ENHANCING CLINICAL EFFICIENCY: AUTONOMOUS DETERMINATION OF CARDIAC EFFECTIVE REFRACTORY PERIOD USING ECG SIGNALS

Richard Redina[1, 2], Marina Filipenska[1]

[1]Department of Biomedical Engineering, Faculty of Electrical Engineering and Communications, Brno University of Technology, Brno, Czech Republic

[2]International Clinical Research Centre, St. Anne's Hospital, Brno, Czech Republic

Abstract

Electrophysiological procedures for managing arrhythmias remain time-consuming, causing patients to wait for critical interventions. To address this pressing need, we introduce a revolutionary algorithm that autonomously calculates the effective refractory period (ERP) of cardiac tissue from electrocardiogram (ECG). The algorithm principally comprises signal filtering techniques and the detection of local extrema within the signal waveform. This algorithm underwent rigorous assessment using an in-house database of ECG signals acquired from ten patients who underwent electrophysiological examinations. Fundamental digital signal processing methods, such as linear filtering and thresholding, were employed in the determination of ERP. The algorithm yielded results congruent with the ERP values established by electrophysiologists in nine out of ten cases, with a standard deviation of 18.97 milliseconds. By being accurate and easy to integrate., this algorithm holds promise for real-time deployment in clinical settings, where it could potentially streamline and automate stimulation protocols, thereby expediting the examination process.

Keywords

Cardiac Electrophysiology, Effective Refractory Period, Arrhythmology, S1–S2 Stimulation, Intracardiac Electrogram

Introduction

In our contemporary landscape, the prevalence of cardiac ailments is steadily mounting, emphasizing the critical need for improved treatment modalities [1]. Within this context, electrophysiology emerges as a realm ripe for innovative breakthroughs in cardiac care.

Electrophysiology is a specialized field dedicated to the investigation of electrical phenomena in biological systems, with a primary focus on the human body. This discipline aiming on the precise measurement of electrical signals originating within cells, tissues, and organs, all in the pursuit of deeper insights into pathological conditions [2].

The cornerstone of electrophysiology's approach to managing cardiac arrhythmias is the electrophysiological examination [3]. This procedure is pivotal in its dual role of elucidating tissue characteristics under scrutiny, identifying aberrant conduction pathways between atria and ventricles, and pinpointing the origins of cardiac arrhythmias. Moreover, it encompasses therapeutic dimensions, involving the isolation of affected myocardial segments through the application of radiofrequency energy.

Our research is chiefly focused on streamlining the diagnostic phase of this procedure, particularly in automating the determination of the effective refractory period (ERP) of the conduction system. Our ultimate goal is to expedite the entire examination process, which is inherently time-consuming, through the automation of this critical step. Additionally, we provide a proficient and unbiased diagnostic tool for the attending physician. This endeavour marks a significant stride toward enhancing the efficiency and precision of cardiac examinations and treatments.

Lekar a technika – Clinician and Technology 2024, vol. 54(2), pp. 37–42, DOI: 10.14311/CTJ.2024.2.01
ISSN 0301-5491 (Print), ISSN 2336-5552 (Online)

Methods

Dataset

An internal database of signals obtained during electrophysiological examinations conducted at the University Hospital Brno was utilized for the development of the algorithm for automated ERP measurement. All participants provided written informed consent. A total of ten signals were randomly selected from various patients undergoing ERP measurements of the atrioventricular (AV) node.

The signal durations ranged from 57 to 208 seconds. The St. Jude WorkMate 4.2 EP, St. Jude Medical, USA system was employed for signal acquisition, with a sampling frequency of 2000 Hz and a voltage resolution of 78 nV/LSB. The acquisition system is equipped with a built-in band-stop filter to suppress the 50 Hz frequency and a high-pass filter with a cut-off frequency of 0.1 Hz to eliminate low-frequency noise.

During the procedure, patients were subjected to conventional twelve-lead surface ECG measurements alongside five intracardiac electrogram leads. These intracardiac electrograms were recorded using ten-pole catheters positioned in the coronary sinus (CS).

