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Estimation of Inhalation Flow Parameters for Asthma Monitoring Using Acoustic Signal Processing and Machine Learning

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Abstract. Asthma is one of the most prevalent diseases. To control this chronic respiratory condition, inhaler devices, such as the dry powder inhaler (DPI) and the pressurized metered dose inhaler (pMDI), are prescribed. However, poor asthma management can significantly deteriorate the patients' health and their quality of life in general. Through regular treatment, asthma patients frequently use inhaled medication in order to help improving their respiratory system. Nevertheless, a lot of patients do not follow the inhalation technique as instructed, including incorrect use of the inhaler and unsatisfactory medication adherence. This may result in poor control of asthma and increased risk of asthma attacks. In this study, an innovative low-cost solution is proposed to monitor the inhalation flow rate. This consists of an acoustic add-on device that generates a sound when using the inhaler. This sound is correlated to the flow rate of the inhalation. The generated sound signal is captured by a smart phone and its features are extracted in order to estimate parameters such as the inspiratory flow rate (IFR), inspiratory volume over the first second (FIV1), total inspiratory lung volume or the inhalation capacity (IC) and other relevant inhalation parameters. Prior to feature extraction, the signal is first passed through a bandpass FIR filter, and then the inhalation segments are detected using a Bayesian sequential detection algorithm. The energy of the pre-processed signal is then used to estimate the inhalation parameters using linear regression. The proposed method is shown to have good performance (e.g. for IFR estimation: $(R^2 = 99\%, p\text{-value} < 0.0001)$.

Keywords. Asthma, inhalation, acoustic signal, Add-on device, DPI inhalers, inspiratory flow rate, inspiratory capacity, FIV1.

1. Introduction

Asthma is a common chronic disease that occurs in 1 to 18% of the population in different countries all over the world. It is estimated that more than 300 million people suf-

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fer from asthma worldwide [1]. In order to achieve a good symptoms control and limit the risk of future exacerbations, a proper long-term asthma management is indispensable [2]. Inhaled pharmaceutical therapy is the most common medical treatment for asthma. In order to fully benefit from the drugs, the prescribed dose has to reach the airways. Therefore, a poor inhalation technique can decrease the efficacy of the inhaler. For an improved asthma control, patients must respect the time as well as the procedure of taking the medication. Thus, temporal adherence and inhalation technique adherence are key success elements for asthma management [3,4]. It is estimated that 70 to 80% of patients do not use their inhaler correctly [4,5,6]. In fact, several factors are responsible for a non-adherence to the instructed inhalation technique, such as an inappropriate inhalation flow rate, exhaling into the inhaler when using a dry powder inhaler (DPI) and not holding the medication long enough in the airways [6,7]. In a study conducted by Lavorini et al. [8], it was shown that inappropriate drug inhalation profile is widely common among asthma patients. For example, sometimes patients inhale too fast ($>$ 90 L/min) using pMDIs [9] or too slow to reach the recommended flow rate ($>$ 30 L/min) using DPIs. This leads to a non-adherence of the medication use [10]. The damage caused by a non adherence to medication use varies from being minor to severe. It can affect symptoms such as coughing and wheezing, but can also lead to more serious consequences such as frequent asthma exacerbations and frequent hospitalizations, and thus higher morbidity and mortality rates [11,12,13,14].

Different methods have been developed to monitor the adherence to medication of users. These methods can be summarized in two main categories: subjective and objective methods [11,15]. The subjective monitoring methods are mainly based on surveys, which consists of patients' self-reports and observations made by physicians. However, the fact that these methods are based on reported information makes them prone to a high risk of bias [11,16,17]. On the other hand, objective monitoring techniques include a variety of biochemical methods and electronic monitoring systems. Biochemical techniques can accurately evaluate the adherence. However, they can be expensive, interventional and demanding in terms of special technical expertise for their implementation [11,18]. Electronic monitoring systems are based on built-in electric sensors and are developed for inhalers often to capture the frequency of the medication use. To our knowledge there are no non-invasive technologies that can objectively monitor the inhalation flow rate in DPI and pMDI inhalers [11,16,18,19,20,21]. Most of these techniques are expensive, difficult to use and focus only on temporal adherence. There is therefore a need for alternative monitoring solutions that mitigate the above-mentioned shortcomings. Moreover, mobile health applications are currently becoming more popular in our daily life, especially for patients with chronic diseases who need a regular control of their health condition. Due to their proven usability and efficiency, developing health monitoring solutions using smart phones appears to be very promising [22].

