ELECTRONICS AND ELECTRICAL ENGINEERING
ISSN 1392 – 1215 *2007. No. 5(77)*
ELEKTRONIKA IR ELEKTROTECHNIKA

MEDICINE TECHNOLOGY
T 115
MEDICINOS TECHNOLOGIJA

Influence of the Variability of Excitation Parameters on a Rhythm in Parasystole Mathematical Model and in Clinic

D. Eidukas, R. Labrencas
Department of Electronics Engineering, Kaunas University of Technology,
Studentų st. 50, LT-51368 Kaunas, Lithuania; tel.: +370 37 300525; e-mail: danielius.eidukas@ktu.lt
I. Grigaliūnienė, M. Skučas
Institute of Cardiology, Kaunas University of Medicine,
Sukilėlių st. 17, LT-50009 Kaunas, Lithuania; tel.: +370 37 302894; e-mail: aritmiki@kmu.lt
R. Lekas
Institute for Biomedical Research, Kaunas University of Medicine,
Eivenių st. 4, LT-50009 Kaunas, Lithuania; tel.: +370 37 302951; e-mail: bmti@bmti.kmu.lt

Introduction

Experimental and clinical data showed that the paroxysms of atria fibrillation can be provoked by changes in the heart rate variability (HRV) under the influence of parasympathetic nerve tone. This served as the reason for studying the relationship of heart rhythm with HRV in clinic [1, 2]. It is expected that simulation of the occurrence of various cardiac arrhythmias by mathematical models could elucidate the conditions of the development of arrhythmias [3, 4]. Our article present the investigation by the mathematical model of parasystole arrhythmias, when oscillators of excitation are simulated simultaneously – a pacemaker "sinus node" (with the impulse period of T_s), and an additional (ectopic) pacemaker (with the impulse period of T_e. The refractory characteristic we ascribed to the excitation medium as capable to respond to the excitation pulse and the length of the modeled refractory period (T_{ref}) did not depend on the pacemaker impulses.

The aims of the study

To investigate the changes in the modeled rhythm using the mathematical computerized model of pure cardiac parasystole, applying accidental variability of the duration of the periods: T_s, T_e, T_{ref}.

To estimate the congruence of the modeled parasystolic arrhythmias with arrhythmias registered in patients during ECG monitoring.

Methods

The computerized model provides a possibility for a random fluctuation of T_s, T_e and T_{ref} within the permissible (concerning the clinical data) limits.

For the investigation, we used a self-designed model of pure parasystole cardiac arrhythmias [5]. Within the model, the phase response curves (PRC) of both pacemakers were

$$PRCs = 0 \text{ and } PRCe = 0. \quad (1)$$

We chose three regimes of excitation pulse periods (T_s and T_e) in both pacemakers (Table 1). In each modeled regime, we compared the changes in the character of the rhythm, when three values of the variability of the randomly fluctuating length of T_s and T_e were selected for each different pulse rate. The choice of these concrete values was based on the known rhythm variability in experimental models of arrhythmia (in isolated rabbit atria) and in RR intervals of monitoring ECG records of patients, (observed even in the absence of cardiac pathology). The modeled rhythm is presented in rhythmograms and Poincare maps.

Table 1. Select duration of T_s, T_e, T_{ref} and its variability, ms. SDNN – the standard deviation of T_s, T_e, T_{ref} values, ms

T_s	500			800			1500		
T_e	530			830			1530		
SDNN of T_s, T_e	0	3.3	16.7	0	5.3	26.7	0	10	50
T_{ref}	200-600			200-900			200-1600		
SDNN of T_{ref}	0-20			0-30			0-53.3		

In patients' ECG monitoring records we calculate the duration of periodical repetitive arrhythmic cycles of parasystole (T_c). Also we calculate T_c theoretical by the equation (2)

$$T_c = \frac{T_s \times T_e}{T_s - T_e} \quad (2)$$

for the verify whether the parasystole of patients corresponded with the modeled rhythm when the sizes of T_s, T_e, and T_{ref} values and variability on patients' ECG were chosen (T_c in Fig. 1 is indicated by an arrow). We also investigated the dynamics of the similarity and difference in the character of the rhythm between the modeled parasystole and the clinical data.

Results

The analysis of the modeled rhythm showed that in different regimes of excitation source periods (T_s, T_e), when $T_{ref} < \frac{T_e}{2}$, the change in the variability of these periods between 0% and 20% did not have any substantial influence on the character of arrhythmias. The influence of the variability we observed only in that the duration of parasystole repetitive cycle (T_c) became more unequal, and rhythm - more irregular. This is seen in rhythmograms, presented in Fig. 1, when the selected periods were T_s=0.8 s, T_e=0.84 s, and T_{ref}=0.2 s, without their variability (Fig. 1, a), and when their variability was 5.3 ms (Fig. 1, b).