S1–S2 stimulation

A crucial aspect of the recording process involved S1–S2 stimulation, a widely employed protocol for assessing the electrophysiological characteristics of the tissue under investigation, particularly in ERP determining [4]. This protocol entails repetitive stimulation of the tissue with an S1 interval, succeeded by one or more stimuli at an S2 interval, typically shorter.

The precise number of stimuli and the duration of the S1 phase can exhibit variability. By incrementally decreasing the length of the S2 interval, a threshold is reached where the examined tissue can no longer respond to the stimulus. The ERP of the tissue is then determined as the shortest duration of the S2 interval to which the tissue remains responsive. A visual representation of this protocol is presented in Fig. 1.

When assessing the ERP of the AV node, stimulation is conducted at the atrial level (CS leads), with response monitoring taking place at the ventricular level (surface ECG).

Automatic ERP measurement

The proposed methodology for automated ERP detection is elegantly straightforward yet highly efficient, encompassing a series of pre-processing and analytical steps applied to both intracardiac and surface recordings (see Fig. 2).

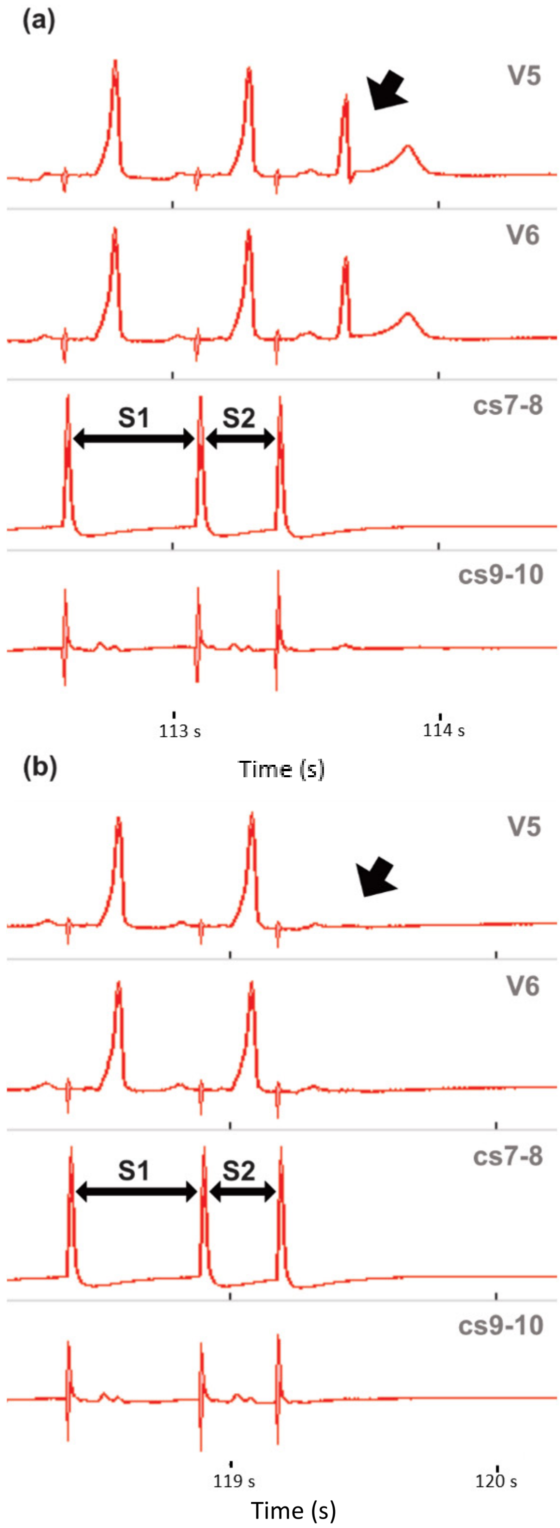

Fig. 1: S1–S2 stimulation. Number of S1 stimuli (T = 500 ms) are followed by shorter S2 stimulus T = 300 ms (a) or T = 290 ms (b). The last one transduced is a stimulus with a period of 300 ms; shorter S2 was not transduced (black arrows).

