Morphological Characteristics of P Waves During Selective Pulmonary Vein Pacing

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OBJECTIVES

We sought to assess the value of 12-lead electrocardiogram (ECG) P-wave morphology to recognize the paced pulmonary vein (PV).

BACKGROUND

Prediction of arrhythmogenic PVs producing ectopy or initiating atrial fibrillation (AF) using 12-lead ECG may facilitate curative ablation.

METHODS

In 30 patients P-wave configurations were studied during sinus rhythm and during pacing at six sites from the four PVs: top and bottom of each superior PV and both inferior PVs. The P-wave amplitude, duration and morphology were assessed, and predictive accuracies were calculated for the most significant parameters. An algorithm predicting the paced PV was developed and prospectively evaluated in a different population of 20 patients.

RESULTS

Three criteria were used to distinguish right from left PV: 1) a positive P-wave in lead aVL and the amplitude of P-wave in lead I ≥50 μV indicated right PV origin (specificity 100% and 97%, respectively); 2) a notched P-wave in lead II was a predictor of left PV origin (specificity 95%); and 3) the amplitude ratio of lead III/II and the duration of positivity in lead V1 were also helpful in distinguishing left versus right PV origin. In addition, superior PVs could be distinguished from inferior according to the amplitude in lead II (≥100 μV).

In prospective evaluation, an algorithm based on the above four criteria identified 93% of left versus right PV and totally 79% of the specific PVs paced.

CONCLUSIONS

Pacing from the different PVs produced a P-wave with distinctive characteristics that could be used as criteria in an algorithm to identify the PV of origin with an accuracy of 79%. (J Am Coll Cardiol 2001;38:1505–10) © 2001 by the American College of Cardiology

It has been shown that most episodes of paroxysmal atrial fibrillation (AF) are initiated by ectopics originating from the pulmonary veins (PVs) (1–3). Although radiofrequency (RF) catheter ablation directed at the PVs can effectively eliminate episodes of AF, it is sometimes difficult to locate the source of AF during the ablation procedure owing to unpredictable firing, multiple sources and frequent induction of sustained AF. Prediction of the location of arrhythmogenic PV before endocavitary exploration on the basis of surface ECG could facilitate and shorten the ablation procedure. The aims of this study were: 1) to analyze the P-wave morphology produced by pacing different PVs, and 2) to develop an algorithm to predict the PV of origin and determine its accuracy.

METHODS

Patient population. This study included 30 patients (20 men; mean age 55 ± 8 years) referred for electrophysiologic evaluation of atrial or junctional tachycardia (including 22 patients with paroxysmal AF), having a patent foramen ovale (n = 16) or requiring a transseptal approach (n = 14). Only five patients had evidence of cardiovascular disease: three had hypertension and two had coronary artery disease. Left atrial size measured by parasternal echocardiography was normal except in two patients with hypertension who had mild left atrial dilation (42 and 44 mm). A separate population with 20 patients (12 men; mean age 50 ± 8 years) referred for electrophysiologic evaluation of atrial or junctional tachycardia (13 patients had paroxysmal AF) was included in the prospective evaluation of the proposed algorithm. All antiarrhythmic drugs except amiodarone were discontinued for at least five half-lives before the study. Informed consent was obtained from all patients before the procedure according to the protocol approved by the hospital’s Human Research Committee.

PV pacing. Direct visualization of all four PVs was performed using selective venography. A 6F or 7F NIH angiocatheter (Cordis-Europe, Netherlands) was introduced through the long sheath into each PV under fluoroscopic guidance. Angiography was performed during held mid-expiration by hand injection of contrast media (about 10 ml) in the anteroposterior view. A quadripolar roving ablation catheter with a 4-mm tip (Cordis-Webster, Diamond Bar, California) was then advanced to the PV of interest. Distal bipolar pacing 1 cm inside each PV was performed with a programmable stimulator (UHS 20, Biotronik, Gmbh, Berlin, Germany) at a 2-ms output pulse width with up to twice diastolic threshold, at a rate 16 beats/min faster than in sinus rhythm. The lowest amplitude allowing constant capture was used to minimize stimulus and post-stimulus artifacts. Six sites were paced in four PVs: the top and bottom of the left superior PV, the top and bottom of the right superior PV, and both inferior PVs. In inferior PVs, pacing was performed at the bottom of
the vein. The 12-lead electrocardiogram (ECG) was recorded on a PPG Midas polygraph at a paper speed of 25 mm/s and an amplitude gain of 1 mV/cm through a band pass filter setting of 0.5 to 40 Hz.

