

Towards Quasi-continuous Heart Rate Variability Estimation using a Patch Type Electrocardiogram Recorder

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Abstract: Changes in different heart rate variability (HRV) measures have been found to possess predictive information in patients with many different diseases, e.g. myocardial infarction, diabetic neuropathy, and patients at risk of developing sepsis. At the same time, the emerging of patch type electrocardiogram recorders facilitates new possibilities for long-term monitoring, real-time data analysis, and wireless transmission of clinically relevant parameters, e.g. short-term HRV measures. This information might in the future assist the healthcare professionals in timely notification of changes in the risk stratification profile obtained from the HRV measures. The purpose of this study is therefore to investigate the possibilities for quasi-continuous estimation of reliable HRV measures using the ePatch heart monitor. We compared the physiologically true values of 11 selected HRV measures with the values obtained using automatically generated RR series from electrocardiograms recorded with the ePatch using four different sampling frequencies (128 Hz, 256 Hz, 512 Hz, and 1024 Hz). We found no significant differences between neither the mean nor the median values of the obtained HRV measures for any of the sampling frequencies. This is very promising for the future application of the ePatch for quasi-continuous monitoring of HRV measures.

1 INTRODUCTION

The application of different heart rate variability (HRV) measures has become increasingly popular as a non-invasive clinical estimate of the state of the autonomic nervous system. One of the major application areas is risk stratification in cardiac patients, e.g. patients with myocardial infarction, congestive heart failure, and left ventricular dysfunction (Huikuri & Stein, 2013). Other promising clinical areas that might highly benefit from risk stratification based on HRV measures include general health management, patients at risk of developing sepsis, patients with diabetic neuropathy, and critically ill intensive care patients (Buchan et al., 2012; ESC and NASPE, 1996). Many of these application areas might benefit from continuous estimation of short-term HRV measures. Together with reliable continuous estimation of other vital sign parameters, this might provide a real-time overview of a potential change in the clinical condition of the patient.

The emerging of patch type electrocardiogram (ECG) recorders with embedded processing capability opens the possibility for this type of continuous monitoring. One of these patch ECG recorders is the ePatch designed by DELTA. The currently CE marked and FDA approved version of the ePatch stores the recorded ECGs internally for offline analysis for up to 72 hours. The ePatch consists of a reusable sensor and a disposable patch. The patch contains three internal measuring points that allow the recording of two bipolar ECG channels without the use of any cables. The ePatch system is further described in (Saadi et al., 2013) and (Saadi et al., 2014).

One of the possible future HRV feedback loops is schematically illustrated in Figure 1. The ePatch sensor is expected to perform real-time embedded detection of each QRS complex. The obtained RR interval curve might then be wirelessly transmitted to a smart phone or a central monitoring station. This device could then automatically calculate preselected clinically relevant HRV measures. This would allow close to real-time feedback on potential

changes in the clinical condition. The information might be calculated with pre-defined intervals depending on the specific application. Hence, we introduce the term quasi-continuous evaluation of HRV measures. The growing clinical accept of patch type ECG recorders increases the real-life applicability of such a system.

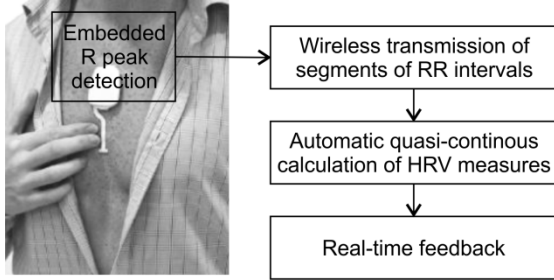


Figure 1: Schematic illustration of a possible future quasi-continuous HRV feedback loop.

One of the important prerequisites for reliable estimation of the HRV measures is the ability to obtain a correct RR interval curve. The obtained RR interval curve might be affected by several factors, e.g. the sampling frequency, the resolution of the digitalized signal, artefacts, the automatic R peak localization procedure, and physiological noise (e.g. beats that does not originate from the sinoatrial node). It is very important to obtain an RR interval curve with as few deviations from the true physiological variability of the heart as possible. In this paper, we therefore define the term “physiologically true R peak position” to describe the best possible localization of the R peak after correction for errors in the digitalization (sampling frequency and signal resolution), errors caused by inaccurate QRS detection (false or missed detections), and uncertainty induced by improper automatic localization of the exact R peak position. We thus use this expression to describe the R peak positions that best describe the true physiological variability of the heart with a minimum of influence from technical errors. The presence of e.g. ectopic beats has also been expected to cause errors and uncertainty in the calculation of the HRV measures (ESC and NASPE, 1996). On the other hand, several different automatic or semi-automatic methods for the editing of the automatically generated RR interval curve have been proposed recently (Citi et al., 2012; HASIBA Medical, 2015). It is therefore not entirely clear whether the manual editing is strictly required. The purpose of this study is thus to explore the possibilities for estimating reliable quasi-continuous HRV measures using the ePatch

ECG monitor.