Lekar a technika – Clinician and Technology 2024, vol. 54(2), pp. 37–42, DOI: 10.14311/CTJ.2024.2.01
ISSN 0301-5491 (Print), ISSN 2336-5552 (Online)

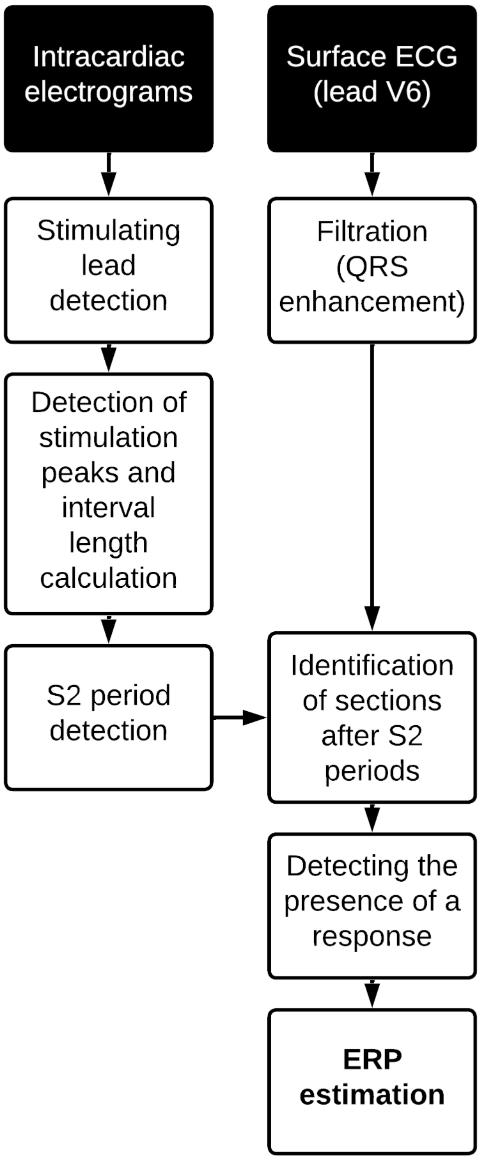

Fig. 2: Block scheme of the algorithm for automated ERP detection.

Initially, a lead showcasing exclusively stimulation spikes, characterized by the highest amplitudes among all recorded signals, is singled out. Within this lead, stimulation spikes are further pinpointed as deviations meeting specific criteria: their peak magnitude must be at least 75% of the signal's maximum value, with adjacent spikes separated by a minimum of 150 milliseconds. In the intervals between individual stimulations, the search commences for subsequent S2 periods shorter than the preceding S1 period.

Subsequently, the analysis shifts to surface lead V6, which undergoes filtration. It is subjected to both a low-pass filter with a cut-off frequency of 45 Hz and a high-pass filter with a cut-off frequency of 15 Hz, utilizing a finite impulse response (FIR) filter order of 35. This process accentuates the QRS complexes while suppressing unwanted components [5].

Following this, segments lasting 500 milliseconds are selected after the already identified S2 periods, beginning 25 milliseconds after the period's ends. These segments are presumed to contain the heart's response to stimulation, manifesting as a QRS complex in the surface ECG. Therefore, QRS complex detection is performed in each selected segment by comparing the maximum deviation of the segment with an empirically set threshold of 2 μV. A subthreshold maximum indicates the absence of a QRS complex in the segment following stimulation, signifying the absence of tissue response to such a brief stimulation period. The last S2 period featuring a present QRS complex is identified as the ERP and reported for further utilization.

Model robustness

One of the crucial attributes of any signal processing algorithm is its robustness against noise that may be present in the data. There can be several types of such noise, and for the purposes of this work, two were selected, the occurrence of which is nearly unavoidable.

The first one is random noise, specifically Gaussian noise. This type of noise is characterized by a probability density function equal to the normal distribution. The second type of noise is power line interference (PLI). The presence of this type of noise is almost inevitable under common conditions due to the ubiquitous electrical grid. An advantage of this noise is its narrow spectral characteristic, primarily limited to the frequency of 50 Hz (or 60 Hz in the US).

