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Abstract: *Diaphragm pacing (DP) is an efficient treatment to artificially restore respiratory function. Commercialized systems do not embed any respiratory monitoring function and cannot adapt patients' electro-ventilation needs. To increase the performance and safety of these systems, in this study, an acoustic respiratory monitoring method based on a microphone is investigated. This method also captures stimulation signal so that it could generate an alarm for stimulation failure or an apnea. This could also help to optimize stimulation configurations individually for each patient. We have recorded the tracheal sound of one patient with tetraplegia implanted with a stimulator. Promising preliminary results are a first step towards the validation of the proposed monitoring algorithm of breathing events under phrenic nerve stimulation.*

Keywords: *respiratory monitoring, diaphragm pacing, phrenic nerve stimulation, tracheal sounds*

Introduction

Central respiratory paralysis induces a dependence on artificial ventilation. The paralysis can be congenital (e.g. Ondine's syndrome) or acquired (e.g. upper spinal cord injury). The incidence of patients with cervical spinal cord injury on ventilation support is estimated around 12.7 per one million inhabitants, among which 6.5% requires long-term mechanical ventilation [1]. The number of patients with Ondine's syndrome is about 100 in which 10%-15% patients have ventilatory dependence. In these situations, if phrenic nerves and diaphragm remain functional, diaphragm pacing (DP) through electrical stimulation can provide a more natural respiration instead of mechanical ventilation [2]. Furthermore, it allows an increased autonomy and reduces health costs, and, reduces infection risk, and significantly improves speech and olfactory sensation [2]–[4].

Even though DP has several advantages over the classical mechanical ventilation, it is not safe enough to maintain a full-time ventilatory assistance because of the absence of any " efficacy alarm" [5]. For example, DP systems alarms warn users of electronic failure, but, contrary to the case of mechanical ventilators, do not warn about ventilatory inefficiency. Indeed, DP systems do not embark any ventilatory monitoring. As a result, patients cannot be left alone during the day and usually return to mechanical ventilation during the night for safety reasons. In addition, all existing systems work in open-loop; indeed, stimulation is delivered with constant pre-defined parameters. It means that stimulation intensity, pulse width and frequency are fixed at the installation of the implant, updated at each control visit, but do not adapt to patient's continuous situation evolution because of the absence of respiratory monitoring. To close the loop, an ambulatory respiratory monitoring solution needs to be developed.

Classic respiratory monitoring methods, including nasal flow captors, pneumotachograph, oximetry, plethysmograph … are cumbersome and have limitations. As an alternative to these sensors we propose to use a microphone to capture the tracheal sounds. Indeed, during respiration, air turbulences in the upper air way make the around tissues to vibrate. This vibration induces the propagation of tracheal sounds so that recordings on the neck are possible [6]. Microphones are reduced in size, portable and have no electric contact with the user so no risk of interaction DP system.

Several studies proposed algorithms for apnea detection from breathing sounds [7]–[9], but those studies were focused on sleep apnea, and few of them were used for real-time monitoring (treatment delay < 5 s). To adapt the use with patients with DP systems, we developed a real-time algorithm combining detections both in temporal and frequency domains for a better accuracy. Moreover, during recordings, the microphone captured the radio-frequency stimulation signals from the wireless implanted link, which are synchronized with respiratory sounds. Instead of considering these signals as interferences, we propose to use them to verify if respiration is induced by the stimulation.

Electrical stimulator

There are presently 3 DP systems available in the market: two intrathoracic phrenic nerve stimulation (PNS) systems: AtroStim® (Atrotech, Finland) and Mark IV Breathing Pacemaker (Avery Biomedical Devices, U.S.); one intramuscular PNS system, NeuRx DPS® (Synapse Biomedical, U.S.). The present work was carried out with AtroStim® PNS system shown in Figure 1.

At the installation of the device, stimulation parameters were set into the external controller. During stimulation, the controller sends power and stimulation commands to implanted radiofrequency receivers. According to the received commands, electrical pulses (stimulus) are sent through the quadripolar electrodes in alternative way.

During the respiratory cycle, inspiration is an active movement whereas expiration is passive. Therefore, PNS is by nature limited to inspiration. Two cycles of stimulation signals of the AtroStim® system are illustrated in Figure 2.

