Entropy and sequence analysis in Portapres® signals

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Abstract—**Continuous non-invasive recording of blood pressure (BP) waveforms in moving subjects is a challenging task. Portapres® is a unique device that accomplish this task with sufficient reliability. The signals acquisition is complex. Itincludes the blood pressure correction due to the increasing and decreasing elevation of cuffs so, inevitably, the signal is corrupted by artifacts. The aim of this paper is to analyze the errors in cardiac parameters extracted from the recorded waveforms and to check the robustness of the frequently implemented analytical methods. The methods include clinically approved sequence analysis that tests the spontaneous baroreflex sensitivity, and entropy analysis (cross-approximate and cross-sample entropy) that are unavoidable in scientific studies.**

Key words – continuous non-invaseve blood pressure monitoring; Portapres®, cardiac parameters, entropy, sequence analysis.

I. INTRODUCTION

The most reliably recording of the continuous blood pressure (BP) waveforms isperformed by sensors implanted into abdominal aorta with wired or (preferably) wireless connection to the remote A/D convertor. Such recordings are highly invasive and could be performed during the surgery, or in experiments with laboratory animals. Completely non-invasive, cuff-less, recording is a subject of extensive studies. In spite of substantial progress that has been made [1]-[9],no commercial device was approved.

Semi-invasive ambulatory recording of continuous waveforms can be performed Finapres® system that use finger cuffs. The Portapres® is a Finapres®-based advanced technological solution that combines two golden clinical standards: a) 24-hour continuous, real-time recordings of arterial blood pressure in ambulatory subjects and b) recording the blood pressure in freely moving subjects. It is functional from 0 to 35 Celsius degrees and battery capacity provides 60 hours in portable regime [10].

Embedded Beatscope® software allows online monitoring, control, storage and offline review of the complete Portapres®data. Beatscope® extracts cardiac parameters, including systolic and diastolic blood pressure (SBP and DBP) and pulse interval (PI). Sampling frequency is equal to 100Hz, yielding a PI signal with resolution of 10ms. An important Portapres®feature that makes its uniqueness is the blood pressure correction, necessary due to increasing and decreasing elevation of finger cuffs.

Cardiac parameters (SBP, DBP and PI) are extracted at beat-to-beat basis (cca 72 times per minute). For the sake of comparison, usual “pressure holter” wearable devices yield one SBP signal per 15 minutes.

Yet, Portapres®still needs a finger cuff. In order to prevent the finger exhaustion during the long measurements, two cuffs at adjacent fingers are used. The cuff functionality periodically changes, with a period of one or two minutes.The periodical change of cuffs induces periodical artifacts in the recorded signal.

The aim of this paper is to analyze the effect of artifacts induced by cuff changes. Three types of analyses were considered: basic analysis, standard in any ambulatory monitoring; baroreflex sensitivity based on standard sequence analysis; and, finally, entropy analysis unavoidable in scientific studies. The signals for analysis are recorded at Bezanijska Kosa hospital, with the courtesy of prof. dr Branislav Milovanovic. To our best knowledge, this is the unique Portapres® in Republic ofSerbia.

II. MATHERIALSAND METHODS

A. Experimental data

The signals were recorded from 25 healthy volunteers. Recording was performed according to the ethical protocol at Medical faculty, University of Belgrade, and ethical protocol of Bezanijska Kosa Hospital. Each subject signed a document of accordance. Eighteen signals were short, while 7 ones were longer than 10 minutes and could be used for entropy study. Blood pressure sampling interval was 10ms, which is sufficient for cardiac time series (although 1ms is a recommendation for ambulatory recording in sitting or lying patients). Time series extracted from BP waveforms were systolic blood pressure (SBP) obtained as local BP maxima and pulse interval (PI), obtained as an interval between the local maximal increasing gradients $(\Delta(BP)/\Delta T)max$, i.e. as maximal pressure change $(\Delta)BP$ per sampling interval $\Delta T=10ms$.