Both types of noise were artificially introduced into the signals, and various levels of signal-to-noise ratio (SNR) were tested to evaluate the algorithm's performance under challenging conditions. The robustness of the model was tested at a total of five SNR levels (20, 15, 10, 5, and 0 dB).

Results

ERP estimation

The presented algorithm was applied to ten records from electrophysiological examinations, and the algorithm's outputs are summarized in Table 1. In nine out of ten cases, the ERP of the AV node was correctly identified. In one case, the ERP of the AV node was not correctly identified due to the presence of a pathological conduction pathway with a lower ERP than that of the AV node. Consequently, the stimulation propagated to the ventricles. However, the propagated stimulus was delayed and exhibited altered morphology. This case is illustrated in Fig. 3.

Lekar a technika – Clinician and Technology 2024, vol. 54(2), pp. 37–42, DOI: 10.14311/CTJ.2024.2.01
ISSN 0301-5491 (Print), ISSN 2336-5552 (Online)

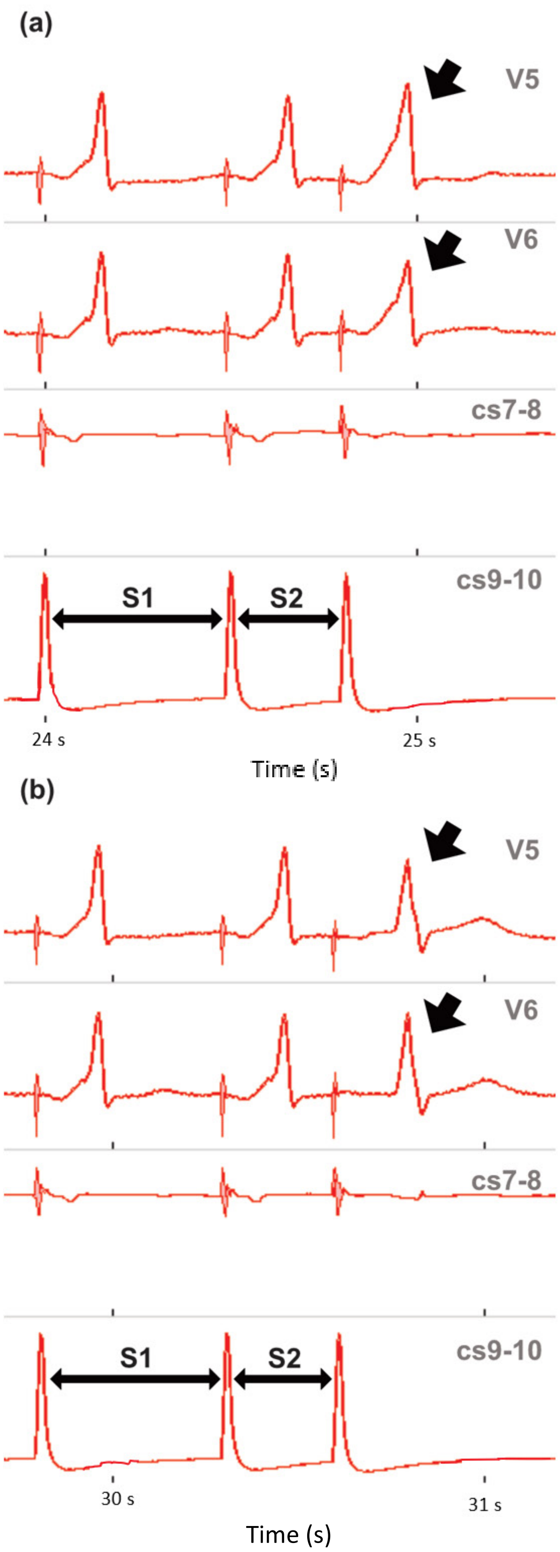

Fig. 3: Noticeable change in the morphology of the QRS complex marking the reaching of the ERP accessory pathway (a). Exceeding the ERP of the accessory pathway results in the disappearance of the characteristic delta wave of the second case (b).

