BRIEF REPORT

Evaluation of a novel PVC and PAC detection algorithm in an implantable cardiac monitor for longitudinal risk monitoring

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Introduction

Insertable cardiac monitors (ICMs) are routinely used for diagnosing cardiac arrhythmias due to the advantages of long-term continuous monitoring and the ability to provide data on a daily basis.[1] ICMs are currently indicated for diagnosing syncope, palpitations, suspected atrial fibrillation (AF) after cryptogenic stroke, and AF management.[2,3] Recently, additional diagnostic information such as temperature and ectopy count have been provided to further improve clinical care.[4] Recent guidelines recommend treatment in patients with frequent premature ventricular contractions (PVCs),[5,6] and PVC burden has been shown to be predictive of incident congestive heart failure (HF), ejection fraction reduction, and mortality.[7] PVC burden can effectively guide treatment options, stratify patient risk, and manage HF progression.[8,9] Furthermore, mounting evidence associates frequent premature atrial contractions (PACs) with the development of new onset AF, stroke, and all-cause mortality.[10] While PVC/PAC burden is often quantified using 24-hour Holter recordings, it may vary significantly day to day, and thus a single 24-hour measure may be misleading.[11]

Here we present a novel algorithm designed to detect both PVCs and PACs in the BIOMONITOR IV ICM (BIOTRONIK, Berlin, Germany). Considering the progressive nature of these cardiovascular diseases, this ICM with a 5-year battery life provides a unique opportunity as a long-term diagnostic tool to monitor both PVC and PAC burden and guide clinical therapy.

KEYWORDS Implantable cardiac monitor; Premature ventricular contractions; Premature atrial contractions; Long term monitoring; Risk stratification (Heart Rhythm O^2 2023;4:592–596)

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Methods

Algorithm description

The novel PVC/PAC discrimination algorithm uses self-adapting measures of RR variability to identify ectopic beats and compares dynamic measures of QRS amplitude of detected ectopic beats with surrounding beats to differentiate PVCs and PACs from normal QRS events. Ectopic beats with amplitudes different from normal QRS complexes are identified as PVCs, while beats that are similar to normal beats are labeled PACs. Users are provided with trends of the daily PVC and PAC burden, as shown in Supplemental Figure 1.

Data and statistical analysis

The PVC/PAC discrimination algorithm was developed and validated using 60-second subcutaneous electrocardiogram (ECG) episodes from BIOMONITOR III and IIIm devices. The validation dataset was independent from the development dataset and consisted of periodic subcutaneous ECG episodes obtained from BIOTRONIK's CERTITUDE registry, a real-world evidence generating research program, including data from BIOTRONIK Home Monitoring and other sources. The CERTITUDE registry has received approval from the Advarra Institutional Review Board (Columbia, MD), and data from the CERTITUDE registry have been published previously.[12] All patients provided authorization for use of their data, and the research reported in this article adhered to the Helsinki Declaration as revised in 2013.

Patients who were implanted with BIOMONITOR III/IIIm for unexplained syncope were selected from the CERTITUDE registry, and up to 5 snapshots were sampled from each patient to create the validation dataset. The validation dataset consisted of 1452 episodes from 435 patients; more information about snapshot selection is provided in the Supplemental Appendix. Snapshots were reviewed by 3 experts, who were blinded to algorithm results, and adjudicated each QRS complex as PVC, PAC, or normal. Runs of 2 or more consecutive PVCs/PACs were excluded from analysis.

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KEY FINDINGS

- In a large dataset containing sECG data recorded in 435 patients, the novel PVC/PAC discrimination algorithm detects PVCs with high sensitivity (73.1%) and specificity (99.95%).
- The PVC/PAC discrimination algorithm detects PACs with high specificity (99.9%) with a tendency to overestimate PAC frequency.
- Patient PVC burden determined by the PVC/PAC discrimination algorithm was highly correlated with true PVC burden, demonstrating that this algorithm provides an accurate measure of underlying PVC burden. Long-term PVC/PAC burden monitoring provides improved diagnostic accuracy over Holter monitoring, which can be prone to short-term fluctuations.

