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Development of an Apnea Detector for Neonates using Diaphragmatic Surface Electromyography

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***Abstract*— Respiratory diseases are among the most important and serious conditions that can affect the newborn baby. A cessation of breathing, longer than 15 seconds, or accompanied by hypoxia or bradycardia, is called apnea of prematurity (AOP) and has been found in more than 50% of premature infants. An apnea detector used in infant monitoring has been designed and constructed and is intended to be applied in a clinical environment. Diaphragmatic surface EMG has been used as the technique for detecting apnea episodes due to a direct relation with the respiratory drive. Both obstructive and central apnea can be determined as well as heart rate. Good performance and feasibility have been shown by the prototype.**

I. Introduction

As a consequence of immaturity at the respiratory control system, periodic breathing is a common event in premature infants and does not merit any treatment. Nevertheless, apnea is a pathological cessation of breathing, in excess of 15 seconds duration or accompanied by hypoxia and bradycardia, that generates hemodynamic disturbances and hence merits treatment [1]. Apnea is found in more than 50% of premature infants and is almost general in infants who are below 1000g at birth [2]. It is classified traditionally into three categories based on the presence or absence of upper airway obstruction: central, obstructive, and mixed. Some studies confirmed the well-known fact that death rates are high in neonates who have repeated episodes of apnea lasting longer than 20 seconds [3].

Several electronic monitoring techniques have been used for apnea detection. Neuman reviewed and divided them into direct and indirect methods depending on the position of the sensor, if it is coupled to the airway and measures the movement or other properties of the air transported into and out of the lungs. Direct methods can be pneumotachography, capnography, temperature of inspired or expired air and sound measurements, and methods as transthoracic electrical impedance, whole-body plethysmography, contacting and non-contacting motion sensors, intraesophageal pressure and electromyography, are considered indirect methods [4]. However, some authors are more convinced that the measurement of the electrical activity of the muscles is a more direct method to monitor respiratory activity, as it represents a step necessary to transform central respiratory drive into an inspiration [5], [6]. The diaphragm is the principal muscle for pulmonary ventilation [7] and some studies have been carried out during the last years focused on sensing diaphragm electromyography (EMGdi). Those studies measured the interaction between muscle activity, flow and lung volume, in order to monitor respiration, especially on neonates [8]-[10].

Conventional apnea monitors, as those made to detect cessation of chest or abdominal movements (pressure pads, mattresses or impedance systems), may fail to alarm because of cardiac triggering (an effect of the increased cardiac stroke volume secondary to apnea and bradycardia), body movements or inability to detect obstructive apnea [11]. A non-invasive electromyography (EMG) device that is easy to handle to estimate lung function would extend diagnostic possibilities and would provide an objective measure to evaluate the respiratory activity and detect episodes of apnea. This physiological signal is less sensitive to motion artifacts [12], but in the case of EMGdi is of low amplitude and strongly contaminated by the electrocardiography (ECG) QRS complex [13], [14] and requires complex signal processing. Nevertheless, monitoring the activity of the diaphragmatic and intercostals muscular system is considered the most direct way to obtain information on respiratory muscle function and could be used as an indirect variable to estimate airway obstruction [5], [6], [8]-[10], in this manner, EMGdi is a very suitable technique for both central and obstructive apnea detection. In this paper, the design and construction of an apnea detector, based on the processing and analysis of the EMGdi signal, are described and some results are showed.

II. Materials and Methods

A. Design criteria

The apnea detector was developed following the general requirements for safety according to the *"Norma*

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Técnica Colombiana NTC-IEC 60601-1", which is equivalent to the UNE-EN 60601-1, 1998.

According to previous studies [6], [8], the expected signals using surface electrodes commonly are 1milivolts peak to peak for the ECG and 20μVpp for the EMG. The frequency component of the ECG is in the range of 0-150Hz, and almost all of the diaphragm EMG frequency content is in the range of 20 to 250Hz [15]. In order to get a reliable final EMG signal, an amplification of at least 1000 is needed, as well as filters with different cut-off frequencies.

As the EMG is a biopotential signal, the pre-amplification stage must have the following amplifier characteristics [16]: high common mode rejection ratio (CMRR), high input impedance, good frequency response and low output impedance for further signal processing.

