Prototype and Graphical Interface for Selective Exhaled Air Acquisition

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Abstract: The recent advances in technology and detection methods, as well as its economic viability have pointed the analysis of exhaled breath as a promising tool for medical diagnosis or therapy monitoring. Since the concentration of the most Volatile Organic Compounds (VOCs) present in the exhaled breath is very low (ppb_v – ppt_v range) it is important to have a selective sampling system for alveolar air. In this work we present the design and instrumentation of a prototype that allows real time monitoring of the breathing cycle and automatically decide the correct moment for acquisition and channel the acquired sample to the Ion Mobility Spectrometer with Multi-Capillary Column pre-separation (MCC-IMS). The prototype is composed by a flow meter, signal packaging circuits and a flow commuting circuit (three-way valve). Two graphical interfaces were also developed to help controlling the whole process of acquisition making it easy, quick and reliable.

1 INTRODUCTION

Nowadays the development of a fast, effective, non-invasive, low-cost and painless diagnosis method is under special interest of medical and scientific community (Mashir and Dweik, 2009). From this point of view breath analysis is extremely attractive, sometimes even appointed as an alternative method of biochemical blood analysis (Baumbach, 2009).

It is well known in the medical community that the Volatile Organic Compounds (VOCs) present in the exhaled air can provide important information about the health status (Kim et al., 2012). More than 200 different compounds have been detected in the exhaled breath and some of them are identified as biomarkers of common diseases such as diabetes, liver or kidney failure, pulmonary cancer (Spanel et al., 1999) or allograft rejection (Miekisch et al., 2004).

The VOCs present in the exhaled breath are in very low concentrations, typically from parts-per-billion (ppb) or microgram/litre (µg/l) to parts-per-trillion (ppt) or nanogram/litre (ng/l). Thus the spectrometric methods used for the detection of the different metabolic processes products must have a high sensitivity (low ppb range) and provide a direct analysis in real time or in a few minutes (Baumbach 2006). All these requirements can be realised by Ion Mobility Spectrometry (IMS). This technique is based on the drift of ions given their mobility in the gas phase, at ambient pressure, under the influence of an electric field (Baumbach, 2006). Compared with other methods of breath analysis, the IMS offers a tenfold higher detection rate of VOCs.

By coupling the ion mobility spectrometer with a multi-capillary column as a pre-separation unit, IMS offers the advantage of an immediate twofold separation of VOCs with visualisation in a three-dimensional chromatogram (Jünger et al., 2010).

From other side, direct breath analysis by analytical methods implies to use an effective sample collection system in order to provide the VOCs of endogenous origin only. These compounds are present in the alveolar air which is in chemical equilibrium with the alveolar capillary blood vessels. Therefore it is necessary to develop selective acquisition systems that are able to identify and collect only the alveolar air.

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2 CAPNOGRAPHY

One of the most used techniques to do that selection is capnography. This technique provides information about the CO_2 levels, pulmonary perfusion, ventilation and respiratory patterns.

Capnography consists in the graphic display of the instantaneous concentration of CO_2 in function of Time or in function of Volume during a breathing cycle.

The time capnogram is the most used and can be divided into two segments, inspiration (Phase 0) and expiration (comprises Phases I, II and III) (Bhavani-Shankar et al., 1995).

There are different terminologies to designate the different phases of a capnogram and we decided to adopt the one suggested by Bhavani-Shankar, Kumar, Moseley and Ahyee-Hallsworth (1995).

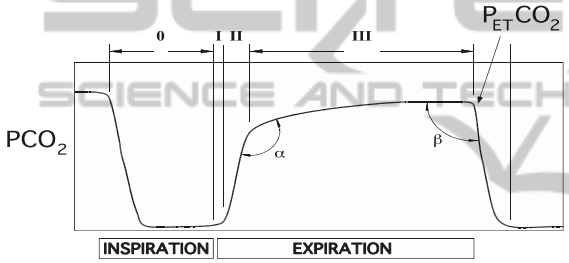

Figure 1: Phases of a time capnogram.