One breathing cycle lasts T_1, including inspiration phase T_2 (it is also the stimulation duration) and the expiration phase (T_1-T_2). Each red vertical line in this figure represents one stimulation pulse which pulse-width is 200 µs. The minimum stimulation intensity (threshold) is I_{TH}. And I_{TV} is the intensity for tidal volume, it is also the maximum stimulation intensity. During T_2, the stimulation begins at the intensity I_{TH}, and increases at each pulse until I_{TV}, then remains at I_{TV} until the end of T_2. Except stimulation pulse-width, all other stimulation parameters mentioned above are manually adjustable depending on patient's situation during and after implanted operation.
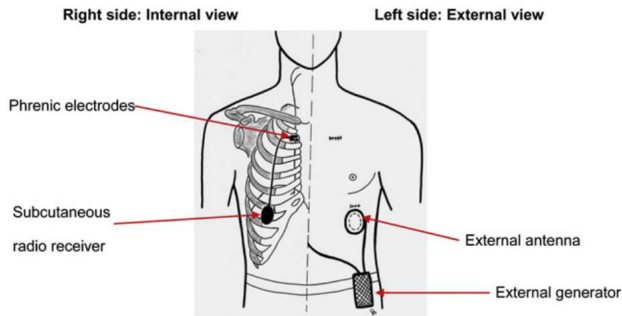

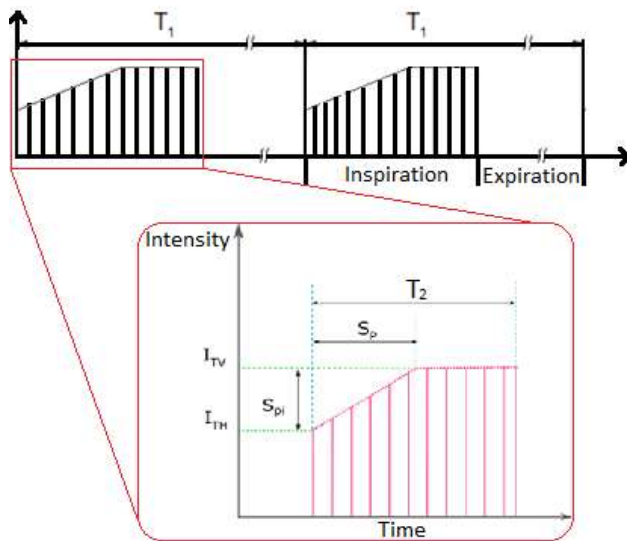Figure 1 : General view of the PNS system [4].

Figure 2: Stimulation signal of AtroStim

A ramp stimulates muscle fibers progressively to avoid a too fast contraction of the diaphragm. This mimics the natural recruitment of motor units during spontaneous inspiration. The inspiration begins when stimulation intensity reaches I_{TV}.

Material and methods

An omni-directional microphone (pro-signal, ABM-705-RC) was used to record tracheal sounds. The microphone was inserted into a 3D printed bell-shape support to increase resonance. Ideally, the support should be positioned over the suprasternal notch for a best quality of signal [10]. This is not practical in tracheotomized patients, the reason for which we chose to attach the microphone just above the tracheotomy, outlined in red in Figure 3.

The signal from the microphone was first amplified (230 times) and filtered (100 Hz-1200 Hz, Band-pass, Butterworth 2nd order) by a custom made analog card, then converted to digital signal by an electronic development card (NUCLEO-F429ZI). Finally, the data were transmitted to a PC by USB link. The sampling frequency was set to 8500 Hz. All the recorded signals were post-processed with MATLAB™ (MathWorks, Massachusetts, U.S.).

Figure 3 : Position of microphone

One participant agreed to participate in this observational study. This patient was equipped with an implanted AtroStim PNS device because of high cervical cord tetraplegia following a ballistic lesion at the C2-C3 level.

One recording of 30 s under stimulation was performed during a routine visit at the hospital. Patient's usual stimulation configuration and parameters were unchanged.
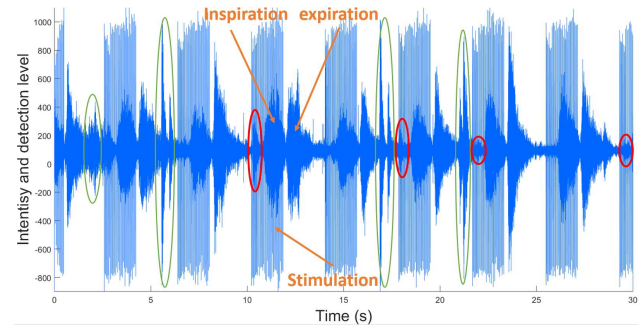
Signals analysis