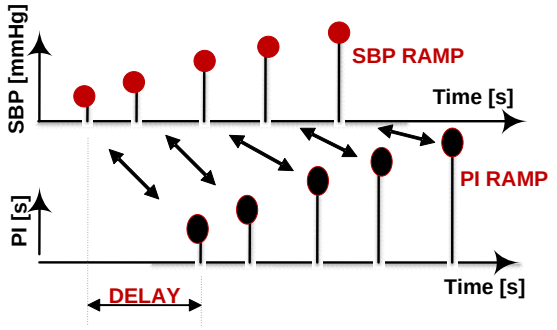

Figure 1. Ramps in SBP and PI time series that form a sequence

B. Methods

Sequence method for baroreflex sensitivity estimation finds increasing (or decreasing) SBP samples (a SBP ramp) that are followed by delayed increasing (or decreasing) PI ramp, as shown in Fig 1. Delay in humans can be 0, 1 or 2 heart-beats. The simultaneously increasing (or decreasing) SBP-PI pairs (usually 2, 3 or 4 pairs) form a "sequence" [11, 12]. A local linear regression can be performed for a sequence, PI = sBRR x SBP + *b*. Averaging the coefficients sBRR over all sequences found in the recorded time series a spontaneous baroreflex coefficient is found.

Cross-entropy estimates deeper connectivity between the observed SBP and PI time series then the linear baroreflex can capture. Entropy was proposed in [13, 14] and well explained in [15, 16]. In brief, one (master) time series of length N – e.g. SBP - is divided into the N-$m$overlapping vectors of length m. Each one of the vectors (e.g. vector no. i) is compared to all the vectors from the second, follower, time series – e.g. PI - to find the probability that the vector $i$is "similar" to the follower series. The criterion of similarity is a distance that should be below the predefined threshold r. If I{} denotes an indicator function, the probability that defines the similarity of vector i from SBP series and PI series is expressed as:

$$\hat{p}_i^{(m)} = \frac{1}{N-m}\sum_{j=1}^{N-m} I\{distance(SBP_i, PI_j) < r\} \quad (1)$$

Difference in Approximate entropy and Sample entropy is that, having obtained probabilities for vectors of length$m$ and m+1, for *ApEn* the averaging the logarithm of probabilities (1) is performed, while for *SampEn* the probabilities (1) are first averaged, and only then the logarithm is taken, making *SampEn* more robust but less sensitive.

III. Results

A. Artifacts: source, statistics and correction

There are three types of typical artifacts in blood pressure waveforms. The first type is due to the tracking procedure (Fig.2, upper panel). The second type is due to the periodical active cuff change (Fig. 2, lower panel). The third type occurs at the end of the recording. The first and the third type are easy to manage: the erroneous start and end of the recorded signals are simply cut out. The visual inspection prior to the signal cuts is necessary, since the tracking length can be variable. Some signals are tuned easily and tracking errors do not exist, while in some patients, several attempts to achieve the locking position has to be made, so the tracking lasts a couple of minutes, and sometimes the recording sessions must be abandoned. The average duration of tracking and interrupts is presented in Table I.

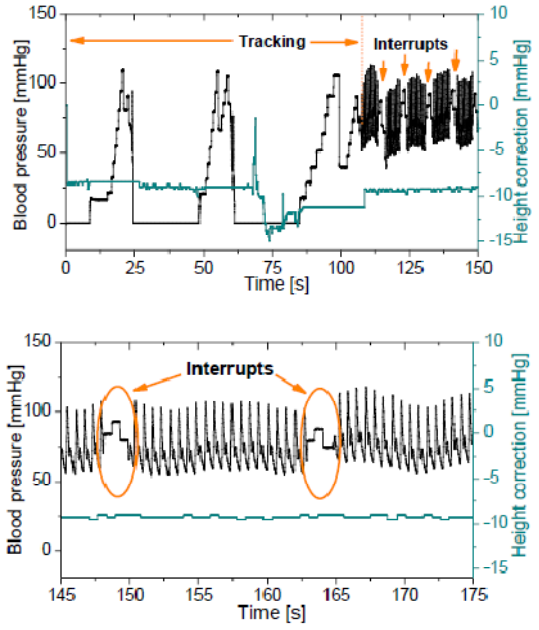

Figure 2. Blood pressure waveforms; upper panel: tracking and start of the signal session; lower panel:enlarged interrupts.