B. Diaphragm electrode position

The frontal EMG diaphragm muscle activity is obtained through two pediatric surface electrodes placed bellow the costal margin on the right and left sides of the body in the nipple line and another placed in the sternum as the reference [6], [8], [17]. The selected electrode position allows an easy replacement for further measurement occasions and it is acceptably close to the insertion of the costal fibers of the diaphragm. Additionally, during tidal breathing only a minimal amount activity of the intercostal muscles contaminate the EMGdi signal [6].

C. Hardware Signal Processing Initial Stage

The electrical activity produced by the diaphragm is recorded using surface electrodes, then the signal goes through isolate wires to a guard-drive connection or a driven right leg circuit and to a very low noise, precision instrumentation amplifier (AMP-01, Analog Devices) used as a pre-amplification of the signal, which accomplishes all the requirements mentioned at the design criteria [18].

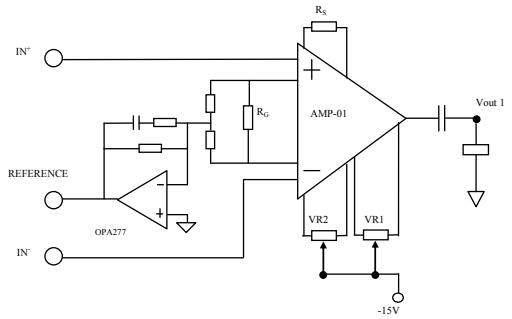

Fig. 1. EMG pre-amplification stage diagram.

The gain of the instrumentation amplifier is:

$$G_{INS} = \left(\frac{20 \times R_S}{R_G}\right) = 51{,}28\,; R_S = 10K\Omega;\ R_G = 3.9K\Omega \qquad (1)$$

The high-pass passive filter has a cut-off frequency at 10Hz. Its main roles are to couple the signal, eliminate electrode offset and reduce some of the low frequency movement artifacts. There are also two trimmers connected to the pins 16-17 and 4-5 to control the offset.

One of the requirements of the NTC-IEC 60601-1 is to isolate the patient from the device. To accomplish the requirement an isolation amplifier (AD210, Analog Devices) is used with a gain of x30. It electrically isolates the previous stage (connected directly to the neonate) and provides it with isolated power supplies and ground, using a high accuracy and complete galvanic isolation technology. The non-isolated side of the amplifier is powered from the main unit [19].

The gain of the isolation amplifier is:

$$G_{Isol} = \left(\frac{R_{S1}+R_{S2}}{R_{s2}}\right) = 29;\ R_{S1} = 560K\Omega;\ R_{S2} = 20K\Omega \qquad (2)$$

Total Gain of initial stage is: $G_{TOT} = G_{Isol} \times G_{INS=}\ 1487.12$

D. EMG Hardware Signal Processing

It would be almost impossible to monitor the newborn respiration from the EMG signal obtained from the initial stage "*Vout 2"*, which is a mixture of ECG and EMG (see Fig. 2). Thus, the signal has been processed to obtain a reliable EMG envelope of the diaphragm. To achieve a clear EMG signal, it was necessary to implement a circuit to eliminate the ECG artifacts in EMGs.

Previous investigations have studied the consequences of using different orders and cut off frequencies in a high-pass filter to substantially reduce the ECG artifact. However, due to the spectral overlap of the ECG and EMG signals, high-pass filtering attenuates the EMG content. The researchers found that the performance is relatively high when the filter order was greater than two and the cut-off frequency was between 50 and 90Hz [20]. Using this information, the signal (Vout2 EMG+ECG signal, Fig.2) was passed through a four order high-pass filter with a cut off frequency at 50Hz; and to get the QRS complex of the ECG artifact, a second order band-pass filter with a cut off frequency at 13Hz-25Hz was implemented.

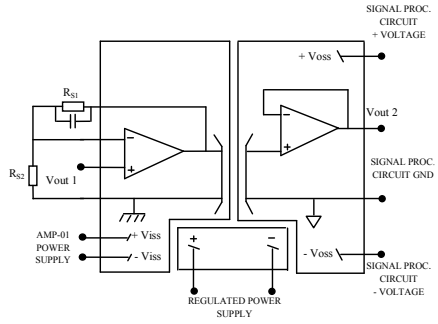

Fig. 2. Isolation amplifier diagram. Modified from an Eagle library, (Cad Soft Computer, Inc).