Analysis of P-wave morphology. Surface 12-lead ECG recordings obtained during selective PV pacing and sinus rhythm were evaluated by two blinded observers, concerning the P-wave amplitude, duration and morphology. Measurements were performed with magnified ECGs (twice the original size) to minimize the error in measurement (Fig. 1).

The P waves were classified into five types: 1) positive = P waves with deflections above the isoelectric line (the T-P segment); 2) negative = P waves with deflections below the isoelectric line; 3) biphasic = P waves having both positive/negative and negative/positive deflections; 4) isoelectric (flat) = low-amplitude P waves; and 5) notched = P waves with only double-positive components (P waves with only double-negative components were not included in the definition of notched P-wave, because they were seen only rarely without specific localizing value). The amplitude of the P-wave was calculated from peak to nadir. Both P-wave duration and amplitude were analyzed, and specificity, sensitivity, positive predictive value (PPV) and negative predictive values (NPV) were calculated for the most significant parameters. Finally, an algorithm was developed based on the above analysis.

Prospective evaluation of the performance of the algorithm. The algorithm was prospectively evaluated in a separate patient population of 20 patients (described above), having a patent foramen ovale (n = 10) or requiring a transseptal approach (n = 10). Four patients had evidence of hypertensive cardiovascular disease. Left atrial size measured by parasternal echocardiography was normal in all 20 patients. Bipolar pacing of each PV was performed as before. All 120 ECG tracings from 20 patients (during pacing from six PV sites) were assessed in random order by four blinded observers (total: 480 assessments) to identify the individual PV paced.

Statistical analysis. All values are expressed as mean ± SD. Statistical analysis was done using the Students t test (paired or unpaired) or chi-square analysis. One-way analysis of variance followed by the Scheffé post hoc test was also used when we needed to compare more than three groups. Differences with p < 0.05 were considered statistically significant.

RESULTS

Amplitude of paced P waves. Significant differences in the amplitudes of paced P waves were observed in all six limb leads and lead V5 depending on the pacing site (Table 1, Fig. 1). In lead I, P waves produced by left PV pacing were

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**Abbreviations and Acronyms**

- AF = atrial fibrillation
- ECG = electrocardiographic/electrocardiogram
- LA = left atrium
- NPV = negative predictive value
- PPV = positive predictive value
- PV = pulmonary vein
- RF = radiofrequency

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*Figure 1.* Surface electrocardiogram P waves in one patient with atrial fibrillation (45-year-old man) during pacing at six sites in four pulmonary veins (PVs) are shown. Pacing in left PVs produced P waves with characteristic features of low amplitude in lead I, negativity in lead aVL, similar amplitude in both leads II and III, notched shape in lead II (most evident during left inferior [LI] pacing in this case), and long positive phase in lead V5. In contrast, P waves during right PV pacing were clearly positive in lead I, relatively flat in lead aVL, and had a low amplitude ratio of lead III/II (<0.8). The P waves during superior PV pacing were taller than those of inferior PV pacing in inferior limb leads. A positive P-wave in lead aVL, seen during RI pacing in this case, is a specific marker of right PV origin of pacing. Bottom-LS = bottom of the left superior PV; Bottom-RS = bottom of the right superior PV; RI = right inferior PV; Top-LS = top of the left superior PV; Top-RS = top of the right superior PV.
very low in amplitude and significantly lower than those of the right (p < 0.0001, Fig. 2A). In lead aVR, all pacing sites showed negative P waves, but superior sites yielded P waves of more negative amplitude than those from inferior sites (Fig. 2B). In lead aVL all pacing sites in the left PV produced negative P waves, whereas positive P waves were observed in 15% of right superior and 85% of right inferior PV (Fig. 2C).