Table 1: Resulting ERP values (ms) measured during the procedure by the electrophysiologist and obtained using the algorithm. The last row represents the standard deviation (ms) for the whole set.

Patient	Physician	Algorithm
1	270	270
2	310	**250**
3	300	300
4	260	260
5	320	320
6	220	220
7	340	340
8	320	320
9	400	400
10	310	310
σ	-	18.97

Robustness to artificial noise

As demonstrated in the study [6], the commonly measured SNR levels in signals typically hover around 10 dB, a level that the model should be able to handle. In the context of our experiment, we independently corrupted the surface ECG signal with both types of noise. The algorithm's performance on the corrupted data is summarized in Tables 2 and 3. The bolded values in the tables highlight the difference from the annotation provided by the physician.

Table 2: ERP values (ms) in individual patients under different Gaussian noise level (dB). The last row represents the standard deviation (ms) for the whole set.

SNR Patient	20	15	10	5	0
1	270	270	270	270	270
2	250	250	250	250	250
3	300	300	300	300	300
4	260	260	260	260	**250**
5	320	320	320	320	**380**
6	220	220	220	**330**	220
7	340	340	**330**	340	**330**
8	320	320	320	320	320
9	400	400	400	400	400
10	310	310	310	**300**	**340**
σ	18.97	18.97	18.97	**19.24**	**34.79**

Although increasing variations with increasing noise level are captured in the tables, a two-way ANOVA test did not confirm a significant effect of intensity level or noise type ($p > 0.05$). Thus, it can be said that the proposed method does not show statistically significant deviations in either category.

Lekar a technika – Clinician and Technology 2024, vol. 54(2), pp. 37–42, DOI: 10.14311/CTJ.2024.2.01
ISSN 0301-5491 (Print), ISSN 2336-5552 (Online)

Table 3: ERP values (ms) in individual patients under different power line interference noise (dB). The last row represents the standard deviation (ms) for the whole set.

SNR Patient	20	15	10	5	0
1	270	270	270	270	270
2	250	250	250	250	250
3	300	300	300	300	300
4	260	**250**	**250**	**250**	**250**
5	320	320	320	320	320
6	220	220	220	220	220
7	**330**	**330**	**330**	**330**	**330**
8	320	320	320	320	320
9	400	**390**	**390**	**390**	**390**
10	**300**	**300**	**300**	**300**	**300**
σ	18.97	19.49	20.00	20.00	20.00

Discussion

The algorithm presented by us serves as a fundamental building block for the automated assessment of ERP during electrophysiological procedures. In our paper, we show that ERP measurements can be largely automated and thus save time during electrophysiological procedures. Despite promising results, this is only a proof of concept.

One of the limitations of the algorithm could undoubtedly be the relatively small dataset on which it was tested. Unfortunately, a small dataset may not adequately capture the wide interindividual variability present among different patients. Additionally, the algorithm does not account for the possible presence of accessory conduction pathways, which may be particularly relevant in younger patients.

As evident from the tables, the algorithm's performance deteriorates with increasing noise levels. To compare the results for the individual types of noise, we can use the standard deviation of the error from the original annotation. A clear comparison emerges, showing that the algorithm handles PLI noise better.

This is likely due to the fact that the signal passes through a low-pass filter with a cut-off frequency of 45 Hz, which should effectively filter out the unwanted influence of PLI.

Conversely, the wideband Gaussian noise is removed less effectively, and the standard deviation value almost doubles with increasing SNR. To achieve better noise removal, it would be necessary to add an additional filter or reduce the cut-off frequency of the mentioned high-pass filter.

The results obtained by our method not only correspond to the results obtained manually by an electrophysiologist during the procedure, but also align with the values obtained experimentally in the study [7].

Despite the mentioned limitations, there is significant potential for testing the algorithm on additional records from different patients. Another avenue for expanding the algorithm is considering the examination of other tissues, thus involving the analysis of various lead combinations. An ancillary product of the algorithm is the identification of the stimulated rhythm, which can provide valuable information for training deep learning systems.