Continue working with the two signals obtained after the high-pass filter and the band-pass filter, the ECG suppression is achieved as is shown in the diagram at Fig. 3 with some signals measured on strategic points in the electronic circuit. The obtained signal in the initial stage "*Vout 2*" passes through the band-pass filter (Fig. 3 (1)), then it is rectified (Fig. 3 (2, 3)) to use the ECG envelope as one of the inputs in the voltage comparator, and the other input is defined by a variable voltage reference. At the end of the stage (Fig. 3 (4)) a pulse is obtained to control the switch (Fig. 3 (6)); the bilateral switch is a signal selector, gating out the ECG artifact immerse in the input signal (Fig. 3 (5)). After the stage (Fig. 3 (6)) a diaphragm EMG signal without

the ECG artifact is amplified by x30 (Fig. 3 (7)), then rectified (Fig. 3 (8, 9)) and finally the signal goes through a high-pass filter (Fig. 3 (10)) for further software processing.

E. Hearth-Rate

Other important factor to consider for detecting an apnea episode is the hearth-rate (HR), because an apnea causes an oxygen desaturation, which in turn triggers a reflex bradycardia [21]. To calculate the HR, the raw EMG waveform in "Vout 2" was passed through the band-pass filter (Fig. 3 (1)) and then trough a comparator amplifier. Finally the output of the comparator is a square wave with frequency equal to the HR (Fig. 3 (d)).

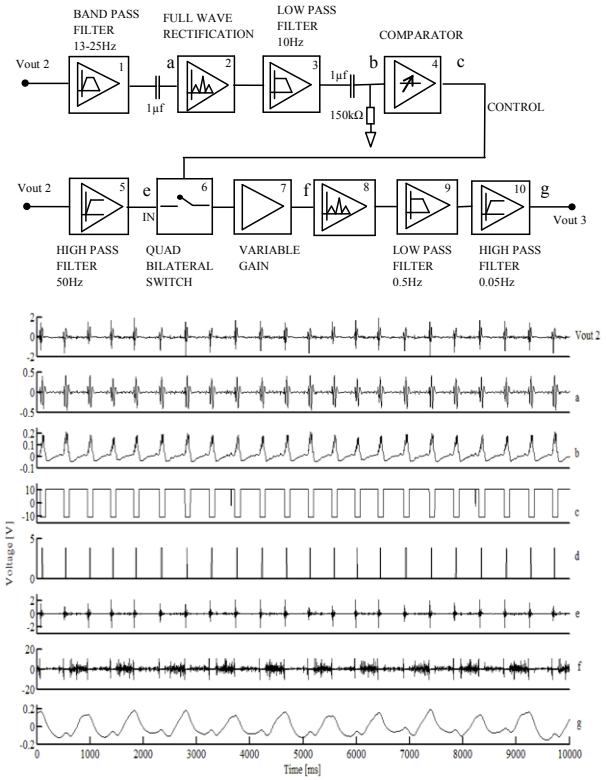

Fig.3. The signal in (Vout 2) shows the diaphragm EMG signal reproduced by the signal generator. It seems that there is an ECG with some EMG artifacts. The curve (c) is a pulse generated by the comparator using the ECG envelope obtained every hearth-beat. The pulse control the switch, and it removes the ECG artifact in the output signal passed through the high-pass filter in (e), which shows less ECG and some respiratory activity present in the baseline. Curve (f) shows the diaphragm EMG amplified by x30, and without the QRS complex. This signal is then rectified and filtered to obtain the envelope (g).

F. Software

A microprocessor board (RabbitCore, RCM4510W RABBIT Semiconductor Inc, Davis, CA) was used to implement the code written in the software Dynamic C (Version 10.23, Rabbit Semiconductor, Inc). The RabbitCore records the EMG envelope of the diaphragm (Fig.3 (g)) through an analog-to-digital (A/D) conversion channel, which has a conversion time of 40ms and a resolution of 10 bits. Using a general purpose I/O channel of the microprocessor, the time between two HB (Fig. 3 (d)) is used to calculate the HR and every 3 seconds the mean of the HR values during this time window is estimated.

$$HR = \frac{60 \times 1Beat}{Time\ \ between\ \ two\ \ pulses\ (ms)} = n(B \cdot min) \quad (3)$$