In this paper, we propose a novel sound-based inhaler system that can remotely assess both the inhalation adherence and the inhalation technique. By analyzing the sound generated during the inhaler use, the acoustic monitoring system can provide an accurate assessment of the inhalation profile.

In this context, a new solution has been proposed in [23] for the monitoring of asthma patients. This solution comprises an inhaler add-on device which is attached to the inhaler; it allows an accurate assessment of flow rate during inhalation based on the sound generated by the add-on device, and can thereby provide an estimation of the in-

halation profile. When a patient is using the inhaler, the add-on device generates a sound that is captured by the microphone of a smart-phone. The acoustic features are extracted and then analyzed using signal processing and machine learning methods, thus allowing the users to assess their inhalation and better control their condition.

In this paper, using the approach proposed [23], we present an *automated* approach to estimate the inhalation flow rate by analysing the sound generated during the use of a DPI inhaler. The sound signal recorded by the smart-phone microphone to first processed by a bandpass FIR filter. The filtered signal is then analysed to detect inhalation segments using a Bayesian sequential detection algorithm. The energy related to these segments are then computed, and used to estimate lung function parameters, such as the inspiratory flow rate, the inspiratory volume over the first second (FIV1) and the total inspiratory lung volume and others, using linear regression. The proposed system is illustrated in Figure 1. This system can be implemented and integrated in a mobile application that may help asthma patients to assess their drug administration for better control, and also to monitor their respiratory function in order to potentially predict the risk of any future exacerbation. The implementation and the integration of the system in a mobile application is beyond the scope of this work and is planned for future studies

The remainder of this paper is organized as follows. In section 2, we introduce our methodology which consists of sound acquisition, signal processing, segmentation algorithm and inhalation parameters estimation. Section 3 is devoted to estimation results. Finally, section 4 presents some perspectives for future work and draws some concluding remarks.

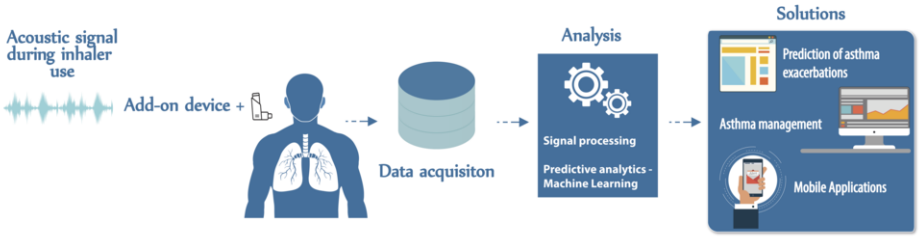

Figure 1. Acoustic monitoring system for asthma patients

2. Methodology

First we start with data acquisition. Second, we pre-process the acoustic signal through filtering and segmentation. The processed signal is then used to extract inhalation metrics that will be used to estimate the flow rate and other parameters. Finally, we use linear regression to estimate the inhalation parameters from the computed energy.

2.1. Inhalation sounds acquisition

The inhalation induced acoustic signals were recorded in a noise-free room at the University of Copenhagen. A dosage unit sampling apparatus (DUSA) was assembled to perform the DPI test as shown in Figure 2. This unit is composed of a vacuum pump (HCP5,

COPLEY), a Critical Flow Controller (COPLEY TPK) and a collection tube (DUSA for DPI, COPLEY) [24].

Figure 2. DUSA set up for DPI test.

First, a mass flowmeter (TSI Incorporated) [25] was attached to the assemblage by a mouthpiece adaptor. The air flow was then adjusted to the test flow rate (15 to 90 L/min with a step size of 5 L/min). Afterwards, the flowmeter was replaced with the inhaler attached to the add-on acoustic device. The sounds were recorded using an iPhone 6 microphone placed at a distance of approximately 1 meter away from the acoustic device. The recording times were between 12 to 15 seconds which is equivalent to three inhalations for each recorded signal. These signals were stored as wave files.