The interrupts shown in Fig. 2 occur within the data region from which the cardiac parameters for further analysis are extracted. From Table I it is clear that average duration of interrupt is cca. 3s, so it affects a couple of SBP-PI pairs.

Beatscope®software automatically corrects this issue, as shown in Fig. 3: it interpolates the positions cardiac parameters so that recorded stream of SBP, PI and other cardiac parameters seem to be without the interruption.

B. Correction and its influence considering the analytical tools

Table II shows the observed parameters: classical measures (mean and deviation of SBP and PI values) and barroreflex sequences values (number of sequences detected and their slope) for signal without the correction (missing samples are neglected), and the changes that correction is induced (missing samples are inserted, as shown in Fig. 3).

TABELA I. ARTIFACT DURATION

ARTIFACTS	DURATION
TRACKING DURATION [S]	42.25 ± 44.01
TRACKING DURATION [BEATS]	52.81 ± 55.12
DURATION OF INTERRUPTS/600 BEATS [S]	50.43 ± 12.77
DURATION OF INTERRUPTS/600 BEATS [BEATS]	16.26 ± 3.77
SINGLE INTERRUPT DURATION [S]	3.12 ± 0.44

Results are presented as mean ± standard deviation

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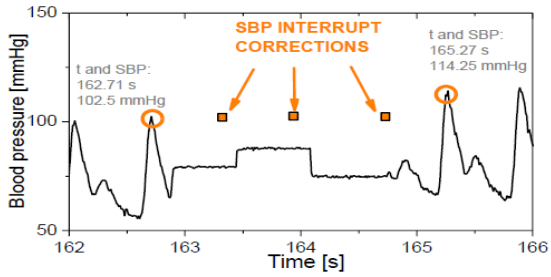

Figure3. Cardiac parameters correction: three SBP samples and the corresponding four pulse intervals (PI) are inserted into the interrupt.

The SBP and PI samples that emulate the missing signal are interpolated according to the existing SBP and PI values. The interpolation is perfectly performed, as the difference between the corrected and non-corrected time series does not exist (less than 0.2%, Table II).

Considering the slope of baroreflex sequences (i.e. the spontaneous sBRR sensitivity), its change is less then 4% andalmost the same for sequence with and without the constraint considering the sequence length. Therefore the impact of interrupt correction is only moderate and the obtained – corrected - signals can be safely used for the baroreflex analysis.

Considering the entropy analysis, the results are not so promising. Table III shows changes of cross entropy analysis using*ApEn* and using *SampEn*, when SBP signal is master and when PI signal is master. Since the length of 7 signals only satisfied the constraints for reliable entropy estimation [15],

TABLE II SBP, PI AND BAROREFLEX SLOPE CHANGES DUE TO THE INTERRUPT CORRECTION

PARAMETER	VALUE
SBP - WITHOUT THE CORRECTIONS [MMHG]	97.38±19.14
PI - WITHOUT THE CORRECTIONS [S]	0.83±0.26
SBPCHANGE [%]	0.17±0.02
PI CHANGE [%]	0.13±0.02
NUMBER OF SEQUENCES CHANGE[%]	5.27±5.29
NUMBER OF SEQUENCES CHANGE, LENGTH > 1 [%]	10.63±17.89
SBRR SENSITIVITY CHANGE [%]	3.93±4.28
SBRR SENSITIVITY CHANGE, LENGTH > 1 [%]	3.94±6.15

Results are presented as mean ± standard deviation; the changes are absolute, expressed in [%] in respect to the case without the correction.

Table III presents the results for all the subjects.

From Table III it may be seen that the entropy results obtained from the corrected and from the source signals are not consistent. Fig. 4 presents the SBP and PI signals with marked correction for Subjects 1 and 7 as their entropy exhibits the least and the most discrepancy in entropy estimation. Although the amount of corrections is similar, and they are scattered in similar way within the signal, the difference of signals is in variability – the correction in low variable signal (number 1) is of low variability itself, and therefore has low impact on temporal analysis such as entropy estimation is. On the other hand, the corrections of high variability (in order to be aligned with the properties of the signal), destroy the temporal properties inherent in signal that affect the entropy study.

