Algorithm Fusion for the Early Detection of Apnea-Bradycardia in Preterm Infants

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Abstract

Episodes of apnea-bradycardia are frequent in preterm infants. The incidence and severity of these events may lead to neurological morbidity or even to the infant death. Even if algorithms for bradycardia detection have been developed, they are inefficient and usually produce false or late alarms. In this work, a new algorithm for the detection of apnea-bradycardia in preterm infants is proposed, based on the fusion of different detection algorithms. A quantitative evaluation of the proposed algorithm and a comparison with two other algorithms proposed in the literature is presented. A database of 40 newborns, with a total of 1188 episodes of apnea-bradycardia was used for the evaluation. The proposed algorithm presents sensitivity and specificity of 97.67% and 97.00%, respectively. Furthermore, the mean time-delay for event detection is decreased to 2.22 beats, which is lower than the mean of the algorithms proposed in literature.

1. Introduction

Transient episodes of apnea and bradycardia are common in preterm infants [1]. These episodes may seriously compromise oxygenation and tissue perfusion and, when they become prolonged and repetitive, they may lead to neurological morbidity or even infant death. Premature infants in neonatal intensive care units (NICU) are continuously monitored through polygraphic recording, to detect bradycardia events and to initiate quick nursing actions (manual or vibrotactile stimulation, oxygenation, ventilation through a mask or intubation) [2, 3]. Typically, when an infant presents a bradycardia event, an alarm is generated by a monitoring device, an available nurse or physician goes to the appropriate NICU room, washes his/her hands, and applies a manual stimulation to the infant in distress. The mean intervention delay, measured from the activation of the alarm to the application of the therapy has been estimated to be around 33 seconds, with a mean manual stimulation duration of 13 seconds, in order to terminate the event of apnea-bradycardia [3].

An event of apnea-bradycardia is defined in the literature [4] as an increase of the beat-to-beat interval over a fixed threshold (the threshold is generally $U_0 = 600ms$, see equation 1), or by more than 33% of the base rhythm (the threshold is denoted by *RRbase*, see equation 2).

$$\left(RR(k_n) \geq U_0\right) \text{ during 4 seconds} \tag{1}$$

$$\left(RR(k_n) \geq (0{,}33)RR_{base}\right) \text{ during 4 seconds} \tag{2}$$

This definition can be difficult to implement directly in a real-time bradycardia detector, presenting a reduced delay in alarm generation.

The objective of this work is to contribute to the reduction of the mean intervention delay by proposing a new real-time algorithm fusion approach for the detection of apnea-bradycardia events, presenting an optimal compromise between detection performance and detection delay.

2. Methods

Two classical methods from the literature (fixed and relative thresholds) have been implemented and a new method, based on abrupt change detection [5], has been proposed.

The fixed-threshold method compares a window-averaged beat-to-beat (RR) interval estimation with a fixed threshold, defined by the user. Most neonatal monitors are based on this detection scheme. The relative-threshold method considers the fact that the mean heart rate of a patient can change through time, and implements a relative threshold of 33% of increase on the mean RR interval in a 4 seconds window. The use of these time-windows reduce the number of false positives, but increase the detection delay. The third method, based on the theory of abrupt-change detection [5, 6], models the bradycardia event as a statistically significant change in the mean RR interval. This algorithm depends on a threshold λ, which has to be optimally defined.

2.1 Proposed detection method

The RR interval series is used in this work to detect bradycardia events. RR intervals are detected from ECG signals acquired in neonatal intensive care units. The ECG signal is preprocessed by a set of filters in order to remove electromyographic interference, 50/60Hz power line interference, baseline drift due to respiration and abrupt base line shifts. After pre-processing, a multi-lead QRS detection scheme based on the work of Pan & Tompkins is applied [7] (see Figure 1).