2 METHODS

An overview of the study design is provided in Figure 2. The overall purpose was to investigate whether RR interval series obtained automatically using the ePatch ECG recorder would be of sufficient quality to provide reliable estimates of clinically relevant HRV measures. To investigate this, we compared HRV measures based on the automatically generated RR series with an estimate of the physiologically true HRV measures. The physiologically true HRV measures were estimated based on manual annotations of QRS complexes in 5-min ECG segments and a method recently designed by our group to accurately locate the physiological R peak position independently of the applied sampling frequency and bit resolution (Ahrens et al., 2015).

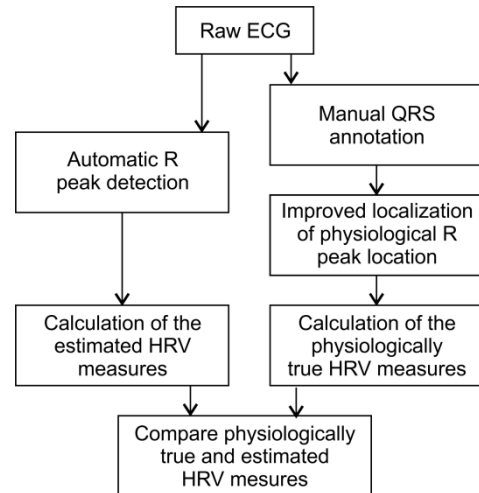


Figure 2: Schematic overview of the study design. The input to the analysis is a raw ePatch ECG signal. The output of the analysis is a comparison between the values of the physiologically true HRV measures and the HRV measures obtained using the automatically generated RR interval series.

2.1 Data Acquisition

The ECG recordings were obtained using the ePatch recorder. The ePatch stores the recorded ECG channels locally for later offline analysis. The ePatch was placed horizontally on the lower part of the chest (see Figure 3). The ePatch can record with four different sampling frequencies (128 Hz, 256 Hz, 512 Hz, and 1024 Hz). With the future

embedded data processing in mind, it is desired to apply a low sampling frequency. However, a higher sampling frequency might induce less R peak jitter, i.e. less error in the exact R peak localization. We therefore found it relevant to investigate the application of all four sampling frequencies. For each sampling frequency, we obtained six 24-hour recordings yielding a total of 24 recordings. The recordings were obtained on healthy, young volunteers. We had 12 different subjects, and each subject was therefore monitored with two different sampling frequencies on two different days. The subjects were instructed to continue all normal daily life activities throughout the monitoring period. This ensures a realistic amount of artefacts and a realistic impression of the normal changes in the HRV measures during a full day of normal daily life activities.

(a) Placement of the ePatch ECG recorder



(b) Raw ePatch ECG snippet

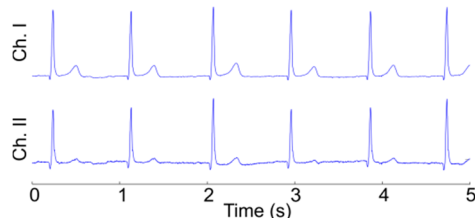


Figure 3: (a) Illustration of the placement of the ePatch on the chest. (b) Illustration of a two-channel ECG snippet obtained with the ePatch recorder. It is observed how this location of the ePatch ensures large R peak amplitudes and relatively small P- and T-waves.

2.1.1 Manual QRS Annotations

Manually annotated QRS positions are required both to estimate the performance of the automatic QRS complex detection algorithm and to obtain the physiologically true HRV measures. To obtain these, we automatically extracted and manually annotated one 5-min ECG segment every third hour of each recording. The manual annotation procedure was similar to previous studies conducted by our group (Saadi et al., 2015). All beats were labelled as normal.

2.2 Automatic QRS Complex Detection

For the automatic QRS complex detection step, we decided to apply an algorithm previously designed by our group (Saadi et al., 2015). We selected this algorithm based on several considerations: 1) It was optimized for QRS complex detection in ePatch ECGs, 2) The algorithm obtained very high clinical performance on both ePatch ECGs and two large standard databases, and 3) The algorithm is computationally efficient enough for real-time embedded functionality. The algorithm is based on bandpass filtering, adaptive thresholding, and a search back mechanism. The algorithm was originally designed for a sampling frequency of 512 Hz. We therefore made small modifications in the algorithm to allow automatic QRS complex detection with all four sampling frequencies. The modifications are described in the Appendix. The RR interval series obtained automatically using this algorithm were applied directly to calculate what we term the “estimated” HRV measures. This would correspond to the output from the potential future feedback loop illustrated in Figure 1. However, in this study, the QRS complex detection algorithm was applied offline in MATLAB R2013b.

2.3 Estimation of Physiological R Peak

The digitalization of the physiological R peak depends both on the sampling frequency and the bit resolution of the recorded data. It might therefore be difficult to conduct an accurate estimation of the physiologically true R peak position based only on the recorded waveform directly. This might induce recording jitter in the HRV measures. Recently, our group has therefore designed a method to estimate the physiologically true R peak position independently of the applied sampling frequency (Ahrens et al., 2015). The input to the algorithm is an approximate QRS location. In our case, this location was the manual annotations. The data is then up-sampled to 8191 Hz. In this high frequency domain, a template matching is performed to maximize the alignment of R peaks and hereby obtain a very accurate assessment of the physiologically true RR interval series. This RR interval series is applied to calculate what we term as the “physiologically true” HRV measures.

