrated distinct body surface map patterns during epicardial pacing at four atrial sites (ie, low RA and low, mid, and high LA). A recent clinical study carried out by the same group using endocardial pacing by catheter at four atrial locations that were comparable to the experimentally selected stimulus sites showed a similar specificity in surface map configuration. The mean paced P-wave integral map produced at segment 12 (inferior wall of the RA near the inferior vena cava) (Fig 7) appears highly comparable with the body surface maps generated at the low RA reported by Kawano and Hiraoka.13

Relation of Surface ECG Signal With Intracardiac Source During Ectopic RA Excitation

Unlike the spread of activation during ectopic ventricular impulse formation featuring radial propagation of a single wavefront, ectopic excitation of the atria is characterized by a markedly nonuniform mode of activation caused by the complex three-dimensional geometry and anisotropic conductive properties of the atria. Epicardial and endocardial mapping of the paced canine atria has demonstrated the simultaneous presence of multiple wave fronts and the occurrence of propagation at higher conduction velocities along prominent anatomic landmarks such as the crista terminalis, Bachmann’s bundle, and the pectinate muscles, whereas other anatomic structures such as the limbus of the fossa ovalis have been shown to act as natural barriers for conduction.10,25–27

Despite the inherent difficulty in assessing the heart-torso surface relationship given the complexity of ectopic atrial impulse propagation, King et al directly compared the epicardial and body surface potential distribution during pacing at the lower RA and LA in the dog. It was shown that two widely disparate RA and LA excitation waves resulted in two distinct maxima and a single minimum on the body surface. However, multiple extrema were not present with less profound epicardial wave-front separation (eg, with two simultaneous waves in either one of the two atria). In comparable canine experiments, Kawano et al predominantly noted a large shift in the position of a single maximum rather than double maxima as the surface reflection of two simultaneous wave fronts in the RA and LA. Although multipolar map patterns were not observed in the present study, we did find frequent surface manifestations of the complex underlying multipolar atrial generator such as initial and late P-wave pattern instability, pseudopod extensions of the voltage distributions, and sudden extreme movement (Figs 3 and 4).
The fact that multipolar map patterns were not present in our clinical data may be explained by the different torso geometry and deeper intrathoracic location of the atria in humans as opposed to canines. These anatomic differences may account for the comparatively lower resolution in electrical source separation obtained in humans. However, despite the decreased ECG sensitivity to detect multiple cardiac wave fronts during the human ectopic atrial excitation sequence, the present data demonstrate conclusively that there is a unique stimulus site-specific interaction between the overall mode of atrial impulse propagation and the spatial distribution of potentials on the torso. Moreover, this specific relation between the atrial current source and the surface P-wave voltages remains present among different patients, as can be noted from the maps and indicated in an anatomic representation of the endocardium of the human RA previously reported by McAlpine. The left and right sides of this representation offer an anteroposterior (AP) and posteroanterior (PA) impression of the RA anatomy, respectively. Main anatomic landmarks are indicated: the superior (SVC) and inferior (IVC) vena cava; the RA appendage (RAA); the smooth (SRA) and trabeculated (TRA) RA; the crista terminalis (CT); the fossa ovalis (FO); the LA; the eustachian valve (EV); the coronary sinus os (CSO); the tricuspid valve (TV); the aorta; and the right (RPA) and left (LPA) pulmonary arteries. The maps are shown without isointegral lines to focus on the essential spatial map features (ie, position and orientation of the extremes and zero-line contour). The anatomic display of the right atrium is reproduced with permission of Springer-Verlag.

