An Acoustic Method to Automatically Detect Pressurized Metered Dose Inhaler Actuations

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Abstract—**Chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) affect over 400 million people and are incurable. The pressurized metered dose inhaler (pMDI) has been the most popular inhaler device in inhaled therapy in recent times. However the pMDIs require good coordination between inhaling and actuating the inhaler to deliver the aerosolized drug most effectively. Poor coordination can greatly reduce the amount of drug delivered to a patient and therefore reducing the control of respiratory disease symptoms. Acoustic methods have been recently employed to monitor inhaler technique quite effectively. This study employs a noninvasive acoustic method to detect actuation sounds in a portable monitoring device. A total of 158 actuation sounds were obtained from a group of healthy subjects (n=5) and subjects suffering from respiratory diseases (n=15). The developed algorithm generated an overall accuracy of 99.7% demonstrating that this method may have clinical potential to monitor pMDI actuation coordination. The informative feedback from this method may also be employed in clinical training to highlight patient actuation technique.**

I. INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD) are two of the most common respiratory diseases today. Both involve persistent obstruction of airflow from the lungs whether it involves the inflammation of the airways, the inability to exhale or simply a chronic cough. According to the World Health Organization (WHO) 235 million people suffer from asthma and 210 million from COPD worldwide. Nine people die every day in the U.S and one person dies every hour in Western Europe from a chronic respiratory disease [1]. There is no cure for these diseases at present however they may be controlled with medication. Inhaled aerosol therapies are the mainstay of treatment of obstructive lung diseases [2] [3].

Inhalers are small portable hand-held devices that are most commonly used to deliver respiratory medication

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directly to the lungs. Inhaled medication offers major advantages over systematic therapy due to the direct targeting of the lungs [4]. The pressurized metered dose inhaler (pMDI) is the most commonly used inhaler with total worldwide sales of pMDI products reaching over $2 billion per year [5]. The pMDI delivers an aerosolized mixture of medication and propellant from the user depressing or actuating a pressurized canister while commencing a slow deep inhalation. The peak inspiratory flow rate (PIFR) is recommended to be below 90L/min [6] [7]. Studies have reported that over 50% of patients are prone to not adhering to the correct inhaler technique [8]. Non-adherence to inhaler technique may have a detrimental effect on a patient's respiratory health as it can limit the precision of drug delivery. The lack of knowledge within healthcare professionals regarding inhaler technique also contributes to patient misuse [9]. Technique errors as reported in [9-11] include the lack of coordination between actuation and inhalation, multiple actuations, not actuating at all, too low or too high inspiratory flow.

Poor actuation-inhalation coordination, or sometimes referred to in the literature as hand-to-lung coordination [12], is the most common pMDI technique error. This refers to actuating the inhaler before inhaling or actuating too late during an inhalation sequence. This may lead to as little as 37% of the total emitted dose being deposited in the lungs and over 50% deposited in the oropharynx [13]. Non-adherence has shown to increase emergency room visits and hospitalizations [12]. Most pMDIs do not contain any dose monitoring system which enables patients to "dump" medication before attending medical checkups.

It has been reported that acoustics can be employed to detect dry powder inhaler sounds [14]. Acoustic methods have proven to be a noninvasive approach to monitoring inhaler technique and can be employed with no modification to existing inhaler designs [15]. However, acoustics methods have yet to be applied to standard pMDI sounds. This study employs time-frequency analysis from pMDI audio recordings to automatically detect pMDI actuations.

II. HYPOTHESIS & AIMS

The aim of this study was to employ an acoustic-based method to identify pMDI actuations. The hypothesis is that acoustic methods can automatically detect actuation-inhalation coordination in pMDI inhalers. This would allow quantitative assessment of asthma patient pMDI technique.

III. METHODS

A. Subjects

Data were collected from a group of healthy subjects to capture all actuation events at key times within a range of PIFRs. Data were also collected from 15 in-hospital patients (6 male, 9 female, age range 21-84) at a Respiratory Clinic in Beaumont Hospital, Dublin, Ireland. All patients recruited were suffering from a chronic respiratory disease and were aware of the mechanics of the pMDI.

1) Healthy Group Protocol

Each subject was trained, using a placebo Evohaler™ pMDI, to actuate the inhaler at three specific times; 1s before inhalation (early actuation), 0-0.5s into an inhalation (correct actuation) and finally approximately two thirds into an inhalation (late actuation). For each actuation time, subjects were trained using a Clement-Clarke *In-Check Dial*™ to inhale at PIFR $\cong$ 25L/min, PIFR $\cong$ 60L/min and PIFR $>$ 90L/min. Each actuation time was recorded three times for each PIFR giving a total of 135 recordings for five subjects. All recordings were visually and aurally assessed by an expert reviewer to ensure an actuation occurred.

2) In-Hospital Patient Group Protocol

In-hospital patients were asked to use a placebo Evohaler™ pMDI three times. The first two consisted of the patient using the inhaler as they would normally on a daily basis. The patients were then informed from a healthcare professional of technique errors made and were then asked to use the inhaler a third time. All patient recordings were visually and aurally assessed by a medical professional and an expert reviewer. A total of 44 recordings (one recording failure instance) were obtained from the in-hospital patients.