2.4 Calculation of HRV Measures

A high number of different short-term HRV measures have been proposed. We decided to investigate three time domain measures, four frequency domain measures, and four dynamic measures: 1) *SDNN* represents the standard deviation of the RR intervals, 2) *RMSSD* is the square root of the mean squared differences of successive RR intervals, 3) *pNN50* is the percentage of interval differences of successive RR intervals that exceeds 50 ms, 4) *VLF* represents the very low frequency power component (≤ 0.04 Hz), 5) *LF* is the low frequency power component (0.04 – 0.15 Hz), 6) *HF* is the high frequency power component (0.15 – 0.4 Hz), 7) *LF/HF* is the relation between the low and high frequency components, 8) *ApEn* is the approximate entropy (a measure of the regularity of the RR intervals), 9) *SD1* is a geometric measure of the short-term variations, 10) *SD2* is a geometric measure of long-term variations, and 11) *SD1/SD2* represents the relation between the two axis in the Poincaré plot. The different measures are described in more details in (ESC and NASPE, 1996).

3 RESULTS

3.1 Performance of QRS Detection

The performance of the automatic QRS complex detection algorithm was evaluated as the sensitivity ($Se = TP/(TP+FN)$) and the positive predictivity ($P^+ = TP/(TP+FP)$), where TP is the number of true positive detections, FN is the number of false negative detections (missed beats), and FP is the number of false positive detections. The performance was evaluated using the *bxh* function in the WFDB Toolbox (Goldberger et al., 2000). The performance of the algorithm is provided in Table 1 for each of the four investigated sampling frequencies. The algorithm only obtained *Se* and/or *P⁺* of less than 99.0% on seven of the 191 segments (three obtained with 128 Hz and two obtained with 256 Hz and 512 Hz, respectively). This lower performance was obtained on segments with high amounts of artefacts. These artefacts are also expected to influence the estimation of the physiologically true HRV measures, and these seven segments were therefore excluded from the HRV investigations described in the following sections. The automatic QRS detection performance on the 184 included 5-min segments is also provided in Table 1.

3.2 Comparison of HRV Measures

The median values of the physiologically true and the estimated HRV measures are provided in Table 2 for each sampling frequency. It generally appears that the automatically generated RR series have a tendency to slightly overestimate the median values of most of the HRV measures for all four sampling frequencies. Therefore, we also investigated the distribution of the differences between the true HRV measures and the estimated values. A few examples of this are provided in Figure 4. It is observed that most of the differences have slightly negative values corresponding to a minor overestimation when the automatically generated RR series is applied. However Mann-Whitney U tests and anova tests showed that the differences observed in the median and mean values, respectively, are not significant for any of the HRV measures for any of the sampling frequencies. Both tests were conducted with a significance level of $\alpha = 0.05$.

The similarity between the true and the estimated 5-min HRV measures were furthermore investigated using correlation plots. A few examples are provided in Figure 5. It is visually observed that there is a high correlation between the true HRV measures and the estimated HRV measures for all four sampling frequencies. This was observed for all of the 11 investigated 5-min HRV measures. The correlation coefficients between the true and the estimated HRV measures are provided in Table 3. Statistical tests showed that all the correlations are significant with a significance level of $\alpha = 0.001$.

Table 1: Evaluation of the automatic QRS detection performances for each sampling frequency with all segments (top line) and with exclusion of segments with very poor performance (lower line). N indicates the number of segments applied.

Fs	N	Total beats	Se (%)	P ⁺ (%)
128 Hz	48	17,664	99.58	99.55
	45	16,029	99.98	99.93
256 Hz	48	18,283	99.97	99.87
	46	17,573	99.99	99.96
512 Hz	48	17,965	99.65	99.64
	46	16,651	99.98	99.93
1024 Hz	47	18,338	99.96	99.95
	47	-	-	-
Total	191	72,105	99.79	99.76
	184	68,582	99.98	99.94

Table 2: Median values of the investigated 5-min HRV measures obtained from the physiologically true RR series (“truth”) and obtained directly from the automatic QRS complex detection (“estimate”) for each sampling frequency. The median values are applied because several of the parameters are not normally distributed.

Parameter	Fs = 128 Hz		Fs = 256 Hz		Fs = 512 Hz		Fs = 1024 Hz	
	Truth	Estimate	Truth	Estimate	Truth	Estimate	Truth	Estimate
SDNN (s)	0.0607	0.0681	0.0640	0.0639	0.0606	0.0650	0.0518	0.0529
RMSSD (s)	0.0350	0.0416	0.0316	0.0342	0.0374	0.0439	0.0314	0.0335
pNN50 (%)	13.896	14.402	10.069	11.780	15.205	16.117	10.671	11.024
SD1 (s)	0.0248	0.0295	0.0223	0.0242	0.0265	0.0311	0.0222	0.0237
SD2 (s)	0.0870	0.0888	0.0862	0.0861	0.0758	0.0829	0.0691	0.0704
SD1/SD2	0.2994	0.3270	0.2511	0.2746	0.3611	0.4122	0.2549	0.2985
ApEn	0.5719	0.5700	0.5403	0.5411	0.5889	0.5713	0.5735	0.5767
VLF (s ²)	3.78·10 ⁵	3.77·10 ⁵	3.53·10 ⁵	3.56·10 ⁵	3.80·10 ⁵	3.80·10 ⁵	3.12·10 ⁵	3.11·10 ⁵
LF (s ²)	568.14	626.54	484.99	454.93	447.06	477.66	455.94	441.18
HF (s ²)	248.23	316.00	224.45	230.97	229.96	319.59	159.42	184.05
LF/HF	2.5396	2.1458	2.5691	2.5391	1.9684	1.3634	3.1721	2.9977