Table 1 Patient demographics and validation dataset characteristics

Number of patients	435
Number of snapshots	1452
Sex	
Male	155 (35.6)
Female	207 (47.6)
Unknown/not disclosed	73 (16.8)
Age	
Mean ± SD, y	71.6 ± 12.5
Median, y	73.3
Range, y	19.3–93.7
Implantation date	11/12/2019 to 06/17/2022
Snapshot date	11/22/2019 to 08/01/2022
Adjudicated beats	
Number of PVCs	620
Number of PACs	165
Total number of beats	145,553

Values are n or n (%), unless otherwise indicated.

PAC = premature atrial contraction; PVC = premature ventricular contraction.

Table 1 summarizes the dataset and relevant demographic information.

Cardiac event adjudications were compared with algorithm classifications to calculate overall and patient-averaged sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). For patient-averaged analysis, counts were pooled across each patient's snapshots and then averaged across all patients. Furthermore, generalized estimating equation estimates for the various performance metrics along with the 95% confidence intervals were calculated to adjust for the multiple PVCs/PACs observed in each subject. Finally, algorithm and adjudicated PVC and PAC burden were estimated for each patient.

Results

Examples of PVCs and PACs detected by the algorithm are shown in Figure 1, including detection multifocal PVCs, PVC bigeminy, and an isolated PAC. Additionally, results of the PVC/PAC discrimination algorithm are summarized in Table 2. The algorithm discriminated PVCs with an overall sensitivity of 73.1% and an overall specificity of 99.95%. The algorithm also discriminated PACs with an overall sensitivity of 60.0% and specificity of 99.9%. Finally, the patient-specific PVC burden between expert adjudications and algorithm classifications was highly correlated ($r = 0.86$, $P < .001$), with a mean error of –0.095%, as shown in Figure 2A. PAC burden between expert adjudications and algorithm classifications was also significantly correlated ($r = 0.57$, $P < .001$), with a mean error of 0.060%. PPV and NPV were not calculated for PACs due to the low prevalence of PACs in this dataset.

Discussion

The prevalence of ectopic beats is an important indicator of cardiac health. Frequent PVCs have been associated with elevated risk of HF and death, and recent guidelines for cardiovascular therapy recommend treatment for patients with high PVC burden.[5,6,7] Similarly, frequent PACs have been associated with elevated risk of new-onset AF, stroke, and death.[10] PVC detection algorithms have previously been implemented in cardiovascular implantable electronic devices such as implantable cardioverter-defibrillators, and in offline analysis of ambulatory ECG recordings such as Holter monitors. These devices have multiple leads that provide consistent ECG signals, and typically utilize prematurity criteria and template-matching algorithms to detect PVCs and PACs with high sensitivity. ICMs, however, record single-lead subcutaneous ECG, and QRS morphology can vary significantly based on posture changes or patient activity; thus, a more dynamic algorithm is needed respond to QRS changes. Additionally, ICMs are designed for extended monitoring periods with limited computational capacity and are not able to implement complex offline algorithms, such as those used to analyze Holter monitor data. Currently, no ICM provides users with both PVC and PAC trends.

The novel PVC/PAC discrimination algorithm described in this report was designed to balance specificity and sensitivity for PVC discrimination, given the computational limitations of ICMs. This PVC discrimination algorithm exceeded performance of the only known published ICM algorithm[13] by 12.1% in PPV (88.0% compared with 75.9%), while maintaining similar