2.2. *Signal Processing and segmentation*

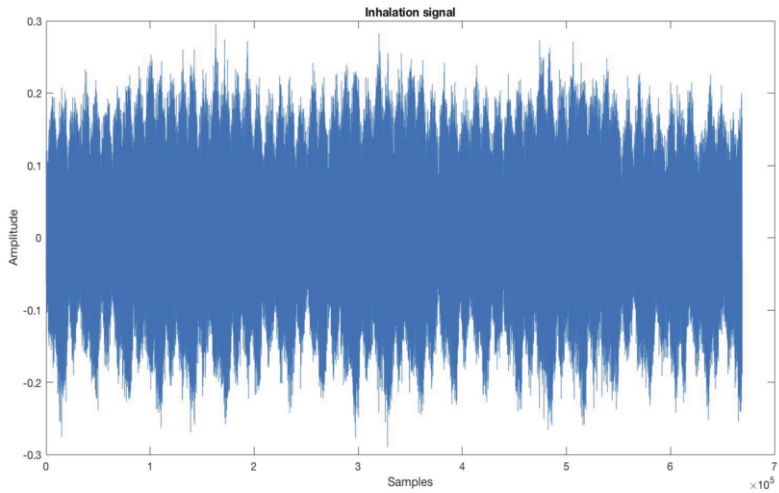

Figure 3. Inhalation recordings with a test flow rate of 20 L/min

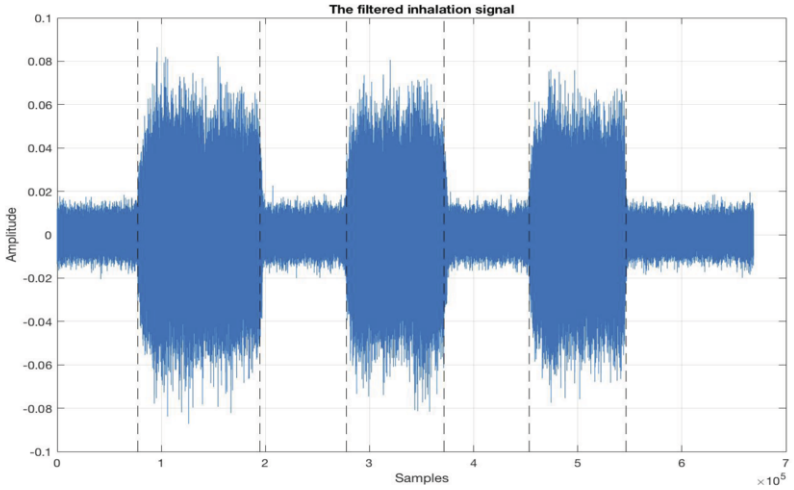

Figure 4. Segmenting the acoustic signal (20 L/min) using the sequential detection algorithm.

All of the acquired signals were processed and analyzed by MATLAB R2017a software. The signals were sampled at 48 KHz sampling rate. The inhalation starts once the air flow is generated using the DUSA. The inspiratory phase ends once the airflow stops. Each inhalation phase is followed by a pause phase. The recorded sound of three consecutive inhalation adjusted to a test flow rate of 20 L/min is illustrated in 3.

In this study, we applied a bandpass FIR filter with lower cutoff frequency 2 KHz and higher cutoff frequency 8 KHz to remove the undesired frequency components. Second, the automatic sequential detection algorithm proposed by Hubert et al. [26] was applied to the filtered signal (see Figure 4).

The adopted detection algorithm can be described as an unsupervised learning method with the only assumption being that a segment involves a change in the signal's energy. Based entirely on a Bayesian inference, this algorithm optimizes the likelihood function of entropy to find the maximum a Posteriori estimate (MAP). Let I denote the number of detected segments in the processed signal. The detection algorithm estimates the start and end of each segment, i.e. for $i = 1, .., I$, we have that

- $\hat{m}_i$: the MAP estimate of the starting time of the i^{th} segment;
- $\hat{q}_i$: the MAP estimate of the ending time of the i^{th} segment.

This sequential detection is a recursive algorithm that returns the concatenated vector $[\hat{m}_1 \hat{m}_1 \cdots \hat{m}_I \hat{m}_I]$. In example shown in Figure 4, we obtained the following vector of six cutting points bounding each inhalation phase: $[\hat{m}_1 \ \hat{q}_1 \ \hat{m}_2 \ \hat{q}_2 \ \hat{m}_3 \ \hat{q}_3] = [77401 \ 194702 \ 277803 \ 371504 \ 453405 \ 546401]$.

2.3. Estimation of inhalation parameters

When using the inhaler, the recorded signal $x(n)$, $n \in A$ with $A = [1, \cdots, N]$, can be expressed as follows :

$$x(n) = \begin{cases} s(n) + w(n) & \text{for } n \in \phi_i,\ i = 1, \cdots I \\ w(n) & \text{otherwise} \end{cases} \tag{1}$$

where $s(n)$ is the desired signal (inhalation signal), $\Phi_i = [m_i,\ q_i]$ is the sample indices corresponding to the i^{th} inhalation segment, and $w(n)$ is the background noise. Let N_i denote the number of samples corresponding to the i^{th} inhalation, i.e. $N_i = q_i - m_i - 1$.