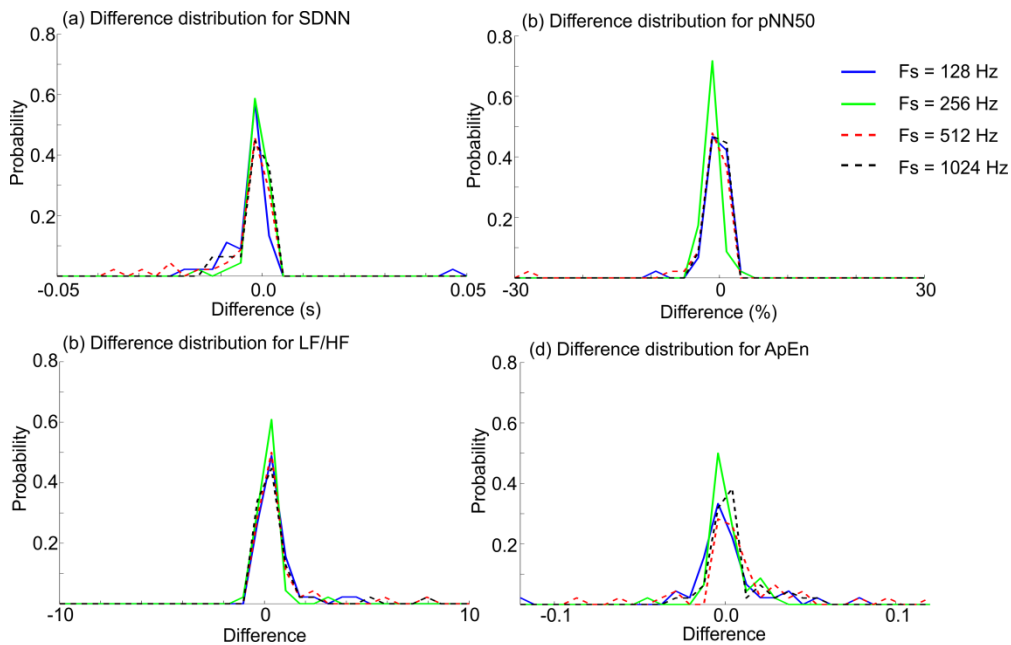


Figure 4: Examples of the distribution of the differences between the physiologically true HRV parameter and the estimated HRV parameter value for each 5-min ECG segment. Negative differences correspond to the estimated value being larger than the physiologically true value. It is observed that the distribution of the differences is comparable for all four frequencies. The probability distributions are calculated as histograms with 30 equally distributed bins.

3.3 Applications of the HRV Measures

One of the interesting applications of quasi-continuous estimation of HRV measures is the possibility to explore transient changes in the HRV measures over time. This could be relevant on larger time scales (e.g. month or years), but also on shorter time scales (e.g. days). We therefore investigated the time course of a few selected HRV measures during the entire duration of our recordings. A few examples are provided in Figure 6. The daily

variations are especially observed for the first subject. In order to automatically detect these transient changes using the estimated HRV measures, it is necessary to ensure that the before mentioned tendency to a minor (non-significant) overestimation of many of the measures does not interfere with the ability to correctly classify between simulated groups of high and low variability, respectively. This ability is also expected to be important with respect to detection of different patient populations based on the HRV measures.

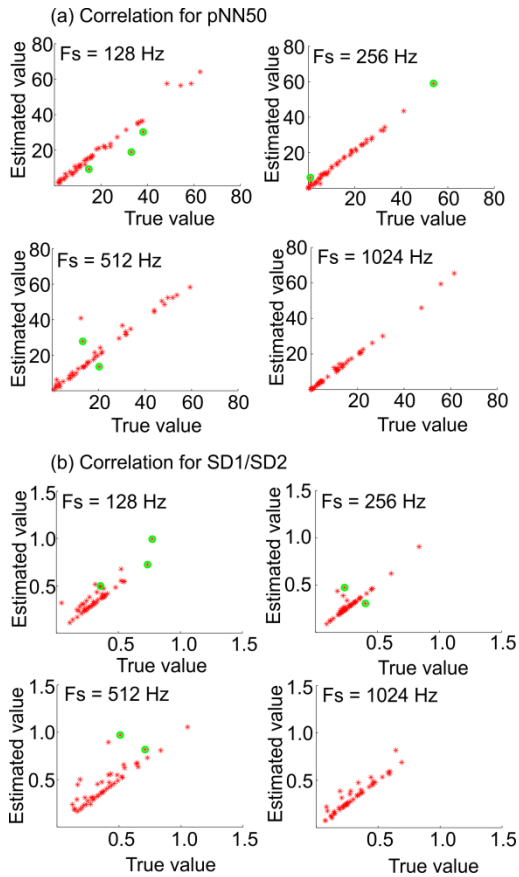


Figure 5: Examples of representative correlations between the physiologically true HRV measures and the estimated HRV measures for the four different sampling frequencies. The green marks indicate segments that were excluded from the HRV comparisons due to poor QRS detection performance.