During the first portion of expiration (Phase I) the PCO_2 is zero. This phase corresponds to the anatomic dead space and the equipment dead space. As expiration continues, a sigmoid curve corresponding to the abrupt rise on CO_2 concentration appears, (Phase II) at this stage there's already a mix of alveolar air and dead space air.

In the last segment of the expiration we find a plateau in the PCO_2 (Phase III) which represents the alveolar region, this is the portion of the exhaled breath we are looking to acquire as it's entirely composed of alveolar air.

3 FLOWMETRY AND REFERENCE RESPIRATORY RHYTHMS

Fluxogram is the graphical monitoring of respiratory air variation with time. A time capnogram overlapped with a fluxogram (Bhavani-Shankar and Philip, 2000) can provide a clear identification for the area of end-tidal breath (see figure 2). By this only a flow meter can be used for selective assessment to the last segment of the expiration which represents the alveolar region with high CO_2 concentration.

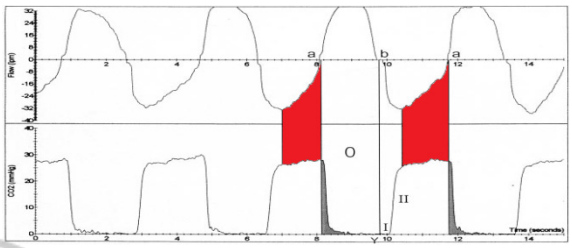

Figure 2: Comparison between respiratory flow rate and time capnogram. (Adapted from Bhavani-Shankar and Philip, 2000).

As a first step it was necessary to create reference rhythms which the user shall follow during the flow measurements. Taking into consideration a probability to need use our breath acquisition system in different situations, we choose to use three kinds of rhythms: Slow, Normal and Fast.

For each of these reference rhythms were determined the average frequency and the mean time for each breathing cycle. Mean values were calculated from the statistical analysis of measurements of respiratory flow of healthy persons of both gender, male and female. Each volunteer have performed the test for approximately 60 seconds at three different paces. The respiratory flow was monitored by SS11LA flow transducer connected to the MP35 acquisition unit from Biopac Systems, INC. The BSL PRO 3.7 graphical software was used for further calculations of the average values for each breathing cycle and determination the reference value for the phase of inspiration and expiration.

The reference values for the breathing cycle were established as follows: for the normal rhythm the total cycle´s time is 3,66 seconds, where 1,63 seconds are for inspiration; the slow rhythm has 7,01 seconds cycle, from which 3,25 seconds are for inspiration; finally the fast rhythm takes 2,23 seconds to fulfill a cycle, being 1,22 seconds of the inspiratory phase.

4 PROTOTYPE FOR SELECTIVE SAMPLING OF ALVEOLAR AIR

The prototype for selective acquisition of exhaled

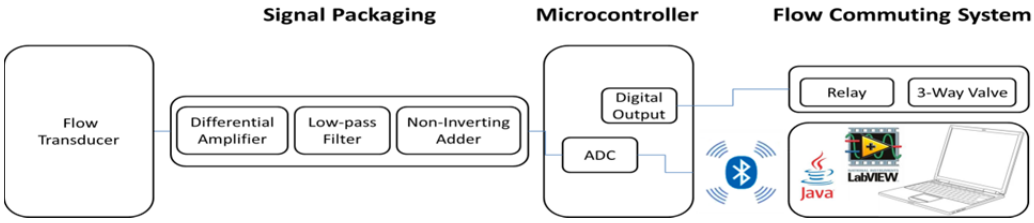

Figure 3: Block diagram from the prototype for exhaled air acquisition.

breath was developed in two different cells, hardware and software.

The hardware is responsible for the data acquisition, analog to digital conversion and data transmission to the computer, a flow commuting system was also developed (see figure 3).

The software is a graphical interface that helps the user pace his breathing cycle and by using some algorithms identifies and triggers the correct sample to be acquired.

4.1 Selective Acquisition System

The developed physical part of the prototype is divided in four blocks: (1) SS11LA flow transducer; (2) the signal packaging circuit; (3) acquisition and communication circuit; (4) flow commuting circuit.