Figure 4 : Recording under stimulation

One example of a recording under PNS is shown in Figure 4. Captured stimulation signals clearly appear as groups of regular peaks. These groups of peaks occur about every 3.5 s, corresponding to the respiratory rhythm (17 times/min) determined by patient's stimulation system.
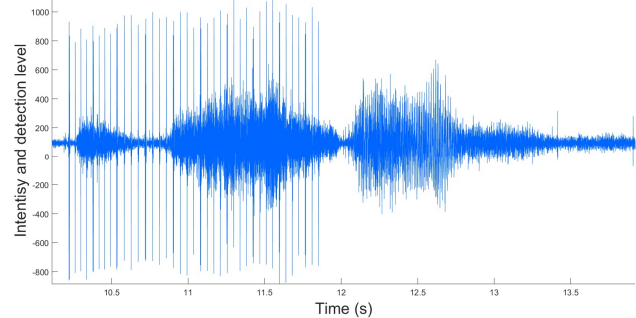

Figure 5 : One enlarged cycle of recording under stimulation

One zoomed zone of the breathing cycle is shown in Figure 5. Each group of peaks lasts about 1.63 s within 40 peaks i.e. 25 Hz, corresponding to the stimulation frequency fixed in the stimulation system. As mentioned before, inspiration is induced when stimulation intensity reaches I_{TV}. According to patient's stimulation parameters, his inspiration should begin 0.64 s later than the first peak of stimulation. But as shown in Figure 4, in many cycles, another weak inspiration induced at the beginning of stimulation is present (identified by red cycles). These pre-inspirations may be caused by some of the first contractions of the diaphragm muscle fibers. It could indicate a higher I_{TH} having been set.
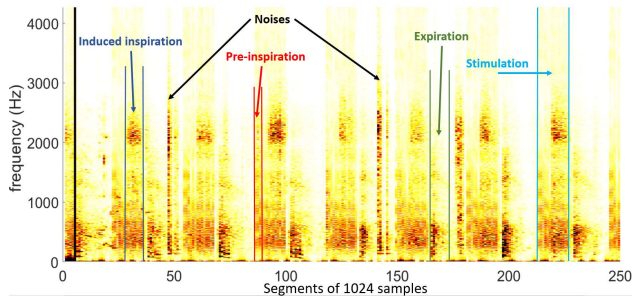

Figure 6: Spectrum of tracheal sounds under stimulation

For spontaneous respiration, respiratory frequency band from tracheal sounds vary depending on recording system, but could normally be detected in 200 Hz-2000 Hz [6]. And there is no obvious frequency difference between inspiration and expiration [11]. With the recording system used in this work, natural breathing has the most information in 300 Hz-900 Hz. This frequency band differs from the one of induced inspiration.

The frequency spectrum of this recorded signal is plotted in Figure 6. Examples of induced inspiration, pre-inspiration, expiration, and stimulation events are labeled in different colors, as well as some external noises. The expiration is always a passive movement, as in natural respiration, its frequency content is centered at 300 Hz-900 Hz. However, the frequency content of the induced inspiration can be divided into two frequency bands: one similar to the one of spontaneous respiration (300 Hz-900 Hz) and another one located in between 2000 Hz to 2500 Hz. This difference in higher frequency band could be a reference to identify the nature of inspiration.

Detection algorithm

Tracheal sounds recordings are processed in real-time with a delay of 0.22 s. This delay is within the acceptable alarm delay for stimulation system, which is around. As shown in the detection flow diagram (Figure 7), 3*1024 samples of recording is first filtered at 300 Hz to remove cardiac noises. Then the filtered signal is processed both in temporal and frequency domains:

- In the temporal domain, the envelope of the signal is obtained by a low-pass filtering at $w_n = 0.01$ rd.s⁻¹. Then one minimum threshold is applied to

detect respiratory event. Once an event is detected, its center time is noted if it lasts more than 0.4 s.