In leads II and III, pacing in superior PVs produced P waves with higher amplitudes (≥100 μV) compared to those from inferior PVs (Fig. 2D). However, unlike lead II, the amplitude of paced P waves in lead III was significantly greater for left compared to right PVs (p < 0.05) (Fig. 2E). Figure 2F demonstrates the values of the amplitude ratio between leads II and III (III/II ratio). All three left-sided pacing sites showed mean values close to 1.0, whereas each of the three right-sided pacing sites produced a mean value <0.8. No significant difference was observed in amplitude between P waves during pacing top and bottom of the superior PVs in all 12 leads except lead aVL (Fig. 2C). The P-wave amplitudes in the two patients with a slightly dilated left atrium (LA) were all within 2 SD of the mean.

Duration of paced P waves. There was significant difference in the P-wave duration between right and left PV at similar levels in most leads (Table 2). However, the degree of difference was too modest (about 20 ms) to distinguish between right and left PV origin except that the duration of the positive phase of the P-wave in lead V1 during left PV pacing was significantly longer (≥40 ms) than those of right PV. No significant difference was observed between P-wave durations during pacing top and bottom of the superior PVs in all 12 leads except lead aVL (Fig. 2C). The P-wave durations of the two patients with slightly dilated LA did not show any findings different from others (all of them were within 2 SD of the mean).

Interobserver variability. The interobserver variability of the P-wave amplitude and width measurement by the two different observers was within 30 μV and 10 ms in 90% of the paced P waves. As for the morphology of the P waves, there was 87% interobserver agreement in the determination of configuration of paced P waves. Differences were resolved by consensus.

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**Table 1. Amplitude of Paced P Waves**

<table>
<thead>
<tr>
<th>SR</th>
<th>Top-LS</th>
<th>Bottom-LS</th>
<th>L1</th>
<th>Top-RS</th>
<th>Bottom-RS</th>
<th>RI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>65.7 ± 32.4</td>
<td>13.3 ± 15.8</td>
<td>13.1 ± 13.4</td>
<td>7.0 ± 15.1</td>
<td>58.7 ± 26.7</td>
<td>59.3 ± 25.5</td>
<td>54.8 ± 21.5</td>
</tr>
<tr>
<td>II</td>
<td>120.4 ± 41.0</td>
<td>169.3 ± 77.4</td>
<td>133.9 ± 57.4</td>
<td>78.9 ± 42.1</td>
<td>162.0 ± 61.9</td>
<td>125.6 ± 48.7</td>
<td>76.1 ± 37.3</td>
</tr>
<tr>
<td>III</td>
<td>63.5 ± 49.0</td>
<td>163.9 ± 71.8</td>
<td>132.1 ± 49.9</td>
<td>77.0 ± 36.8</td>
<td>119.3 ± 54.8</td>
<td>82.8 ± 41.9</td>
<td>40.2 ± 38.1</td>
</tr>
<tr>
<td>III/II</td>
<td>0.48 ± 0.39</td>
<td>0.98 ± 0.09</td>
<td>1.06 ± 0.32</td>
<td>1.00 ± 0.26</td>
<td>0.73 ± 0.18</td>
<td>0.65 ± 0.18</td>
<td>0.43 ± 0.54</td>
</tr>
</tbody>
</table>

p values were calculated without the data during SR. All values (except III/II) are expressed in μV.