Table 3: Correlation coefficients between the true and the estimated value of each investigated HRV measure for all four sampling frequencies. Examples of correlation plots are provided in Figure 5.

Parameter	128 Hz	256 Hz	512 Hz	1024 Hz
SDNN	0.97	0.98	0.95	0.99
RMSSD	0.93	0.96	0.87	0.95
pNN50	0.99	1.00	0.97	1.00
SD1	0.93	0.96	0.87	0.96
SD2	0.62	1.00	0.80	0.93
SD1/SD2	0.86	0.94	0.88	0.95
ApEn	0.93	0.99	0.96	0.99
VLF	1.00	1.00	1.00	1.00
LF	0.94	0.95	0.89	0.98
HF	0.94	0.99	0.93	0.99
LF/HF	0.89	0.99	0.86	0.97

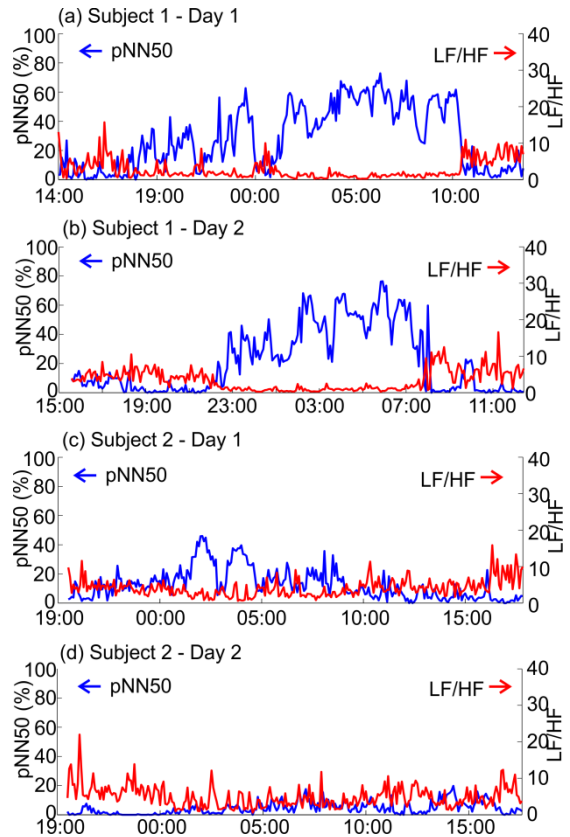


Figure 6: Illustration of the time course of pNN50 (blue line) and LF/HF (red line) calculated using the estimated HRV measures from every 5-min segment throughout the recording on two different days for two different subjects.

To investigate the ability to classify between different states of low and high HRV measures, we divided the included 5-min segments into two groups. The first group represents the lowest half of the HRV measures and the second group represents the highest half for each parameter. The division was based on the physiologically true HRV measures. We first confirmed that there was a statistical significant difference between both the mean and the median values of the two obtained groups using the true HRV measures. This was confirmed for all 11 HRV measures for all four frequencies. This division can thus be applied to simulate two truly different groups. We then investigated whether the difference was still significant when the estimated HRV measures were applied. A few representative examples of the two obtained distributions are provided in Figure 7. It is generally observed that there is a clear difference between the two groups using the true HRV measures. This difference is furthermore observed to be correctly reproduced by the estimated HRV measures. The results were