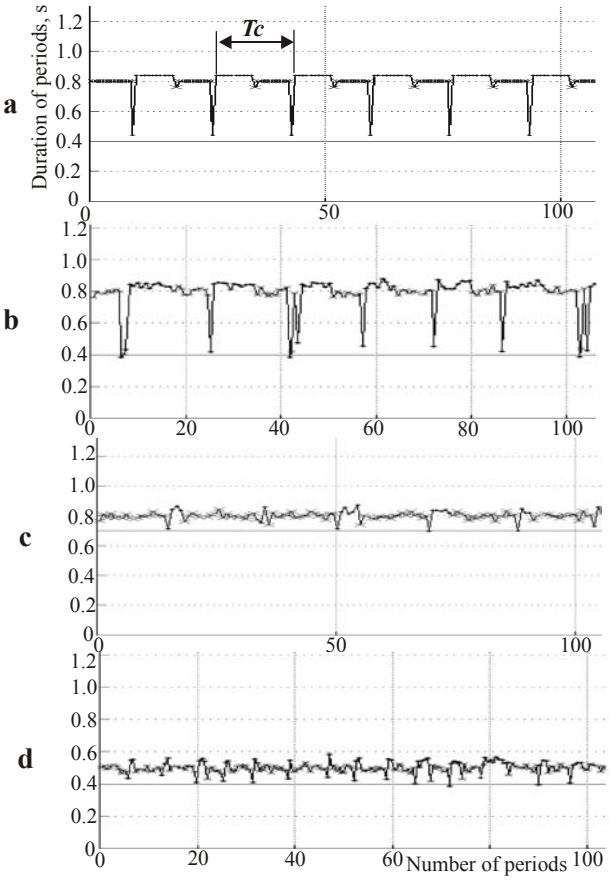

Fig. 1 Rhythmograms of modeled regimes T_s=0.8 s, T_e=0.84 s, T_{ref}=0.2 s: **a** – (without variability); **b** – (variability of 5.3 ms); **c** – (variability of 26.7 ms); **d** – on regime T_s=0.5 s, T_e=0.54 s, T_{ref}=0.4 s, (variability of 26.7 ms)

The comparison with the rhythmograms where the variability of the duration of T_s and T_e was increased to 26.7 ms (Fig. 1, c), showed that such changes in variability did not have any major influence on the character of the rhythm in the model. However, the rhythm changed significantly when the same values and variability of T_s and T_e were used, but T_{ref} was prolonged. Then the rhythm changed essentially because the long arrhythmic intervals disappeared, and only periodically arising single "extrasystole" intervals (T_{Ex}) whose length corresponded to T_{ref}=0.4 s remained (Fig. 1, d).

When imitating tachycardia (when T_s=0.5 s, and T_e=0.54 s) or bradycardia (when T_s=1.5 s, and T_e=1.54 s), the dynamics of rhythm did not differ significantly, and was changing in the same manner. Poincare maps (Fig. 2, a) present the distribution of responses to excitation impulses in the model, in the tachycardia regime (when T_s=0.5 s, and T_e=0.54 s), when the selected T_{ref}=0.2 s, and the variability of the values of all these parameters was 3.3 ms. Fig. 2, b presents the distribution of the response values in the model, in the same T_s, T_e, and T_{ref} regimes, whereas the variability was 16.7 ms.

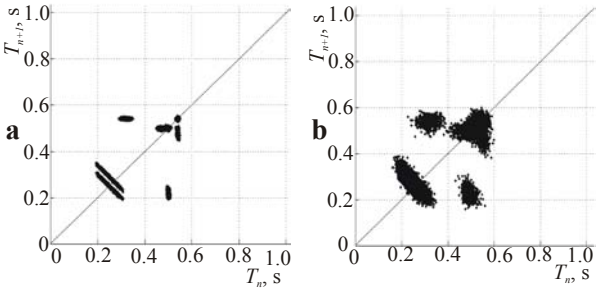

Fig. 2. Poincare maps of the model. Modeled regimes: **a** – T_s 0.5 s, T_e 0.54 s, T_{ref} 0.2 s (variability - 3.3 ms); **b** – T_s 0.5 s, T_e 0.54 s, T_{ref} 0.2 s (variability - 16.7 ms)