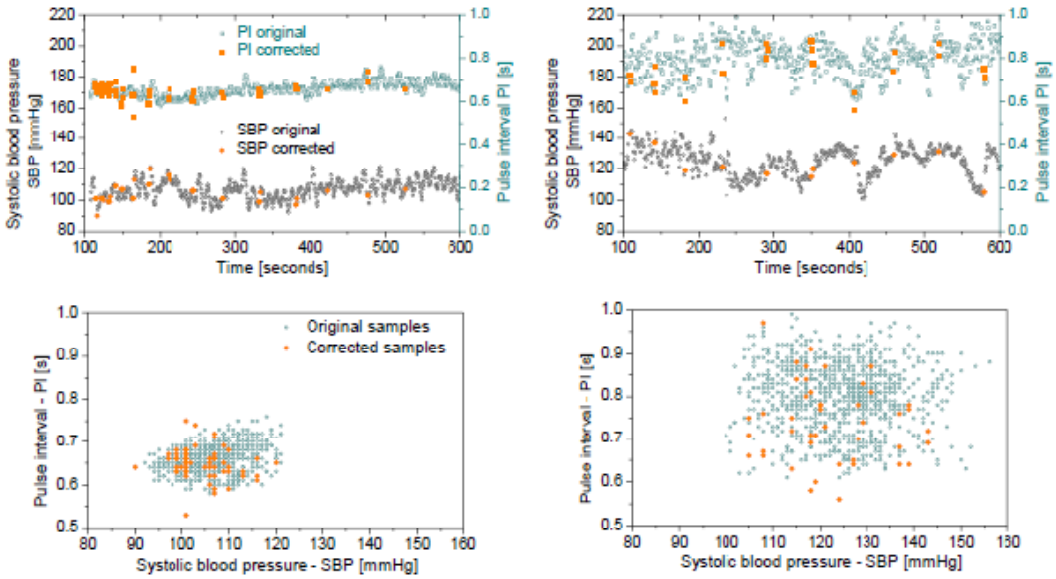

Figure 4. SBP and PI time series (top panels) and signal pairs in SBP-PI plane (bottom panels). Panels in left: signal with no changes in entropy after the correction is performed (yellow points added); panels in right: signal with substantial change in entropy.

TABLE III CROSS-ENTROPY CHANGES DUE TO THE INTERRUPT CORRECTION IN SBP AND PI TIME SERIES

	Cross-ApEn changes [%[		Cross-SampEn changes [%[	
SUBJECTS	**SBP vs. PI**	**PI vs. SBP**	**SBP vs. PI**	**PI vs. SBP**
1	1.5	-7.28	-0.01	-0.02
2	6.47	37.95	36.08	36.16
3	3.66	0.97	6.6	6.64
4	20.54	2.78	14.85	14.81
5	5.08	-0.38	4.2	4.22
6	-1.09	0.16	8.79	8.75
7	39.16	56.31	50.27	50.21
ABSOLUTE MEAN	**11.07**	**15.12**	**17.26**	**17.26**
STANDARD DEVIATION	**12.99**	**20.95**	**17.33**	**17.32**

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SAŽETAK

Kontinualno neinvazivno snimanje talasnih oblika krvnog pritiska na pokretnim pacijentima je veoma izazovan posao. Portapres® je jedinstven uređaj koji, sa dovoljnom pouzdanošću,

može da snima talasne oblike na pacijentima koji se kreću. Međutim, snimanje je komplikovano i uključuje i korekciju pritiska, koja je neophodna jer ruka na kojoj se nalazi senzor menja svoj visinu tokom hodanja. Zbog toga artefakti ne mogu da se izbegnu. Cilj ovog rada je da anlizira greške u kardiovaskularnim signalima koji se izvode iz talasnog oblika krvnog pritiska i da proveri koliko su dobijeni signali robusni ako se koriste pojedine analitičke metode. Razmatrana je sekvencijalna analiza spontane barorefleksne osetljivosti unakrsna-entropija, nezaobilazna u naučnim istraživanjima, i to i aproksimativna entropija i entropija uzorka.

ENTROPIJA I SEKVENCIJALNA ANALIZA PORTAPRES®SIGNALA

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