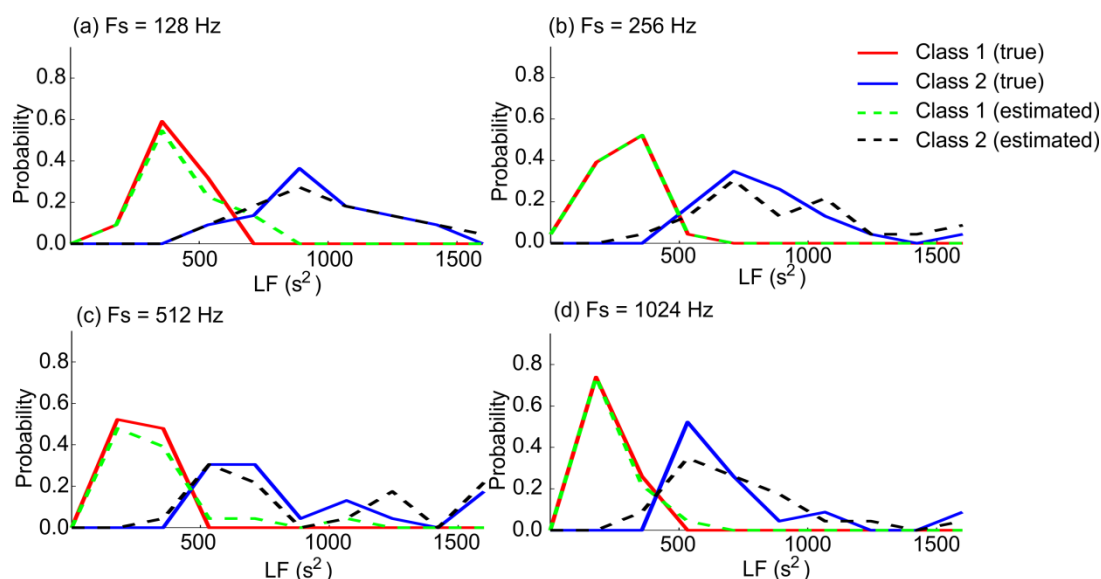


Figure 7: Illustration of division of the LF measure into a high and a low variability group. Each curve illustrates the distribution of the LF measure for class 1 using the physiologically true values (red lines), class 2 using the physiologically true values (blue lines), class 1 using the estimated values (green lines), and class 2 using the estimated values (black lines). The probability distributions are calculated as histograms with 10 equally distributed bins.

similar for all 11 HRV measures for all four sampling frequencies. Mann-Whitney U tests and anova tests revealed that the difference between median and mean values, respectively, were still significant ($\alpha = 0.01$) with the estimated values of the HRV measures.

4 DISCUSSIONS

The performance of the automatic QRS complex detection algorithm was found to be high for all four frequencies. This was especially clear when the seven worst segments were removed. The exclusion of these segments was considered necessary to ensure reliable estimation of the HRV measures due to the lack of manual editing in our setup. However, this suggests that a reliable HRV estimate can be obtained in more than 96% of the segments. This is considered acceptable with the quasi-continuous application in mind. In future studies, it should be investigated how these segments could be excluded automatically. This could for instance include an automatic pre-qualification of the quality of each segment. Furthermore, the next generation of the ePatch is able to record simultaneous accelerometer data. This could be applied to detect periods of high activity and thus base the quasi-continuous HRV estimation on segments with potentially low noise levels. Furthermore, several studies have recently

investigated the possibility for automatic correction of errors in the RR interval curve (Citi et al., 2012). These methods might also be able to decrease the influence of poor QRS detection performance and hereby allow inclusion of more of the segments. However, it should be noted that this study was conducted on young, healthy, and physically active volunteers where the amount of abnormal beats is expected to be low. In cardiac patients or healthy elderly, it is probably necessary to account for abnormal beats in the automatically generated RR interval series before the HRV measures are estimated. As mentioned, several studies have recently designed methods to account for these automatically based on outliers in the RR interval curve (Citi et al., 2012).

Generally, there was a tendency to overestimate most of the HRV measures for all the sampling frequencies. This might indicate that a certain amount of high frequency noise is induced due to the finite sampling of the signals. However, looking at the distributions of the differences in Figure 4, it appears that the overestimation is quite similar for all four frequencies. Furthermore, the correlation was found to be high for all the investigated HRV measures for all four sampling frequencies and we found no statistical significant differences for any of the sampling frequencies. This suggests that all four frequencies can be applied to obtain a very accurate assessment of the true physiological variability. With the embedded implementation in mind, it is

therefore appealing to apply the lower sampling frequencies. However, the usual recommendation has been to apply a higher sampling frequency, especially when the HRV measures are expected to have low values which is often the case in autonomous dysfunction (Citi et al., 2012; ESC and NASPE, 1996; García-González et al., 2004; Tapanainen et al., 1999). Our findings should therefore be confirmed on a larger population that includes different clinically relevant patient groups. It is especially important to investigate whether the findings can be reproduced in populations with more complicated ECGs, e.g. patients with ectopic beats, and patients with reduced HRV measures, e.g. patients with autonomic dysfunction and critical care patients. However, it is very promising that our simulated division into low and high variability groups are quite similar using the true and the estimated HRV parameter values.

Figure 6 contains an example of the application of quasi-continuous HRV measures to investigate daily variations in the autonomic tone. It is generally observed that a clear increase in pNN50 is associated with a clear decrease in LF/HF. This is as expected: A high value of pNN50 indicates more high frequency variations and more high frequency content is associated with a decrease in LF/HF. An increase in the high frequency components are believed to be associated with an increase in the parasympathetic nervous system. For the first subject, it is clearly observed how the high frequency components are more pronounced during the night in both recordings. For the second subject, this difference is only observed on the first day. It is furthermore observed that there is a decrease in pNN50 and hereby a decrease in the high frequency components, in the middle of the night. That might indicate that the subject woke up at night. This illustrates how quasi-continuous estimation of HRV measures might assist in keeping an eye on the development of changes in the autonomic tone. This could for instance prove useful for the monitoring of critical care patients or patients at risk of developing sepsis. It might also be helpful in general health management or for monitoring of improvements obtained by exercise or stress management programs. These examples illustrate how new knowledge about the constantly changing autonomic tone might be gained by working towards quasi-continuous monitoring of HRV measures. This paper is a very early step in the direction of real-time quasi-continuous monitoring of changes in the autonomic tone through HRV measures, but the results are promising and suggest that more research

in this area might prove beneficial.

Generally, there are three requirements for obtaining reliable estimates of clinically relevant HRV measures:

1. The patient should be able to comply with wearing the system for the necessary amount of time.
2. The system should be able to correctly reproduce the physiological variability of the heart in quasi-continuous segments.
3. The system should be able to automatically select the ECG segments that are suitable for reliable estimation of the HRV measures.