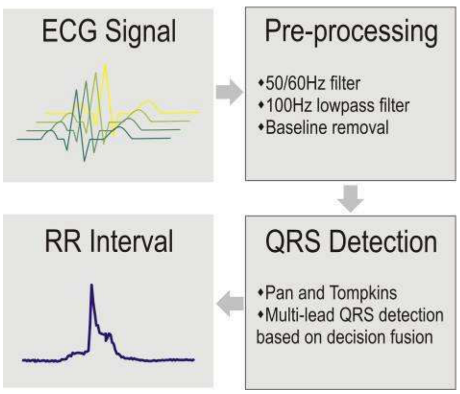

Figure 1. Processing chain to obtain RR series

The proposed detection approach is based on the *Cumsum* test [5]. In this approach, the RR interval *RR(k)* is considered as a constant piecewise function, perturbed by a noise *e(k)* with zero mean ($\mu=0$) and a known variance (σ^2). Two hypotheses can be defined for the detection of significant changes on this series:

$$H_0 : RR(k) = \overline{RR_o} + e(k) \text{ for } 0 \le k \le r-1$$

$$H_1 := RR(k) = \overline{RR_1} + e(k) \text{ for } r \le k \le n$$

where $\overline{RR_0}$ and $\overline{RR_1}$ are the mean values of *RR(k)* before and after the beginning of the bradycardia event, respectively.

In order to detect these events, the H_1 hypothesis must be accepted (the increase of *RR(k)*) in front of hypothesis H_0 (no change of state of the infant). The likelihood ratio associated to both hypotheses (H_0, H_1), taking the observations as independent, is defined as:

$$g = \frac{\prod_{k=1}^{r-1} . P_o(RR(k)) \prod_{k=r}^{n} . P_1(RR(k))}{\prod_{k=1}^{n} . P_o(RR(k))} = \frac{\prod_{k=r}^{n} . P_1(RR(k))}{\prod_{k=r}^{n} . P_o(RR(k))} \quad (3)$$

Where *r* represents the instant of abrupt change (initial instant of the bradycardia).

By using the Kolmogorov-Smirnov test [8], some authors showed [9] [10] [11] that the hypothesis that the heart rate variability follows a normal law cannot be rejected. Therefore the likelihood ratio can be expressed as:

$$\begin{aligned} \Lambda_n(r) &= \frac{\overline{RR_o} - \overline{RR_1}}{\sigma^2} \sum_{k=r}^{n} \left(RR(k) - \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \\ &= \frac{1}{\sigma^2} S_r^n \left(RR(k), \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \end{aligned} \quad (4)$$

The instant of occurrence of a bradycardia event, *r*. is considered by estimating the maximum of the likelihood ratio under H_1, in other words:

$$\begin{aligned} \hat{r} &= \arg\max_{1\le r\le n} \left[\prod_{k=1}^{r-1} . P_o(RR(k)) \prod_{k=r}^{n} . P_1(RR(k)) \right] \\ &= \arg\max_{1\le r\le n} \left[S_r^n \left(RR(k), \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \right] \end{aligned} \quad (5)$$

Finally, a bradycardia event is detected if:

$$\Lambda_n(\hat{r}_n) = \max_r \left[S_r^n \left(RR(k), \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \right] \underset{H_1}{\overset{H_1}{\lessgtr}} \lambda \quad (6)$$

where λ is the detection threshold.

This test can be expressed in a recursive form (for a real-time implementation) as follows:

$$\Lambda_n(\hat{r}_n) = S_r^r \left(RR(k), \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \min_{1\le k\le n} \left[S_1^k \left(RR(k), \frac{\overline{RR_o} - \overline{RR_1}}{2} \right) \right] > \lambda \quad (7)$$

However, the values of $\overline{RR_0}$ and $\overline{RR_1}$ are unknown. $\overline{RR_0}$ can be considered as the mean value of the analyzed RR series over a time window, and $\overline{RR_1}$ as an increase of this base value $\overline{RR_1} = \overline{RR_0} + \nu$, where ν is chosen empirically.