First, we estimate the power of the noise-corrupted signal corresponding to each inhalation, as well as the power of the noise-only signal as follows:

$$P_i = \frac{1}{N_i} \sum_{n=m_i}^{q_i} x(n)^2 \tag{2}$$

$$P_w = \frac{1}{|\Omega|} \sum_{n \in \Omega} x(n)^2 \tag{3}$$

where $\Omega = A \setminus \Phi_1, \cdots, \Phi_I$ and $|\Omega|$ its cardinality.

The average energy of the noise-free signal, that will be used as a predictor for the flow rate estimation, is calculated as follows:

$$E_s = \frac{1}{I} \sum_{i=1}^{I} (P_i - P_w) t_i \tag{4}$$

where t_i is the time duration (in seconds) of the i^{th} inhalation, which is determined using m_i, q_i and the sampling frequency.

Finally, we estimate the inhalation flow rate using a simple linear regression model where E_s is the predictor, i.e.

$$\hat{f} = \beta \times E_s + \alpha. \tag{5}$$

where the parameters α and β are estimated using the available datasets and the least square method.

3. Results

In our experiments, a total of 54 inhalations were recorded and adjusted to different test flow rates (15 to 90 L/min with a step size of 5 L/min). The acoustic signals were stored in .wav files. Using Matlab, the signal is filtered and analysed as described above. The actual value of the inspiratory flow rate (IFR) was extracted during the experiments; it was displayed on the mass flow-meter. Subsequently, the actual values of (IC) and (FIV1) were easily extracted from the inhalation segments.

The results show that the signal energy E_s is highly correlated to the inhalation flow rate and can significantly explain 99% of its variance, i.e. ($R^2 = 99\%$, with p-value$<$ 0.0001)..

We tested our methodology on 3 acoustic signals that were not included in our training model (Eq. (5)). Based on the flow rate estimation, estimates of the other inhalation

parameters such as the inhalation capacity (IC) and the forced inspiratory volume in one second (FIV1), are easily derived.

Experiment No.	IFR (L/min)			IC (L)			FIV1 (L)		
	Estimated	Actual	RMSE	Estimated	Actual	RMSE	Estimated	Actual	RMSE
E1	25.424	25	0.4241	2.058	2.0243	0.034	0.0032	0.0042	1e-03
E2	31.258	30	1.258%	3.134	3.008	0.126	0.0032	0.0050	0.001
E3	39.619	40	0.381	3.972	3.837	0.135	0.0034	0.0067	0.003

Table 1. Comparison of the estimated inhalation parameters IFR, IC, FIV1 and their actual values

Table 1 compares the actual values vs. the estimated values of the inhalation parameters. This table also includes the root mean square error (RMSE) as an important indicator of the accuracy. The RMSE on FIV1 estimation was slightly higher compared to other parameters; this can be explained by the amplitude of the acoustic inhalation signal. Since the energy signal is correlated with IFR, we can see in Figure 4 that low amplitudes correspond to the first seconds of inhalation. Therefore, the observed error are due to the fact that we assumed a steady test flow when estimating the actual FIV1. However, the overall RMSE for IFR and IC is remarkably low, which illustrate the merits of the proposed method.

4. Conclusion and future work

Most related works on acoustic monitoring systems require microphones to be placed near to the sound source, which can be sometimes uncomfortable to use for to the patient. In this work, we propose a new technology to monitor inhalation performance using an acoustic device. Using an inhaler add-on and a smartphone, we were able to capture good quality acoustic signals and accurately estimate different inhalation parameters. These promising results motivate us to incorporate the proposed technology into an acoustic monitoring system for asthma patients, that will include an inhaler with an add-on device (both DPIs and pMDIs) which in turn is connected to a smartphone via an m-health application. This would provide asthma patients with all the important instructions when using their inhaler in case of a non-adherence, and also help them gain control of their asthma condition and prevent potential exacerbations by allowing them to have a close look at their lung function through the inhaler sensor. In continuation of this research, we are planning to test this new technology on asthma patients in the region of Rabat (Morocco) and we intend to include other relevant data in our prediction models such as the patient's self-reports, weather and air quality measurements through a geographical information system (GIS). These clinical trials will enable us to improve the prediction quality of our models, thus making this technology very useful in the field of asthma management and control.

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