In these Poincare maps, the position of the lowermost points and the position of the farthest points, situated in left side, correspond to the chosen T_{ref} length. The situation in Poincare maps was significantly transformed when T_{ref} was increased to 0.4 s. The rhythmogram (presented in Fig. 1, d) shows the latter case. Here one can that the limits of discrete T_c become unidentifiable, the marked T_{Ex} have disappeared, and the rhythm becomes different to the parasystole one. When choosing the bradycardia regime (when T_s=1.53 s, T_e=1.5 s, and T_{ref} =0.2 s) and setting random fluctuation of the values of these periods to ≤20%, the arrhythmic intervals still remained by 3-4 times longer than the rhythmical intervals, but when choosing T_{ref} =0.4 s in the same regimes, the arrhythmic intervals shortened significantly.

The investigation of long-time monitoring records ECG of patient A.B. showed that periodical cycles arrhythmias, when T_{Ex} ranged between 576 ms and 680 ms and variability of T_c duration amounted to 17%, were parasystole. However, the calculation of the total length of the repeating "clinical" cycles according to T_s and T_e values in patient A.B. showed that "clinical" T_c were by 200-400 ms longer, compared to T_c, calculated in the formula (2) according to the clinical values of T_s and T_e, and the variability of T_c was somewhat lesser (Fig. 3). 15 minute-long ECG monitoring records were used to compare the variability of rhythmical RR intervals situated in the interstice between recurrent parasystole cycles (Table 2, positions 1, 2, and 3), and the variability of extrasystoles occurring between rhythmical RR intervals (Table 2, position 4).

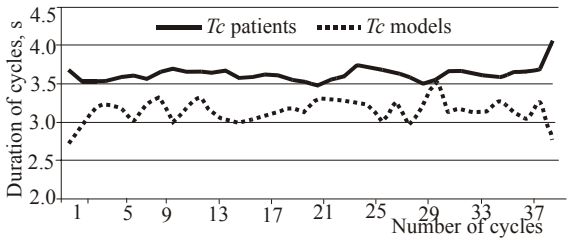

Fig. 3. Duration of parasystole cycles T_c in ECG of patient A.B. (continuous line) and theoretically calculated T_c duration, using formula (2), according to T_s and T_e values of this patient (dotted line)

Table 2. Heart rate and T_{Ex} variability (data in *ms*) during 15 min, in states of strain and repose of patient A.B. SDNN - the standard deviation of all normal-to-normal RR intervals (NN)

	State of patients	Normal-to-normal RR intervals		T_{Ex}	
		Mean RR	SDNN (p<0.05)	Mean T_{Ex}	SDNN (p<0.05)
1	Strain	895	19.0±2.0	591.0	30.2±3.8
2	Strain	593	5.1±0.25	-	-
3	Repose	920	33.8±5.6	613.2	48.1±6.3
4	Repose	849	26.5±1.58	-	-

The duration of T_c did not depend on T_{Ex}, like T_c did not depend on T_{ref} in the model. T_{Ex} in ECG records can reflect the T_{ref} values. Additionally, the variability of RR intervals in patients' ECG Poincare maps indicates that T_{Ex} in parasystole cycles has an analogous meaning to T_{ref} in the model. The analysis of clinical parasystole arrhythmias using Poincare maps showed that the heart variability in such cases reached to 30 ms (Fig. 4, a). We also noticed that cardiac rhythm variability decreased after the disappearance of arrhythmia and with increasing heart rate (Fig. 4, b).

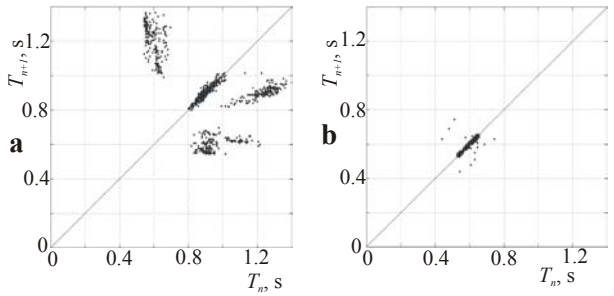

Fig. 4. Variability of RR intervals in Poincare maps, constructed from monitoring of ECG patient A.B. during 15 min: **a** – repose, **b** –exertion

The analysis of the recurrent parasystole cycles in ECG of two patients when each cycle was formed of four arrhythmic periods – T_{Ex}, T_k (the compensation pauses after extrasystole) and two following its RR intervals showed, that the correlation coefficient (r) between the ratio T_k/T_{Ex} and T_c for patient A.B. was r=0.79, n=40 cycles (p<0.01), and for patient D.K. – r=0.62, n=17 cycles (p<0.01).