Finally, the equation for the real-time implementation is given by:

$$\begin{aligned} &\Lambda_0(r) = 0 \\ &\Lambda_n(r) = \sum_{k=r}^{n} \left(RR(k) - \overline{RR_o} - \frac{\nu}{2} \right) \\ &m_n(r) = \min_{1\le k\le n} \Lambda_n(r) \\ &\therefore (\Lambda_n(r) - m_n(r) \ge \lambda) \cap \left(r = \arg\min_{1\le k\le n}(m_k) \right) \end{aligned} \quad (8)$$

An event detection occurs when the following conditions are satisfied:

$$\Lambda_n(r) - m_n(r) \ge \lambda \text{ and } r = \arg\min_{1\le k\le n}(m_k)$$

The behavior of the likelihood ratio $\Lambda_n(r)$ and the values of ν and λ for a typical bradycardia event are shown in Figure 2.

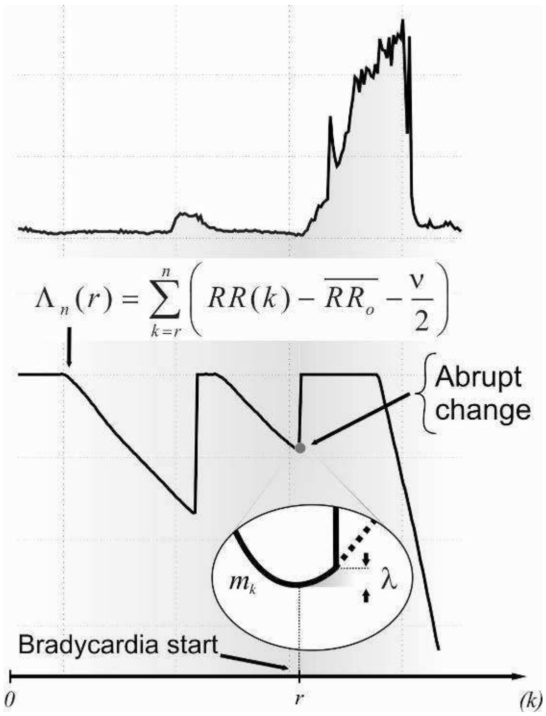

Figure 2. Likelihood ratio in an abrupt change

2.2 Algorithm fusion

The three bradycardia detectors presented in the previous sections are based on different hypotheses and can be considered as complementary. The objective of this work is to combine these detectors in order to maximize detection performance while minimizing the detection delay.

Different fusion rules can be used to combine local detections (obtained from each algorithm) into a final decision *u*. Some simple rules are based on a "k out of n" function. Special cases of this function include the AND and the OR rules. However, there has been an important effort to obtain optimal fusion rules, based often on the weighted combination of each local detection, that provide a higher weight to the more reliable detectors. In this work we have used the optimality criterion proposed by Chair and Varshney [12].

2.3 Evaluation methodology

A quantitative evaluation of each individual detector as well as the algorithm fusion approach was performed, by using a database composed of records from 40 preterm infants, acquired at the University Hospital of Rennes [13]. A total of 1188 apnea-bradycardia episodes and 722,849 beats were analyzed. References for the time instants of the beginning and end of each episode were obtained by applying offline the above-mentioned definition from the literature. These time instants were manually verified by an expert. The ECG signal has been acquired at 1000 Hz using a data acquisition system (PowerLab®/Chart v4.2®) installed on a Pentium III. Database files are analyzed using MATLAB.

Detection performance was evaluated by estimating three parameters for the whole database and for different threshold values: i) sensitivity, ii) specificity and iii) mean detection delay. Classical definitions of sensitivity (Se) and specificity (Sp) were used:

$$Se = \frac{TP}{TP + FN} \tag{9}$$

$$Sp = \frac{TN}{FP + TN} \tag{10}$$

where *TP* are the true positives, *FP* are the false positives, *FN* are the false negatives and *TN* are the true negatives.