Figure 7. The 17 mean P-wave integral maps (top) and their corresponding RA segments of ectopic impulse formation (bottom). The mean integral maps are displayed without isointegral lines (see text for more details) and are related to the endocardial segments by the circled numbers. These numbers are depicted above the maps and indicated in an anatomic representation of the endocardium of the human RA previously reported by McAlpine. The left and right sides of this representation offer an anteroposterior (AP) and posteroanterior (PA) impression of the RA anatomy, respectively. Main anatomic landmarks are indicated: the superior (SVC) and inferior (IVC) vena cava; the RA appendage (RAA); the smooth (SRA) and trabeculated (TRA) RA; the crista terminalis (CT); the fossa ovalis (FO); the LA; the eustachian valve (EV); the coronary sinus os (CSO); the tricuspid valve (TV); the aorta; and the right (RPA) and left (LPA) pulmonary arteries. The maps are shown without isointegral lines to focus on the essential spatial map features (ie, position and orientation of the extremes and zero-line contour). The anatomic display of the right atrium is reproduced with permission of Springer-Verlag.
the high qualitative and quantitative pattern uniformity within the different groups of P-wave integral maps.

It was interesting to note that endocardial pacing could be achieved well into the superior but not into the inferior vena cava. In one patient, we were able to pace the lateral superior vena cava (segment 3) at a site that was 3.2 cm from the junction with the upper RA. These findings are in agreement with intraoperative epicardial mapping results of Spach et al, who reported excitability 2 to 5 cm into the superior vena cava while no electrical activity could be recorded in the inferior vena cava.

### P-Wave Configuration During Pacing at the Lower RA Septum Around the Coronary Sinus Os

Although clinically paced rhythms produced in the os of the coronary sinus have been shown to result in a negative P-wave polarity in the inferior leads of the 12-lead ECG, both experimental and clinical studies have contested these findings. Moore et al demonstrated in a canine model that pacing at the RA septum just superior to the os of the coronary sinus caused positive P waves in leads II, III, and aVF and argued that the finding of a negative P-wave polarity in these leads was related to intra-atrial or interatrial conduction abnormalities. Waldo et al investigated the ectopic P-wave polarity in the inferior leads of the standard ECG during endocardial pacing at 11 septal sites in the vicinity of the coronary sinus os in patients with various cardiac pathology undergoing surgery. These authors found negative P waves when pacing inferior and posterior to the coronary sinus os (comparable to the location of segments 13 and 14) and biphasic or positive P waves when stimulating superior to the coronary sinus os (comparable to the location of segment 15). In subsequent exposed dog heart experiments, the same authors performed epicardial and endocardial mapping while pacing superior or inferior to the os of the coronary sinus. They obtained similar results regarding P-wave polarity as in their previous clinical study and explained their findings by the location at which predominant transseptal crossing of impulse propagation occurred. With transseptal propagation across Bachmann’s bundle, left atrial excitation proceeded in a superoinferior direction (pacing superior to the coronary sinus os), whereas transseptal conduction via a low interatrial route resulted in inferosuperior activation of the LA (pacing inferior to the coronary sinus os). In the present study, however, pacing around the os of the coronary sinus (segments 13 through 15), including the middle septum (segment 16), always produced a superoinferior direction of the electromotive forces on the mean P-wave integral maps (Fig 7) and consequently negative P waves in the inferior leads of the standard ECG. Our different findings cannot be explained by abnormal intra-atrial or interatrial wave-front propagation, given the absence of structural heart disease in this patient population. The discrepancy