Discussion

The HRV analysis was used for the evaluation of the influence of the nervous system on cardiac function. It has been found that not only antiarrhythmic drugs reduce HRV. Also the HRV is reduced in patients with ischemic heart disease. But according to D. Žemaitytė [6] when RR intervals shortened, a decrease in HRV on exertion was observed (Fig. 5). The theory of the development of paroxysmal arrhythmias as based on the HRV dynamics is not very clear. Although experiments showed that arrhythmias could be initiated by stimulating cardiac nerves, the causes of atria fibrillation episodes remain unclear in as many as 30% of patients [4].

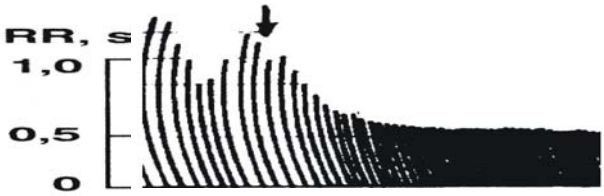

Fig. 5. Decrease in the HRV of patient together with rate acceleration by strain (according to D. Žemaitytė [6]). Start of a strain on heart is indicated by an arrow

Mathematical models were used for investigations of HRV. The presented self-designed parasystole model includes the possibility for a selective alteration of the variability of T_s and T_e. The characteristic of refractoriness for the excitation medium was modeled so that the duration of T_{ref} was not dependent on the length of T_s and T_e. In the model the decrease in the variability of all these parameters had a lesser effect, compared to the increase in T_{ref} duration. This gives us reason to think that in clinic, it is expedient to search for the means that could rapidly and for a longer period of time restore the required duration of T_{ref}. More efforts could be directed not only towards changing of HRV, but also towards the regulation of T_{ref} duration. Since direct measurements of the duration of T_{ref} in cardiac muscle are complicated, RR rhythmograms or Poincare maps are advisable in ECG monitoring.

It is easy to verify that in the Poincare maps of patients' long-term ECG monitoring, the position of the lowest and the left-side points corresponds to T_{Ex} and reflects the duration of T_{ref} length at the given moment. These data show that the Poincare maps are useful for the control of the treatment of parasystolic arrhythmias. Like in the model, T_c did not depend on T_{Ex}. Model remain unclear why the duration of T_c of "clinical" recurrent cycles was by ca. 400 ms longer than theoretically calculated, when T_s and T_e values of patients were entered into the formula (2). One could presume that in clinic, when heart rate increases during exertion, the main role falls on the sinus node. Ikeda N. et al. [4] offered a bidirectional modulated parasystole model, which simulates not only heart sinus node pulses with random variability, but also the influence of the pulses of an "ectopic" source as feedback to sinus node. The model simulates stable paroxysm of bigeminy and/or rhythm, similar to the Wenckebach rhythm, and is based on the influence of experimental external current stimuli on pacemaker cells, which imitate the influence of autonomic cardiac nerves. The authors present the general equation of modulated parasystole. However the authors did not indicate the possibilities for the application of this model.

It is necessary to note that although the suddenly reduction HRV is interpreted as a sign indicating poor prognosis in cases of heart ischemia [7]. Fig. 3 and 4 demonstrate that increased heart rate also reduces HRV. That can be provoked by influence of sympathetic nervous system in time a strain or exercise on heart. Changes in HRV should also be associated with the development of arrhythmias; otherwise, the scale of HRV could be interpreted incorrectly. We believe that the obtained findings data may be relevant for the prognostication of parasystole arrhythmias as well as for its treatment control.

Conclusions

1. The model of pure cardiac parasystole provides the possibility to change the variability of the impulse periods of two competitive excitation sources (T_s and T_e) and the variability of refractory period of the excitation medium (T_{ref}), which allowed for determining that the increase in the variability of these parameters up to 20% did not result in the character of the rhythm, whereas in the same conditions, changes in the duration of T_{ref} allow for transition from stable rhythm to various arrhythmias.

2. The modeled parasystole rhythm and the investigation of patients' long-term ECG monitoring records showed that T_{ref} in RR intervals in Poincare maps correspond to T_{Ex}, and therefore it is expedient to use these maps for the control of changes in ECG RR intervals and/or the efficiency of arrhythmias treatment.