The code is divided in two main parts, the *"Training Mode"* and the *"Detecting Mode"*. The Training mode (TM) was written to personalize the device, because the EMG diaphragm muscle activity varies from neonate to neonate. In the TM, the microprocessor takes time windows of 3 seconds during 90 seconds, each time window contains the EMG signal read through the A/D channel and a mean of the time between pulses read in the I/O channel. When a time window is recorded some features are extracted from the EMG signal: the mean, the length, and the numbers of peaks. Then, the 30 data obtained for each feature during the 90 seconds are saved in 4 different vectors to calculate a confidence interval. The confidence intervals are calculated as follows:

$$P(\bar{X} - 1.96 * \sigma \leq \mu \leq \bar{X} + 1.96 * \sigma) \quad (4)$$

In 95% of the cases μ will be between the ranges, but in 5% of the cases it will not be (refer to (4)). After calculating the confidence intervals the program runs into the Detection Mode (DM), until the device is turned off. In the DM the Rabbit takes time windows of 3 seconds, the same features are extracted from the waveform, and they are evaluated to detect the type of apnea episode (Obstructive or central apnea) and activate an alarm. There is possible to determine which kind of apnea is taking place through the EMGdi and HR value, using the muscle activity increment as obstructive apnea and the muscle activity decrement as central apnea.

The apnea detector also has a graphical LCD 128x64 pixels (TG12864B-05, Tinsharp), which shows the envelope of the diaphragm EMG signal every moment, the HR and the type of apnea detected if this is the case.

III. Results and Discussions

The most frequently used method of respiratory monitoring in infants is transthoracic electrical impedance but several limitations can lead to errors. The electrical resistance of rib cage tissues is less than air; therefore alternating current passing across the thoracic cavity reflects mainly tissue impedance. The technology is therefore more prone to motion and cardiogenic artifacts. This method is also unable to assess thoraco-abdominal coordination, so it cannot be used to distinguish central or mixed apnea from obstructive apnea. Other method is pulse oximetry, but accurate interpretation decreases at lower levels of O_2 saturation (i.e. < 70-80%). Monitoring pulse oximetry in infants requiring supplemental O_2 is problematic and body motion has been a problem with false alarms or loss of signal [21].

A previously acquired neonate signal is used to test the electronic circuit performance. This signal was sent by L.A. van Eykern [22], and it was reproduced by a signal generator (Tektronix AFG3101), connected immediately after the pre-amplification stage (as a "Vout 2" signal). The signal contains about 38 minute's signals of raw EMGdi, sampled

at 300 Hz. The sample frequency is low because it was recorded for testing purposes. Also some central and obstructive apnea as well as some movement signals can be found (At the discretion of Catalina Osorio MD, Neonatologist). A flow signal is included separately to confirm whether there is a real apnea or not.

For the training stage of the program, a normal breathing signal reproduced by the signal generator was used to calculate proper confidence intervals. After the training mode, randomized episodes of apneas, central and obstructive, present in the test signal were identified successfully, showing a good performance of the electronic circuit and the algorithm implemented. The EMGdi envelope is displayed on the graphical LCD as well as the HR value and, what type of apnea is taking place when an apnea episode is detected.

The apnea detector prototype meets basic requirements of a neonatal monitoring system: is reliable; is relatively simple to operate and provide information in an easy manner to interpret; is safe for patient use, which is especially important in the neonatal population because the portion of the system that comes in contact with the patient must be appropriately sized and non-irritating to sensitive skin; is non-invasive; provides continuous and real-time information; and is reasonably small and portable. The prototype was also classified as safety class II and applied part of type CF by Luis Carlos Álvarez Vélez, leader engineer of the Biomedical Metrology Institute at the 'Hospital Universitario San Vicente de Paúl'. But to guarantee the previous classification according to the UNE-EN 60601-1, the prototype needs to be tested with specialized equipments.

Clinical experimentation is required in order to give a valid concept of the prototype's behavior compare with others monitors. It has been developed under the requirements for a clinical environment and would be tested directly in patients. At the moment an approval from the CES University ethics committee is pending and some preliminary work is carried out at 'Hospital General de Medellín (HGM)', a recognized local Hospital, where clinicians have given valuable contributions for future testing of the prototype.

IV. Conclusion

An apnea detector has been designed and tested with a previously acquired neonate signal, showing good performance and feasibility. The major features of the design are: (1) make use of a non-invasive and directly related with the respiratory drive technique; (2) on-line ECG artifact rejection and smooth envelope of the EMGdi signal; (3) detection of both obstructive and central apnea through (4) an personalized EMGdi analysis with previous algorithm training, and related to (5) a bradycardia detector; (6) a continuous visualization of the respiratory signal in a graphical LCD; and (6) a portable and easy to use device.

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