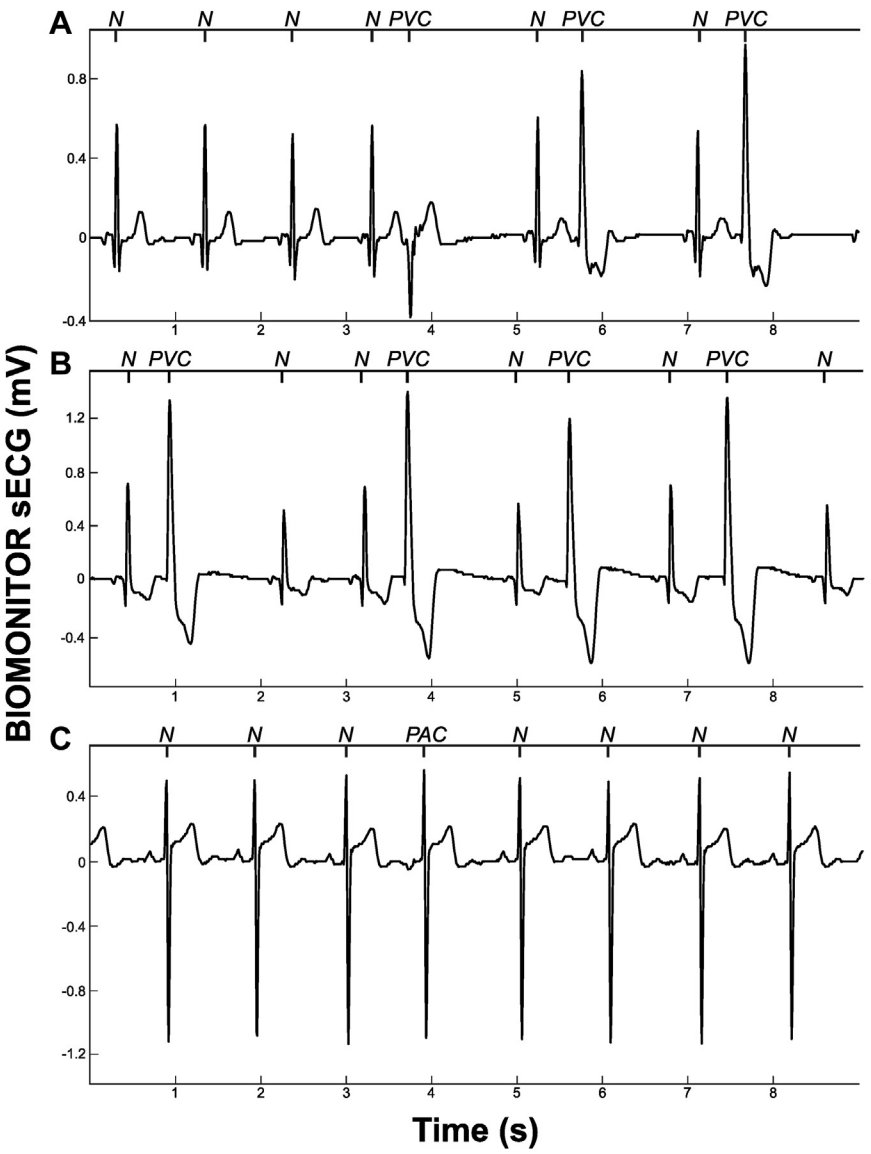

Figure 1 Example subcutaneous electrocardiogram (sECG) strips showing premature ventricular contraction (PVC), premature atrial contraction (PAC), and normal (N) beats classified by the algorithm. **A:** Multifocal PVCs and bigeminy rhythm detection. **B:** Detection of onset of PVC bigeminy. **C:** Detection of an isolated PAC.

sensitivity (73.2% compared with 75.2%). The algorithm performance was also robust across the entire dataset, with patient-averaged performance exceeding the previously published algorithm in both sensitivity (74.5% compared with 69.9%) and PPV (84.8% compared with 40.6%). However, due to the low prevalence of PACs and occasional variability in the QRS amplitude, PACs were sometimes misclassified as PVCs, leading to a lower sensitivity for PAC discrimination. Similar to the previously published ICM algorithm, this algorithm is limited in its ability to detect runs of consecutive PVCs/PACs: the algorithm utilizes ectopic timing and morphology comparisons to surrounding beats, both of which are unreliable in the case of couplets and runs. Although the algorithm cannot detect consecutive ectopic beats, it is able to detect unifocal and multifocal PVCs, as well as bigeminy and trigeminy episodes of both PVCs and PACs, as shown in Figure 1.