- In the frequency domain, the summation of frequency contents between 300 Hz and 600 Hz is calculated for every segment of 1024 samples. One minimum threshold is applied, but also a moving threshold depending on the average of power on previous, actual and next segments. As in temporal domain, the center time is noted for each detected event.
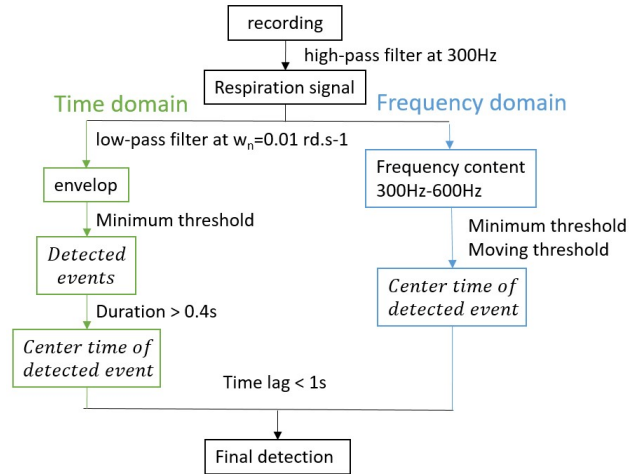

Figure 7: Detection flow diagram

At the end, if one respiratory event is detected in both temporal and frequency domains, and if the time lag between these two detections (evaluated by their center times) is less than 1s, the event is considered as detected in the final result.

Results

The detection result is presented in Figure 8**Erreur ! Source du renvoi introuvable.**. The temporal detection result is shown in yellow, the frequency detection result is shown in purple and the final detection is shown in red. Each detection signal has two levels: a high level presents a detected respiratory event; a low level presents pause or apnea.
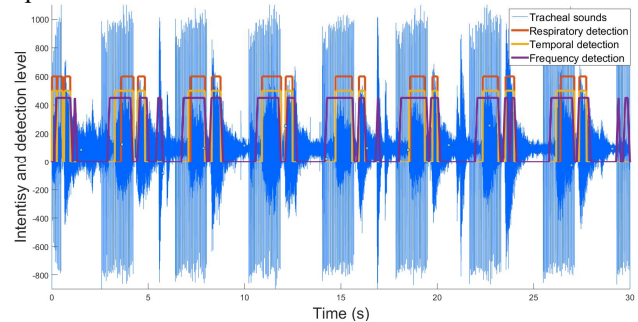

Figure 8: Example of a detection result

For this recording of 30 s, 9 induced inspirations and 8 expirations are all detected successfully. Some noises at 2 s,

6 s, 17 s and 21 s are eliminated. And all pre-inspirations are not considerate as respiratory events.

Discussion

We have proposed a respiratory detection method for DP monitoring, which allows detecting breathing events and electrical stimulation signal. The results obtained with one recording on one patient are very promising.

Some short noises (shown in green circles in Figure 4) were considered as respiratory events by the frequency detection (presented in Figure 8). Temporal detection allows to eliminate these noises are eliminated by analyzing their durations. On the other hand, temporal detection may be influenced by the stimulation signal, and this is when frequency detection can help because the inspiration frequency content differs from the one of stimulation.

Furthermore, the captured stimulation signal could indicate a dysfunction of the pacing system and recorded tracheal sounds could give a feedback of the electro-ventilation quality. The synchronization of these two information could indicate if the stimulation settings (intensity, frequency ...) should be adapted. For example, in the present case, I_{TH} may be set too high because some small pre-inspirations are induced at the beginning of the stimulation.

Moreover, one possible application of this system during the implantation surgery would be to help verifying electrodes contacts and adjust stimulation settings instead of relying on the visual observation of diaphragm contractions as it is assessed usually.

For the target population, the cardiac signal would also be an important vital indication. But in the present study, the microphone was located quite higher because of the tracheotomy, therefore cardiac sounds were too weak to be captured. Tracheal sounds could not be recorded under mechanical ventilation because air flow did not reach the microphone which was placed above the tracheotomy. For the next study, we may place the microphone closer to the chest, or integrate it within the tracheotomy tube for a better flow sounds recording.

In the present work, only one short recording was done on one patient in a calm room, more recordings on different patients in various environments need to be analyzed to further validate the approach. Tracheal sounds may vary between different patients; it means that respiratory features could not be the same. A noise-reduction algorithm needs to be added because acoustic methods are always sensitive to noises. Besides, artificial intelligent methods could be studied because respiratory sounds and stimulation signals are so repetitive.

We believe that monitoring tracheal sounds could be a useful way beyond the very limited niche of patients with DP. Indeed, it would provide a non-invasive way to approximate inspiratory flow that would be useful in all patients requiring respiratory monitoring in acute situations (e.g. as a safety measure during the administration of morphine for acute pain) and in chronic situations (e.g. home mechanical ventilation).

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