Since one of the limitations mentioned is the relatively small dataset used for testing, performing cross-validation on larger datasets from diverse patient populations can provide a more comprehensive assessment of the algorithm's performance and its ability to generalize across different patient cohorts.

Given the algorithm's inability to account for accessory conduction pathways, conducting sensitivity analyses or simulations to assess the impact of these pathways on algorithm performance could be valuable. This could involve introducing simulated accessory pathways into the data and evaluating how the algorithm responds.

Conclusion

In our paper, an algorithm for the automatic detection of AV node ERP was introduced. The algorithm demonstrated success in nine out of ten cases, establishing its reliability. Further development of the algorithm could potentially lead to fully automated real-time measurement of the ERP in various parts of the conduction system during examinations.

The use of our method can reduce the time of S1–S2 stimulation, which can take several minutes. The automatic assessment of the cardiac tissue response can free the hands of the physician, who can focus on other activities during the examination—e.g. inserting therapeutic catheters.

Partial results from this work were previously published at the Trends in Biomedical Engineering 2023 conference [8].

Acknowledgement

Brno Ph.D. Talent Scholarship Holder funded by the Brno City Municipality.

During the preparation of this work the authors used OpenAI's ChatGPT and Google Bard for pre-correcting English syntax and grammar. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

References

[1] Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The Global Burden of Cardiovascular Diseases and Risk: A Compass for Future Health. Journal of the American College of Cardiology. 2022 Nov;80(25):2361–71. DOI: 10.1016/j.jacc.2022.11.005

[2] Katritsis DG, Boriani G, Cosio FG, Hindricks G, Jaïs P, Josephson ME, et al. European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLAECE). EP Europace. 2016 Nov 17;19(3):465–511. DOI: 10.1093/europace/euw301

[3] Martin E, Alan B, Martin F. Základy srdeční elektrofyziologie a katétrových ablací. Grada Publishing a.s., 2012. 264 p.

[4] Nothstein M, Luik A, Jadidi A, Sánchez J, Unger LA, Wülfers EM, et al. CVAR-Seg: An Automated Signal Segmentation Pipeline for Conduction Velocity and Amplitude Restitution. Frontiers in Physiology. 2021 May 24;12:673047. DOI: 10.3389/fphys.2021.673047

[5] Thakor NV, Webster JG, Tompkins WJ. Estimation of QRS Complex Power Spectra for Design of a QRS Filter. IEEE Transactions on Biomedical Engineering. 1984 Nov;BME-31(11):702–6. DOI: 10.1109/TBME.1984.325393

[6] Blanco-Velasco M, Weng B, Barner KE. ECG signal denoising and baseline wander correction based on the empirical mode decomposition. Computers in Biology and Medicine. 2008 Jan;38(1):1–13. DOI: 10.1016/j.compbiomed.2007.06.003

[7] Corino VD, Sandberg F, Platonov PG, Mainardi LT, Ulimoen SR, Enger S, et al. Non-invasive evaluation of the effect of metoprolol on the atrioventricular node during permanent atrial fibrillation. Europace. 2014 Oct 31;16(suppl_4):iv129–34. DOI: 10.1093/europace/euu246

[8] Ředina R, Ronzhina M. Estimation of myocardial conduction velocity using a coronary sinus catheter. In: Novak V, editor. Proceedings II of the 29th Conference STUDENT EEICT 2023; 2023 Apr 25. Brno: Brno University of Technology, Faculty of Electrical Engineering and Communication; c2023. p. 156–60. DOI: 10.13164/eeict.2023.156

Richard Ředina
Department of Biomedical Engineering
Faculty of Electrical Engineering and Communication
Brno University of Technology
Antonínská 2, CZ-601 00, Brno

E-mail: 195715@vut.cz
Phone: +420 541 146 676

Lekar a technika – Clinician and Technology 2024, vol. 54(2), pp. 37–42, DOI: 10.14311/CTJ.2024.2.01
ISSN 0301-5491 (Print), ISSN 2336-5552 (Online)