Future improvements could be made to allow detection of PAC and PVC couplets, allow classification of ventricular and supraventricular tachycardia (characterized by runs of 3 or more PVCs or PACs, respectively), and improve PAC discrimination. Future studies could also assess the performance of the algorithm on data collected from 24-hour Holter monitors, which serve as a standard for assessing ectopic prevalence and have the benefit of greater computational

Table 2 PVC/PAC discrimination algorithm performance metrics

	Overall performance (%)	Patient average performance (%)	GEE (95% CI) (%)
PVC performance			
Sensitivity	73.1	74.5	70.6 (62.9–78.3)
Specificity	99.95	99.9	99.97 (99.93–100.0)
PPV	88.0	84.8	81.0 (73.8–88.1)
NPV	99.9	99.8	99.9 (99.9–100.0)
PAC performance*			
Sensitivity	60.0	58.5	52.3 (36.8–67.8)
Specificity	99.9	99.9	99.9 (99.8–99.9)

CI = confidence interval; GEE = generalized estimating equation; NPV = negative predictive value; PAC = premature atrial contraction; PPV = positive predictive value; PVC = premature ventricular contraction.
*PPV and NPV were not calculated for PACs due to low PAC prevalence.

power through offline analysis. Additionally, ICMs with PVC/PAC detection capabilities could be used to assess the impact of PVC/PAC burden on longitudinal risk of HF or stroke. Prospective studies in specific patient cohorts such as HF, post–myocardial infarction, new-onset AF, or stroke are also needed to further evaluate the performance of the algorithm and its impact on therapy decisions and outcomes.

Conclusion

The PVC/PAC detection algorithm detected PVCs with similar sensitivity to the only known published PVC discrimination algorithm in ICMs and provided improved specificity/PPV. Furthermore, the algorithm was highly specific for detection of PACs, providing the first PAC detection available in ICMs. Additionally, the algorithm reported the patient-level PVC and PAC burden with a high degree of accuracy. This PVC/PAC detection algorithm would provide a valuable clinical diagnostic to monitor PVC/PAC burden trends for therapy guidance. Measurement of PVC burden combined with the 5-year longevity of the BIOMONITOR ICM could provide an innovative approach to optimize clinical management of patients.

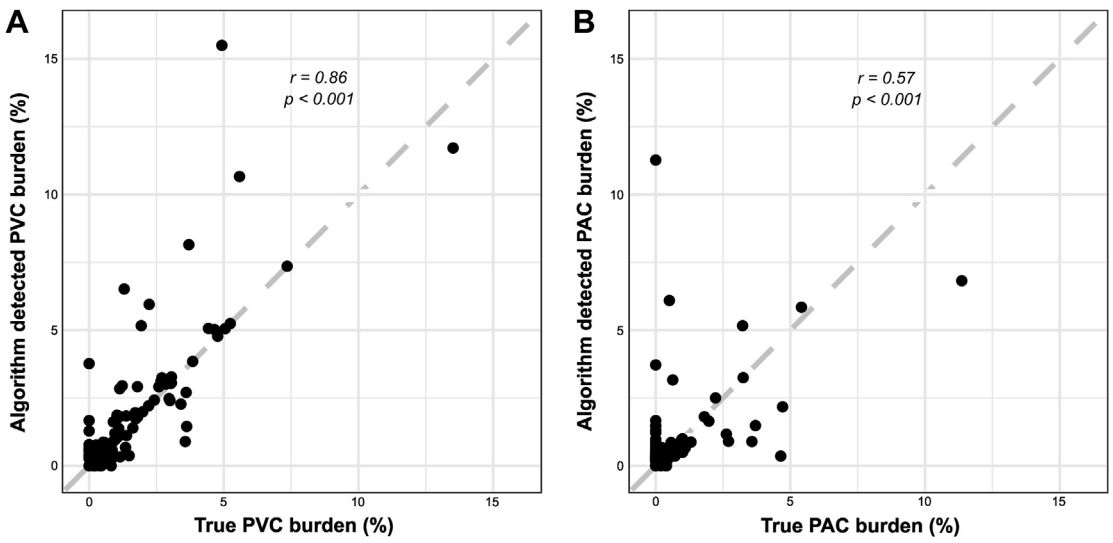

Figure 2 Correlation of premature ventricular contraction (PVC) burden **(A)** and premature atrial contraction (PAC) burden **(B)** based on expert adjudications and algorithm classifications, with a Pearson correlation coefficient of r = 0.86 for PVC burden and r = 0.57 for PAC burden.

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Patient Consent: All patients provided authorization for use of their data.

Ethics Statement: The CERTITUDE registry has received approval from the Advarra Institutional Review Board (Columbia, MD), and data from the CERTITUDE registry has been published previously. The research reported in this article has adhered to the Helsinki Declaration as revised in 2013.

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