References

1. **Andersen D., Bruggemann T**. Heart rate variability preceding onset of atrial fibrillation // J. Cardiovasc. Electrophysiol. – 1998. – 9. – P.26–29.
2. **Demidova M. M., Tikhonenko V. M.**. Circadian dynamics of heart rate variability in patients with attacks of atrial fibrillation // Kardiologiia. – 2006. – 3. – P.24–30.
3. **Skučas M., Grigaliūnienė I., Barauskienė V. et al**. The dynamics of extrasystolic periods with respect to refractory period in mathematical model of parasystole // Electronics and Electrical Engineering. – 2006. – No. 3(67). – P.87–92.
4. **Ikeda N., Takeuchi A., Hamada A et al**. Model of bi-directional modulated parasystole as a mechanism for cyclic bursts of ventricular premature contractions // Biol. Cybern. – 2004. – Vol.91. – P.37–47.
5. **Skučas M., Grigaliūnienė I., Pyragas K.** Competition of two excitation generators in isolated atria // Electronics and Electrical Engineering. – 2003. – No. 4(46). – P.21–25.
6. **Žemaitytė D**. Authonomic regulation of heart rhythm, Palanga. – 1997. (In Lithuanian).
7. **Foranelli M., Piecoli M., Mileto G. M. et al**. Analysis of heart rate variability five minutes before the on set of paroxysmal atrial fibrillation // Pace. – 1999. – Vol.22. – P.743–749.

Submitted for publication 2007 02 27

D. Eidukas, R. Labrencas, I. Grigaliūnienė, M. Skučas, R. Lekas. Influence of the Variability of Excitation Parameters on a Rhythm in Parasystole Mathematical Model and in Clinic // Electronics and Electrical Engineering. – Kaunas: Technologija, 2007. – No. 5(77). – P. 37–40.

The study introduced the possibility of a random variability of T_s and T_e (simulated as impulse periods of the "sinus node" and the "ectopic" focus) and T_{ref} (as the refractory period of the excitation medium) in the mathematical model of cardiac parasystole. The influence of the variability of these parameters on the modeled rhythm was estimated. We have found that the increase in the variability of up to 20% only makes the rhythm more disorderly, whereas the character of the rhythm is determined by changes in T_{ref} value. We believe, that the T_{ref} is reliably reflected in Poincare map as the duration of the shortest RR intervals registered in the monitoring ECG of patients with parasystole arrhythmias**.** This parameter also is therefore useful by the control of the efficiency of antiarrhythmic treatment. Ill. 5, bibl. 7 (in English; summaries in English, Russian and Lithuanian).

Д. Эйдукас, Р. Лабренцас, И. Григалюнене, М. Скучас, Р. Лякас. Влияние вариабельности параметров возбуждения на ритм в математической модели парасистолии и в клинике // Электроника и электротехника. – Каунас: Технология, 2007. – № 5(77). – С. 37–40.

В математической модели парасистолии сердца введена возможность изменения вариабельности периодов T_s и T_e, симулируемых как периоды синусового узла и эктопического очага, и рефрактерности возбуждающейся среды T_{ref}. Установлено, что моделируемый ритм при увеличении вариабельности T_s, T_e и T_{ref} становится более беспорядочным, в то время как изменение значения T_{ref} меняет характер ритма. Анализ диаграмм *Poincare,* построенных по RR интервалам, зарегистрированным во время мониторинга ЭКГ пациентов, подтвердил, что продолжительность кратчайших RR периодов достоверно отражает T_{ref}, поэтому целесообразно это использовать при контроле эффективности лечения аритмий. Ил. 5, библ. 7 (на английском языке; рефераты на английском, русском и литовском яз.).

D. Eidukas, R. Labrencas, I. Grigaliūnienė, M. Skučas, R. Lekas. Sužadinimo parametrų variabilumo įtaka ritmui parasistolijos matematiniame modelyje ir klinikoje // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2007. – Nr. 5(77). – P. 37–40.

Širdies parasistolijos matematiniame modelyje panaudota galimybė parinkti norimą modeliuojamų sinusinio mazgo ir ektopinio židinio impulsų periodų T_s ir T_e bei sužadinimo terpės refrakterinio periodo T_{ref} variabilumo dydį. Ištirta šių parametrų variabilumo įtaka modelio formuojamam ritmui. Nustatyta, kad variabilumą didinant iki 20 % ritmas darosi dar netvarkingesnis, o T_{ref} dydis turi įtakos ritmo pobūdžiui. T_{ref} dydis patikimai atsispindi Puankare diagramose kaip trumpiausių RR intervalų trukmė, užregistruota pacientų EKG stebėsenos metu. Todėl šį parametrą tikslinga panaudoti klinikoje gydymo efektyvumui kontroliuoti. Il. 5, bibl. 7 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).