<table>
<thead>
<tr>
<th>Group</th>
<th>Pacing Sites, n</th>
<th>Patients, n</th>
<th>Intragroup Map r</th>
<th>Positive P-Wave Integral Amplitude, mVms</th>
<th>Negative P-Wave Integral Amplitude, mVms</th>
<th>P-Wave Duration, ms</th>
<th>Endocardial Segment Location</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0.91 ± 0.03</td>
<td>3.03 ± 0.67</td>
<td>2.59 ± 0.36</td>
<td>54 ± 8</td>
<td>Septum High</td>
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<td>2</td>
<td>11</td>
<td>5</td>
<td>0.98 ± 0.01</td>
<td>6.61 ± 1.02</td>
<td>5.55 ± 1.06</td>
<td>77 ± 8</td>
<td>SVC Medial</td>
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<tr>
<td>3</td>
<td>6</td>
<td>3</td>
<td>0.97 ± 0.01</td>
<td>6.29 ± 0.89</td>
<td>4.88 ± 0.88</td>
<td>78 ± 9</td>
<td>SVC Lateral</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>3</td>
<td>0.95 ± 0.03</td>
<td>4.81 ± 0.96</td>
<td>5.53 ± 0.60</td>
<td>91 ± 14</td>
<td>Lateral High</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>4</td>
<td>0.95 ± 0.02</td>
<td>4.50 ± 1.13</td>
<td>5.22 ± 1.29</td>
<td>78 ± 11</td>
<td>RAA −−−</td>
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<tr>
<td>6</td>
<td>3</td>
<td>3</td>
<td>0.94 ± 0.01</td>
<td>4.09 ± 0.74</td>
<td>4.86 ± 1.80</td>
<td>93 ± 21</td>
<td>Lateral High-mid</td>
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<tr>
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<td>5</td>
<td>0.89 ± 0.10</td>
<td>4.94 ± 1.51</td>
<td>6.01 ± 1.05</td>
<td>105 ± 12</td>
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</tr>
<tr>
<td>8</td>
<td>9</td>
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<td>0.93 ± 0.06</td>
<td>3.71 ± 0.49</td>
<td>6.41 ± 1.93</td>
<td>102 ± 20</td>
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<td>3.78 ± 0.68</td>
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<td>0.90 ± 0.06</td>
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<td>7.68 ± 2.14</td>
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<td>4.12 ± 0.23*</td>
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<tr>
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<td>0.79 ± 0.01</td>
<td>3.50 ± 0.48</td>
<td>3.80 ± 0.28</td>
<td>76 ± 20</td>
<td>Septum Low</td>
</tr>
<tr>
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<td>2</td>
<td>0.93 ± 0.06</td>
<td>1.88 ± 0.24</td>
<td>4.43 ± 1.20</td>
<td>71 ± 27</td>
<td>Septum Mid</td>
</tr>
<tr>
<td>17</td>
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<td>1</td>
<td>2.24 ± 0.01</td>
<td>6.11 ± 0.11†</td>
<td>88 ± 0†</td>
<td></td>
<td>Anterior Low</td>
</tr>
</tbody>
</table>

**SVC** indicates superior vena cava; **RAA**, RA appendage; **IVC**, inferior vena cava; and **CSO**, coronary sinus os.

*Terminal portion of P wave obscured by initial part of QRS complex in one of the three paced sequences of this group.
†Terminal portion of P wave obscured by initial part of QRS complex.
in the results, however, may be attributed to interspecies differences in lower transseptal impulse propagation or cardiothoracic anatomy11,21 or to the recording conditions in the aforementioned clinical pacing study, which included an open chest and a right atriotomy.22

It is of interest to note that the integral maps produced at the segments 13 through 15 (lower RA septum around the coronary sinus os) show superior and slightly rightward directed electromotive P-wave forces that might be mistaken with a lower LA source of ectopic excitation. These particular map patterns may be understood when the geometry of the lower RA septum is taken into consideration. From endocavitary casts of the human heart generated by Anderson and Becker,33 it can be appreciated that the lower RA septum demonstrates a considerable degree of inward curvature right at its proximal level close to the AV ring, which may offer an anatomic explanation for the aforementioned direction of P-wave forces.

Study Limitations
One obvious limitation of this study and in fact any study in which detailed analysis of the low voltage P wave is carried out relates to the requirement of a hardware setup that enables high-quality signal acquisition with low noise interference in the electrophysiology laboratory. In the design of our mapping system, we have taken the necessary steps to meet these stringent demands, as can be noted by a low peak-to-peak noise level of 2 μV despite the lack of signal averaging techniques. Moreover, we particularly choose to use a method based on beat-to-beat analysis because it is our aim to use body surface mapping clinically as a practical technique for the noninvasive localization of atrial tachycardia.24 During the latter arrhythmia, the P wave is sometimes buried in the TU wave of the previous cardiac cycle, in which case intravenous adenosine or carotid sinus massage may be used to temporarily block AV conduction so that one unobscured P wave can be obtained for subsequent single-beat analysis. An additional measure to reduce outside electrical interference included the use of P-wave integral maps rather than sequential potential maps for the database formation. Nevertheless, we cannot exclude the possibility of noise interference in the low-level potential maps of the early or late P wave that may have obscured our interpretation of the more complex instantaneous voltage distributions.