The first requirement is clearly fulfilled by the patch type ECG recorders. The second requirement is bound by the ability to automatically detect and localize the R peaks with sufficient accuracy. The focus of this study was to investigate this second requirement. Overall, we found that when the ECG is of sufficient quality (defined by the ability to obtain sufficient automatic QRS complex detection), it was possible to reproduce the physiological variability using the ePatch recorder and an automatic QRS complex detection algorithm. Our findings thus suggest fulfilment of the second requirement. However, as mentioned, this was based on segments from healthy volunteers with expected low arrhythmia burden and with high QRS detection performance. This leads to the third requirement that is related to the ability to automatically select the segments that are suitable for the quasi-continuous estimation of the short-term HRV measures. This might include automatic selection of segments with sufficient signal quality, automatic selection of segments without arrhythmias, or automatic correction of abnormal beats in the RR series before calculation of the HRV measures. This area should thus be the subject of further research in the future.

5 CONCLUSIONS

We found a high correlation between the physiologically true HRV measures and the measures estimated with an automatically obtained RR interval series for four different sampling frequencies (128 Hz, 256 Hz, 512 Hz, and 1024 Hz). This indicates that the described ePatch system is able to obtain reliable estimates of clinically relevant HRV measures. These findings should be further investigated in larger patient populations with more complicated ECGs and in patient populations with expected low variability in the heart rate. However,

the findings are still promising for the future application of the ePatch ECG recorder in the growing area of risk stratification based on HRV measures.

REFERENCES

- Ahrens, E., Sorensen, H. B. D., Langberg, H., Hoppe, K., & Saadi, D. B. (2015). Investigation of the Minimum Conditions for Reliable Estimation of Clinically Relevant HRV Measures - Introducing a Novel Approach to the Validation of HRV Measurement Systems. In *CARDIOTECHNIX 2015: Proceedings of the International Congress of Cardiovascular Technologies 2015*. SciTePress. Accepted.
- Buchan, C. A., Bravi, A., & Seely, A. J. E. (2012). Variability analysis and the diagnosis, management, and treatment of sepsis. *Current Infectious Disease Reports*, *14*, 512–521. doi:10.1007/s11908-012-0282-4
- Citi, L., Brown, E. N., & Barbieri, R. (2012). A real-time automated point-process method for the detection and correction of erroneous and ectopic heartbeats. *IEEE Transactions on Biomedical Engineering*, *59*, 2828–2837. doi:10.1109/TBME.2012.2211356
- ESC and NASPE (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology). (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, *17*, 354–381.
- García-González, M. A., Fernández-Chimeno, M., & Ramos-Castro, J. (2004). Bias and uncertainty in heart rate variability spectral indices due to the finite ECG sampling frequency. *Physiological Measurement*, *25*, 489–504. doi:10.1088/0967-3334/25/2/008
- Ghaffari, A., Homaeinezhad, M. R., & Daevaeiha, M. M. (2011). High resolution ambulatory holter ECG events detection-delineation via modified multi-lead wavelet-based features analysis: Detection and quantification of heart rate turbulence. *Expert Systems with Applications*, *38*, 5299–5310. doi:10.1016/j.eswa.2010.10.028
- Goldberger, A. L., Amaral, L. A. N., Glass, L., Hausdorff, J. M., Ivanov, P. C., Mark, R. G., Mietus, J.E., Moody, G.B., Peng, C.-K. & Stanley, H. E. (2000). PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals. *Circulation*, *101*, e215–e220. doi:10.1161/01.CIR.101.23.e215
- Huikuri, H. V., & Stein, P. K. (2013). Heart rate variability in risk stratification of cardiac patients. *Progress in Cardiovascular Diseases*, *56*, 153–159. doi:10.1016/j.pcad.2013.07.003
- Li, C., Zheng, C., & Tai, C. (1995). Detection of ECG characteristic points using wavelet transforms. *IEEE Transactions on Biomedical Engineering*, *42*. doi:10.1109/10.362922
- Martínez, A., Alcaraz, R., & Rieta, J. J. (2010). Application of the phasor transform for automatic delineation of single-lead ECG fiducial points. *Physiological Measurement*, *31*, 1467–85. doi:10.1088/0967-3334/31/11/005
- HASIBA Medical GmbH. (2015). Cardioscope(TM) Analytics. Retrieved October 12, 2015, from <https://cardioscope.com>
- Pan, J., & Tompkins, W. (1985). A real-time QRS detection algorithm. *IEEE Transactions on Biomedical Engineering*, *32*, 230–236. doi:10.1109/TBME.1985.325532
- Saadi, D. B., Fauerskov, I., Osmanagic, A., Sheta, H. M., Sorensen, H. B. D., Egstrup, K., & Hoppe, K. (2013). Heart rhythm analysis using ECG recorded with a novel sternum based patch technology. In *CARDIOTECHNIX 2013: Proceedings of the International Congress on Cardiovascular Technologies 2013*, SciTePress, 15-21. doi:10.5220/0004640900150021
- Saadi, D. B., Sorensen, H. B. D., Hansen, I. H., Egstrup, K., Jennum, P. J., & Hoppe, K. (2014). *ePatch(R) - A Clinical Overview*. Retrieved from http://orbit.dtu.dk/fedora/objects/orbit:135692/datastreams/file_56776d8b-c232-4bcb-af6c-20f3a00382a9/content
- Saadi, D. B., Tanev, G., Flintrup, M., Osmanagic, A., Egstrup, K., Hoppe, K., Jennum, P., Jeppesen, J.L., Iversen, H.K. & Sørensen, H. B. D. (2015). Automatic Real-Time Embedded QRS Complex Detection for a Novel Patch-Type Electrocardiogram Recorder. *IEEE Journal of Translational Engineering in Health and Medicine*, *3*, 1900112. doi:10.1109/JTEHM.2015.2421901
- Tapanainen, J. M., Seppänen, T., Laukkanen, R., Loimaala, A., & Huikuri, H. V. (1999). Significance of the accuracy of RR interval detection for the analysis of new dynamic measures of heart rate variability. *Annals of Noninvasive Electrophysiology*, *4*, 10–18. doi:10.1111/j.1542-474X.1999.tb00359.x