- Bottom-LS = bottom of the left superior pulmonary vein; Bottom-RS = bottom of the right superior pulmonary vein; L1 = left inferior pulmonary vein; RI = right inferior pulmonary vein; SR = sinus rhythm; Top-LS = top of the left superior pulmonary vein; Top-RS = top of the right superior pulmonary vein.
Evaluation of the predictive accuracy of significant criteria. Seven criteria were evaluated (Table 3). Positive P waves in lead aVL, as a predictor of right PV origin, showed the highest specificity (100%) and PPV, but low sensitivity and NPV. Amplitude of P waves in lead I exceeding 50 μV demonstrated high specificity (99%) and PPV in predicting a right PV origin, with moderate sensitivity and NPV. A notched P-wave in lead II showed 92% specificity in predicting a left PV origin, and this value increased to 95% when the two patients with a notched lead II P-wave in sinus rhythm were excluded (one of these two criteria). The combination of the above three criteria (a positive P-wave in lead aVL, higher amplitude of P-wave in lead I greater than 50 μV and the presence of notch in lead II) were selected because they indicated right and left PV origins with the highest specificities. Remaining P waves were classified as being of right- or left-sided PV origin depending on the lead III/II amplitude ratio or the duration of positivity in V1. Finally, P-wave amplitude in lead II (≥100 μV) differentiated superior PV from inferior PV. The algorithm and 81% sensitivity. The ratio of P-wave amplitude during pacing to that in sinus rhythm (≥1.0 for superior PV) failed to improve the predictive accuracies compared to the simpler criterion of using the height of paced P-wave alone (p = 0.11 ~ 0.15).

Development of the algorithm. From the analysis of morphological features of P waves during selective PV pacing, we developed an algorithm predicting the PV origin of pacing (Fig. 3). The initial criteria (a positive P-wave in a lead aVL or amplitude of P-wave in lead I greater than 50 μV and the presence of notch in lead II) were selected because they indicated right and left PV origins with the highest specificities. Remaining P waves were classified as being of right- or left-sided PV origin depending on the lead III/II amplitude ratio or the duration of positivity in V1. Finally, P-wave amplitude in lead II (≥100 μV) differentiated superior PV from inferior PV. The algorithm

### Table 2. Duration of Paced P Waves

<table>
<thead>
<tr>
<th>Criteria</th>
<th>SR</th>
<th>Top-LS</th>
<th>Bottom-LS</th>
<th>LI</th>
<th>Top-RS</th>
<th>Bottom-RS</th>
<th>RI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>104.8 ± 9.8</td>
<td>123.3 ± 22.7</td>
<td>121.2 ± 21.8</td>
<td>121.9 ± 18.6</td>
<td>115.6 ± 17.8</td>
<td>110.0 ± 16.6</td>
<td>113.9 ± 13.8</td>
<td>0.065</td>
</tr>
<tr>
<td>II</td>
<td>112.6 ± 12.0</td>
<td>140.0 ± 13.9</td>
<td>138.5 ± 15.2</td>
<td>137.0 ± 15.6</td>
<td>119.3 ± 13.0</td>
<td>117.6 ± 14.9</td>
<td>113.3 ± 15.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>109.6 ± 12.9</td>
<td>140.0 ± 14.7</td>
<td>138.1 ± 15.2</td>
<td>135.6 ± 16.7</td>
<td>117.4 ± 13.5</td>
<td>113.9 ± 14.9</td>
<td>111.1 ± 17.4</td>
<td>&lt;0.0001</td>
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<tr>
<td>aVR</td>
<td>113.0 ± 9.5</td>
<td>126.7 ± 15.7</td>
<td>127.2 ± 15.7</td>
<td>128.2 ± 15.9</td>
<td>120.7 ± 13.3</td>
<td>117.6 ± 14.7</td>
<td>114.1 ± 15.5</td>
<td>0.002</td>
</tr>
<tr>
<td>aVF</td>
<td>103.0 ± 12.4</td>
<td>131.9 ± 17.6</td>
<td>128.5 ± 19.1</td>
<td>131.5 ± 18.5</td>
<td>115.4 ± 16.7</td>
<td>112.4 ± 19.5</td>
<td>112.3 ± 17.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>aVL</td>
<td>110.0 ± 11.8</td>
<td>139.3 ± 15.7</td>
<td>138.1 ± 14.2</td>
<td>140.0 ± 16.9</td>
<td>120.5 ± 13.8</td>
<td>116.3 ± 15.0</td>
<td>114.1 ± 17.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>105.2 ± 16.0</td>
<td>129.3 ± 19.4</td>
<td>128.1 ± 19.6</td>
<td>131.5 ± 14.9</td>
<td>117.4 ± 15.6</td>
<td>117.6 ± 16.0</td>
<td>118.3 ± 17.7</td>
<td>0.002</td>
</tr>
<tr>
<td>P-V1/V1</td>
<td>34.8 ± 37.3</td>
<td>94.1 ± 31.0</td>
<td>95.2 ± 28.7</td>
<td>116.0 ± 35.6</td>
<td>54.1 ± 36.0</td>
<td>55.9 ± 26.9</td>
<td>61.5 ± 29.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>P-V1/V1</td>
<td>0.33 ± 0.35</td>
<td>0.73 ± 0.22</td>
<td>0.76 ± 0.24</td>
<td>0.88 ± 0.24</td>
<td>0.46 ± 0.31</td>
<td>0.47 ± 0.23</td>
<td>0.52 ± 0.23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>V1</td>
<td>108.2 ± 17.1</td>
<td>131.1 ± 17.2</td>
<td>131.2 ± 18.0</td>
<td>133.0 ± 17.3</td>
<td>122.4 ± 15.3</td>
<td>118.5 ± 15.6</td>
<td>118.9 ± 16.0</td>
<td>0.001</td>
</tr>
<tr>
<td>V2</td>
<td>108.9 ± 10.5</td>
<td>126.3 ± 17.6</td>
<td>124.6 ± 19.4</td>
<td>125.2 ± 18.7</td>
<td>120.2 ± 14.2</td>
<td>118.7 ± 15.5</td>
<td>120.2 ± 17.3</td>
<td>0.47</td>
</tr>
</tbody>
</table>