A slow pacing rate was selected to optimally isolate the paced P wave and its preceding stimulus spike from the previous TU wave, despite the associated shortening of the PR interval and possible superposition of the PTa wave over the early part of the QRS complex. Although QRS superposition of the terminal TA wave occurred frequently (Fig 4), we observed this phenomenon only with the terminal component of the P wave in 2 of the 86 paced sequences when stimulation was conducted in close proximity to the AV node (segments 14 and 17). However, the nonobscured part of the P wave was considered to be adequate in duration to enable reliable integral map computation (ie, P-wave interval of 80 and 88 ms) in these latter two paced complexes.

Because comparative LA paced body surface mapping was not conducted, we are currently not able to comment on the specificity of the 17 P-wave integral map patterns to ectopic RA excitation. This is an important issue, given the reported difficulty in separating right-sided from left-sided focal atrial tachycardia on the basis of P-wave polarity in the standard ECG leads, particularly when tachycardias arising from the right upper pulmonary vein in the LA are to be differentiated from tachycardias originating from the high crista terminalis in the RA.25 The ability to reliably distinguish these tachycardias on the basis of their surface ECG morphology also bears important practical consequences because this may allow an a priori decision to consider a transeptal puncture before an anticipated left-sided catheter ablation.26 The as-yet limited amount of clinical data reported by Kawano and Hiraoka13 demonstrates that body surface maps generated by pacing at the middle or high LA are indeed quite different from any of our 17 paced P-wave integral maps produced in the RA. However, the map pattern that these authors acquired during stimulation at the lower LA did show a similar direction of electromotive forces compared with the mean P-wave integral map obtained at segment 13 (inferior wall near the os of the coronary sinus). Clearly, further systematic study of the spatial surface map variation during ectopic LA rhythms is warranted.

It has been suggested that abnormal atrial conduction resulting from structural heart disease hampers localization of ectopic atrial rhythms using the P-wave morphology on the 12-lead ECG.27 The high ECG localization resolution attained with paced body surface mapping in the present report was acquired in patients with normal biatrial anatomy. Therefore, we do not know whether similar spatial resolution results are indeed feasible when structural atrial disease is present. However, in a recent preliminary study, we were able to obtain highly comparable body surface integral map patterns of the dominant component of the flutter wave in patients with typical atrial flutter regardless of the presence or absence of structural heart disease, including atrial dilatation.28

Clinical Impact and Conclusions
This study demonstrates that a spatial approach to the interpretation of P-wave morphology based on 62-lead ECG mapping enables detailed differentiation of ectopic RA foci into 17 distinct segments of impulse formation. These findings are in sharp contrast to the overall disappointing results obtained with the clinical application of 12-lead ECG scalar P-wave analysis to localize ectopic atrial rhythms. Given the often subtle spatial differences in the paced P-wave map patterns, it becomes apparent that a scalar polarity or morphology-based assessment of the P wave in the 12 standard ECG leads cannot capture the discrete variation in the complex spread of atrial activation when ectopic impulses originate from different RA sites. The clinical importance of the current findings relates to the possibility to use the mean P-wave integral map patterns as a reference database to match and localize focal atrial tachycardia to navigate and accelerate the mapping procedure on-line during catheter ablative therapy. From a practical perspective, it is shown that noise-related interference during clinical signal acquisition of the low-voltage P wave can largely be overcome with the currently available advanced body surface mapping technology, even when a beat-to-beat analysis approach is adopted. We believe
that the encouraging results of this report show that spatial P-wave analysis based on surface mapping techniques holds great promise in reinforcing the role of the ECG in the noninvasive diagnostic evaluation of atrial arrhythmias.

Acknowledgments
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Body Surface Mapping During Pacing at Multiple Sites in the Human Atrium: P-Wave Morphology of Ectopic Right Atrial Activation

Arne SippensGroenewegen, Heidi A. P. Peeters, Emile R. Jessurun, Andre C. Linnenbank, Etienne O. Robles de Medina, Michael D. Lesh and Norbert M. van Hemel

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