The mean detection delay has been estimated from the individual differences (in beats) between each event annotation and the corresponding instant of occurrence of the detected event. Detected events with delays higher that 20 beats or lower than -20 beats were considered as false positives.

3. Results

Performance results for each detector are presented in Table 1.

Algorithm	Sensitivity	Specificity	Mean delay
Fixed threshold	30.02%	100%	7.23
Relative threshold	34.57%	100%	6.35
Abrupt change (λ = 81)	96.84%	96.60%	-2.85
Optimal fusion (λ = 92)	97.67%	97.00%	-2.22

Table 1. Algorithms Performance

It can be observed that the fixed and relative threshold algorithms provide an excellent specificity, but a poor sensitivity and an important mean detection delay. These problems are mainly due to the necessity of using a moving average window on the RR interval, which implies the use of a buffer and the introduction of an additional delay when implemented in real-time.

In order to evaluate the abrupt change detector, an ROC curve was constructed (Figure 3) by calculating the sensitivity and specificity of the detector for λ values in the interval [0, 1000]. An optimal λ value of 81 was obtained for the abrupt change detector by estimating the ROC point minimizing the global probability of error (e.g. the distance between each ROC point and the perfect detection point). The third line of Table 1 shows the performance of the abrupt change detector, when using this optimal λ value. It should be noticed that a negative mean detection time is obtained with this approach, meaning that the detection is produced before the event annotation. Finally, the decentralized decision fusion approach was applied and the results obtained are displayed in Figure 3 with a λ value of 92.

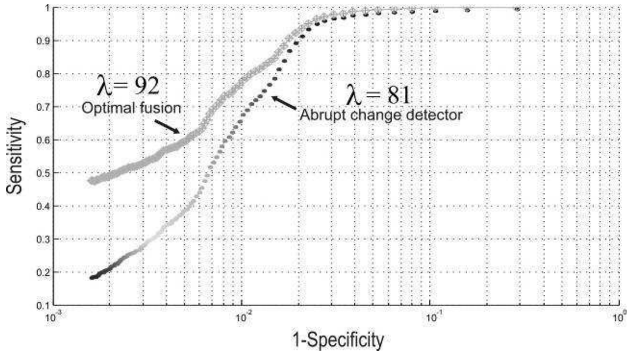

Figure 3. ROC curves for the proposed algorithms

Results obtained from the weighted decision fusion are similar to those of the abrupt change detector, but with a slightly higher sensibility and λ value different. Figure 4 shows the results of the sensitivity versus the mean detection delay for different thresholds of the abrupt change detector and the fusion approach. It can be observed that the fusion approach provides higher sensibilities for the same detection delays. This method has thus been retained for the real-time early detection of bradycardia events.

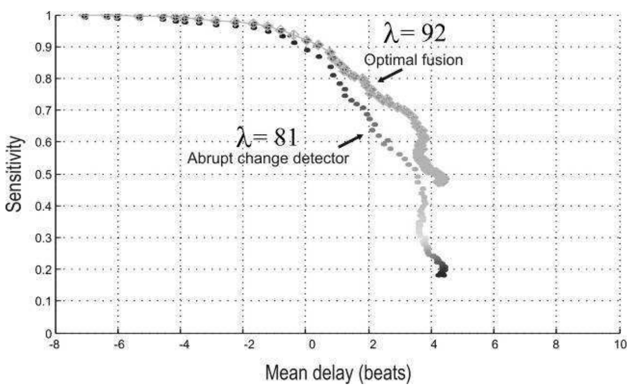

Figure 4. Sensitivity vs. mean detection delay for the abrupt change detector and the fusion approach

4. Discussion and Conclusions

The proposed approach based on decision fusion shows better performance than the fixed and relative threshold algorithms. In addition, the real time implementation on a PC system of this approach can provide an early bradycardia detection. This detector is suitable to be implemented on a micro-controller, and integrated on a monitoring device. This approach can be used to include other detection algorithms providing complementary information.

Acknowledgements

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