### Table 3. Evaluation of Surface Electrocardiographic Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Predicted PV</th>
<th>Sp (%)</th>
<th>Se (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Positive in lead aVL</td>
<td>Right</td>
<td>100</td>
<td>38</td>
<td>100</td>
<td>62</td>
</tr>
<tr>
<td>2) Amplitude of lead I ≥50 μV</td>
<td>Right</td>
<td>99</td>
<td>72</td>
<td>98</td>
<td>77</td>
</tr>
<tr>
<td>3) Notch in lead II</td>
<td>Left</td>
<td>95</td>
<td>39</td>
<td>89</td>
<td>61</td>
</tr>
<tr>
<td>4) Positive phase in V1 ≥80 ms</td>
<td>Left</td>
<td>73</td>
<td>85</td>
<td>76</td>
<td>83</td>
</tr>
<tr>
<td>5) Amplitude ratio of lead III/II ≥0.8</td>
<td>Left</td>
<td>75</td>
<td>96</td>
<td>79</td>
<td>95</td>
</tr>
<tr>
<td>6) Amplitude of lead II ≥100 μV</td>
<td>Superior</td>
<td>74</td>
<td>81</td>
<td>86</td>
<td>67</td>
</tr>
<tr>
<td>7) Amplitude ratio of pacing/SR in lead II ≥1.0</td>
<td>Superior</td>
<td>85</td>
<td>72</td>
<td>91</td>
<td>61</td>
</tr>
</tbody>
</table>

NPV = negative predictive value; PPV = positive predictive value; PV = pulmonary vein; Se = sensitivity; Sp = specificity.
did not differentiate top versus bottom of the superior veins. Out of 480 assessments of 120 PV sites, 93% of left versus right PV, 85% of superior versus inferior PV and 79% of the specific PV paced were correctly identified with the algorithm. The pacing sites in superior PVs were diagnosed with significantly higher accuracy (84%) compared to inferior PVs (68%, p < 0.05). Interobserver variability for the accuracy of diagnosis was small (6.0 ± 3.5%), endorsing the reliability of the algorithm.

DISCUSSION

Major findings. This study showed that selective PV pacing at each of four PVs produced distinct P-wave characteristics that could be used to identify the PV of origin of pacing with an accuracy of 79%.

Left PV pacing produced low P-wave amplitude (flat P-wave) in lead I, negative polarity in lead aVL, similar amplitudes in both leads II and III, a notched morphology in lead II, and longer duration of positivity in lead V1. Conversely, right PV origin was suggested by a positive P-wave in lead I ≥50 μV, a relatively flat P-wave in lead aVL, and a low amplitude ratio of lead III/II (less than 0.8). In addition, a clearly positive P-wave in lead aVL was a specific marker of right PV origin.