The user breathes through the flow transducer which has a differential output proportional to the measured flow.

The signal packaging circuit is divided in three parts, a differential amplifier which detects the differential output, single waves it and gives it a 4000 gain, one low-pass filter which cuts the existing noise and a non-inverting adder that places the whole signal in the digital window of the microcontroller.

The acquisition and communication circuit uses a microcontroller that through its AD converter digitalizes the electrical signal from the packaging circuit and sends this data to a computer with the help of a Wireless Bluetooth module.

The flow commuting circuit is composed of a relay, a three-way valve and a coupling circuit connecting it to the microcontroller.

4.2 Graphical Interfaces

We have developed two graphical interfaces, one in LabVIEW® and the other in Java™, both with the ability to instruct the user to follow a desired breathing rhythm.

The LabVIEW® graphical interface (see figure 4) was developed to determine if this way of collecting exhaled air samples was valid and accurate. This aim was confirmed in interaction with the selective acquisition system.

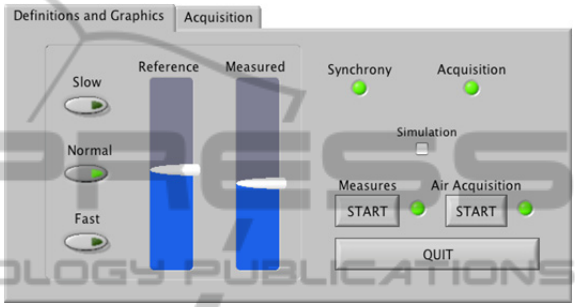

Figure 4: LabVIEW® graphical interface.

Therefore, we developed another user interface using Java™ (see figure 5) aiming to do the same process, but using a programming language that did not need purchase of commercial software.

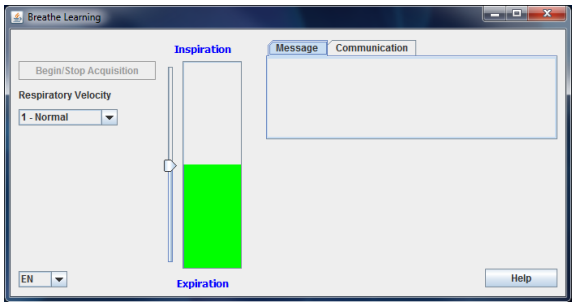

Figure 5: Java™ graphical interface.

In both interfaces, the user is asked to breathe according a slide representation of a previously chosen reference signal (breathing rhythm).

In a first step, the developed algorithm checks if the signals are synchronous at least for the three complete respiratory cycles. When this condition is reached the initial and final instant of the alveolar region of the breathing cycle are identified. At this time a command is sent to the microcontroller, which in turn operates the relay valve, allowing the valve to remain open only between these instants. This process ensures that only alveolar air is

sampled into the system for its further analysis by Ion Mobility Spectrometry or some other suitable analytical technique.

5 CONCLUSIONS

The proposed method for monitoring and selective sampling of exhaled air through the respiratory flow represents a reliable alternative method to the capnography.

The developed prototype is cheaper than any fast capnograph and it can be used for a long period of time. It can also be easily assembled to the MCC IMS apparatus for further sensitive analysis of the VOCs from alveolar air.

The successfully developed graphical interfaces make a process of breath samples collection more user friendly for the operator, as well as for the patients.

However some parts of the implemented algorithm have to be optimized for better performance in real healthcare environments.

However some parts of the implemented algorithm have to be optimized for better performance, especially for the patients with some diseases or respiratory problems.

So the future work will concern to the extensive statistical tests of the developed prototype with large groups of population, regarding the specificity of its age and gender. This is important in order to improve the accuracy of the reference rhythms of breathing. Within this topic it shall be acquired respiratory rhythms from children and people with limited medical conditions, as well as create models and special menu for this kind of patients.

It can also be added an instructional movie or help menu to allow to the patient follow the respiratory reference rhythm in a better way.

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