APPENDIX

The automatic QRS complex detection algorithm was originally designed for a sampling frequency of 512 Hz (Saadi et al., 2015). The performance of this version of the algorithm on the MIT-BIH Arrhythmia Database (MITDB) is compared to other published algorithms in Table 4. Two modifications were required to adapt the algorithm to the other three sampling frequencies. The first adaptation was an adjustment of a threshold that decides the variability mode of the algorithm. The original threshold was $T_{\theta, \text{original}} = 35$ samples. This threshold was updated to $T_{\theta} = 8$ samples for $f_s = 128$ Hz, $T_{\theta} = 17$ samples for $f_s = 256$ Hz, and $T_{\theta} = 70$ samples for $f_s = 1024$ Hz. The second modification was related

to the digital filters. The original filter coefficients for $f_s = 512$ Hz are provided in (Saadi et al., 2015). For $f_s = 1024$ Hz, all coefficients were doubled. Thus the length of all the cascaded filters was doubled. This keeps the bandpass region for a doubled sampling frequency. Likewise, every other filter coefficient was removed to adjust for a sampling frequency of 256 Hz. This modification was not possible for $f_s = 128$ Hz. Instead, the two first bandpass filters were therefore modified according to (1) and (2).

Table 4: Comparison of performances obtained on the MITDB by different algorithms published in the literature. In this study we applied the algorithm designed by (Saadi et al., 2015). This algorithm was designed and optimized for detection of QRS complexes in ePatch ECGs.

Algorithm	Se (%)	P^+ (%)
(Saadi et al., 2015)	99.90	99.87
(Ghaffari, Homaeinezhad, & Daevaeiha, 2011)	99.94	99.91
(Martinez, Alcaraz, & Rieta, 2010)	99.71	99.97
(Li, Zheng, & Tai, 1995)	99.89	99.94
(Pan & Tompkins, 1985)	99.75	99.54

$$h_{BP1}[n] = \{-\delta[n+3] + \delta[n+2] + \delta[n-1] - \delta[n-2]\}. \quad (1)$$

$$h_{BP2}[n] = \{-2\delta[n+4] - \delta[n+3] + [n+2] + 2\delta[n+1] + 2\delta[n] + \delta[n-1] - \delta\delta[n-2] - 2\delta[n-3]\}. \quad (2)$$

For the average filters, half the coefficients were removed relative to the filters applied for $f_s = 256$ Hz. The bandpass filter characteristics for the four different sampling frequencies are provided in Figure 8. It is observed that the filter characteristics are very similar. It is expected that the performances obtained by the three modified algorithms ($f_s = 128$ Hz, $f_s = 256$ Hz, and $f_s = 1024$ Hz) will be comparable to the performance stated in Table 4 for the original algorithm ($f_s = 512$ Hz).

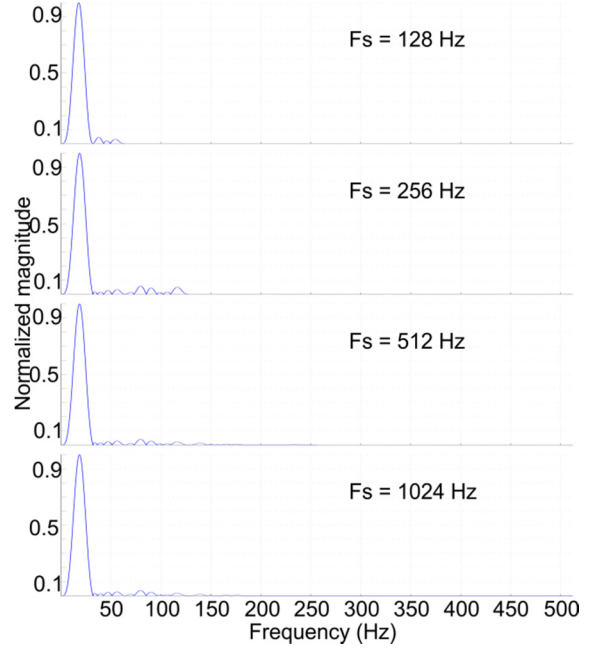


Figure 8: Amplitude characteristics for the combined bandpass filters for each sampling frequency.