The difference in the amplitude ratio of lead III/II between right and left PV pacing in our study probably reflects the more vertical axis of activation from left PVs as opposed to the more leftward axis (in the frontal plane) of depolarization from right PVs. The longer duration of positivity in lead V1 may reflect more posterior locations of left PV insertions into the LA compared to the right PV.

The accuracy of diagnosis for inferior PV origin was significantly lower than that of superior PV, which may be due to anatomical variations in the level of PV insertion into the posterior left atrial wall among individuals. Accordingly, the difference between P waves during pacing from top and bottom of the same superior PVs was small.

Previous studies. Morphologic features of P waves in ectopic atrial rhythms have been studied and reported; however, they focused on distinguishing between right and left atrial origin or sites within the right atrium (4,5). In a recent report Saksena et al. (6) performed simultaneous catheter mapping of initiating ectopics in right and left atrial regions, and they concluded that the P-wave morphology on surface ECG did not correlate with the site of origin in specific atrial regions. Significant differences existed in methods between their study and ours; we studied the correlation between the pacing sites and the P-wave morphology, whereas they correlated the earliest mapping site (all of them were outside of PV) and the P-wave morphology, which makes it difficult to compare the results.

Pace mapping has been evaluated for localizing the origin of ectopic atrial rhythms. Where MacLean et al. (7) reported that P-wave polarity and morphology were not useful for localization as the P-wave pattern was relatively similar for different pacing sites, our data indicate that paced P-wave morphology does have localizing value. The researchers performed epicardial pacing in patients after cardiac surgery for structural heart disease and did not conduct pacing inside the PVs, and these methodologic differences may be responsible for differences in results. Man et al. (8) reported that the spatial resolution of unipolar atrial pace mapping in amplitude and duration of P-wave was about 17 mm. Accordingly, our study was able to differentiate the paced PV among four PVs located more than 17 mm apart from each other. To our knowledge, the usefulness of P-wave configuration in multiple surface ECG leads has not been reported so far for identifying the origin of ectopics among the four PVs.

Clinical implications. Recently, electrical disconnection of arrhythmogenic PV from the LA has been performed to treat paroxysmal and chronic AF (9). However, it is sometimes difficult to locate the source of AF during the procedure owing to unpredictable firing, multiple sources and frequent induction of sustained AF. Rapid localization of arrhythmogenic PV on a single initiating ectopy may be facilitated by surface ECG P-wave analysis. Even with anatomic strategy targeting all the PVs, it is necessary to ablate the arrhythmogenic vein first so as to permit complete disconnection of PVs in stable sinus rhythm. Identification of arrhythmogenic PV is also difficult in cases with few or no ectopy during the procedure. Prediction of the target veins by the P-wave configuration on surface ECG may be helpful for directing mapping and ablation as it is relatively easy to document ectopics at some other moment in the patient’s past. This is particularly useful in the youngest patients, who typically have a single arrhythmogenic PV (9).

Study limitations. This algorithm is valid only for pacing from the PVs, and it has been developed in the prospect of use in conjunction with a subtraction system (10) to unmask the ectopic P wave superimposed on T waves. There is a minority of patients with focal AF where the trigger is not located in any of the PVs (9), and the algorithm in this study was not developed to localize such focal atrial sources outside of the PVs or to differentiate superior vena cava from right superior PV focal origins. Another limitation is that P-wave morphology during stimulation (at a rate of 10 beats/min faster than sinus rhythm) may be different from that of spontaneous ectopics with shorter coupling intervals, because of altered activation sequences.

Conclusions. Pacing from the different PVs produced distinct P-wave characteristics. An algorithm based on these characteristics identified 93% of left versus right PVs, 85% of superior versus inferior PVs, and in all 79% of the specific PVs paced. To analyze P waves superimposed on T waves during spontaneous ectopics, the algorithm should be used in combination with an ECG subtraction technique.
REFERENCES