B. Inhaler Recording Setup

The study employed an Analog Devices ADMP401 MEMS omnidirectional medium quality microphone (Fig. 1). The microphone was placed outside facing inwards, towards the location of the actuation site, at the lower end of the inhaler casing. The microphone was then connected to a Creative Sound Blaster [Creative Labs Ireland (Ltd.), Dublin, Ireland] sound card. The sampling rate employed was 44.1kHz at 16 bits/sample. Fig. 2 shows the acoustic signal from a pMDI recording. A 0.5" force sensitive resistor (FSR) was placed on top of the inhaler canister to obtain a gold standard temporal indication of the canister being depressed. The FSR was connected as a feedback resistor in a buffer circuit with low resistance (R=120Ω) to obtain a linear force-voltage relationship as is in the manufacturer's guidelines [SparkFun Electronics, Colorado, USA]. FSR data were recorded at 1kHz sampling rate.

Figure 1. (Left) Top-down view of the recording rig showing FSR on canister. (Right) Side view of recording rig showing microphone placement.
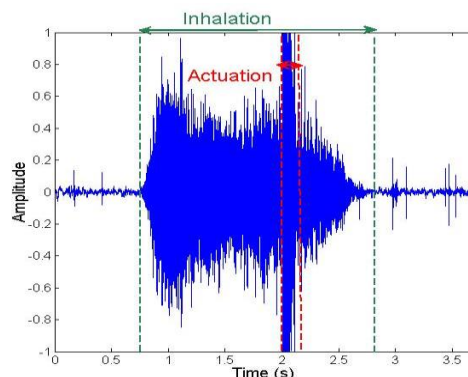

Figure 2. Acoustic signal from a pMDI consisting of an inhalation (0.7-2.7s) with a late actuation occurring at (2-2.15s)

C. Signal Processing

It was hypothesized that the plume expelled from the inhaler canister creates a burst of high frequency energy for a small duration in time. The signal processing was divided into two phases. Phase one consisted of time-frequency analysis of pMDI acoustics. Phase two employed a summation of high frequency content followed by a peak assessment routine.

1) Phase One

Wavelet transformations have been previously employed to classify between healthy subjects and subjects with respiratory diseases [16]. The continuous wavelet transform (CWT) was employed to highlight discontinuities in the inhaler audio signals. The CWT with scaling parameter a and position parameter b is given as

$$T(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{+\infty} x(t)\varphi * \left(\frac{t-b}{a}\right) dt \quad (1)$$

where φ is the analyzing wavelet if it verifies the admissibility condition [16].

The CWT was chosen as it gives high temporal resolution at high frequencies. The Morlet wavelet, consisting of a sinusoid multiplied by a Gaussian window, was employed as it is commonly used and its scale-frequency relationship requires less computation to define as the peak frequency is equal to the center frequency of the wavelet. The Morlet wavelet is given as

$$\varphi(t) = \frac{1}{\pi^{\frac{1}{4}}} \left(e^{i2\pi f_0 t} - e^{-(i2\pi f_0)^2/2}\right) e^{-t^2/2} \quad (2)$$

where f_0 is the center frequency of the mother wavelet.

Scales 2 to 1.625, corresponding to 17,916Hz to 22,050Hz, in decrements of 0.005 were chosen to view high frequency content of the audio signal. This represents a total of 76 pseudo frequencies to utilize for time-frequency analysis of pMDI acoustics.

2) Phase Two

The second phase of signal processing reduced the dimensionality of the output wavelet matrix and detected sharp peaks that may identify actuation plumes. Each wavelet coefficient was squared to obtain all positive coefficients. A one dimensional vector containing a summation of all high

frequency content over all coefficients at each sample point, similar to the method discussed in [17], was obtained. The method employed for this study can be represented as

$$Y(t) = \sum_{a=1.625}^{2} T^2(a,b) \ for \ b = 1,2,3 \dots N \quad (3)$$

where N is the total number of samples in the input signal.

The CWT and high frequency summation output can be seen in Fig. 3. A peak assessment routine was then employed to detect and assess peaks above a threshold of 0.38. It was observed that the actuation acoustic signal was of very small duration, 100-150ms. Each peak was initially marked as a potential actuation plume. Power values were taken ±56ms from the peak point to observe if the value decreased by a threshold of 25% of the peak both before and after the peak point to flag as an actuation plume. Fig. 4 shows a flow chart of the signal processing employed to detect an actuation sound. An FSR was employed as a gold standard time stamp signal to combine with expert visual-aural assessment to time stamp actuation events. An adaptive threshold of 80% of the maximum voltage triggered a logic pulse to time stamp canister actuation.

IV. RESULTS

A random selection of 20 pMDI acoustic recordings from the healthy group data was employed for algorithm training. The developed algorithm was applied to 159 test recordings taken from a group of healthy (n=115) subjects in a controlled environment and also to recordings from in-hospital patients in a respiratory clinic (n=44). A total of 158 actuations were obtained for testing. Recordings consisted of no actuations (n=6). Others contained multiple actuations (n=4), as a result from patient incorrect technique.
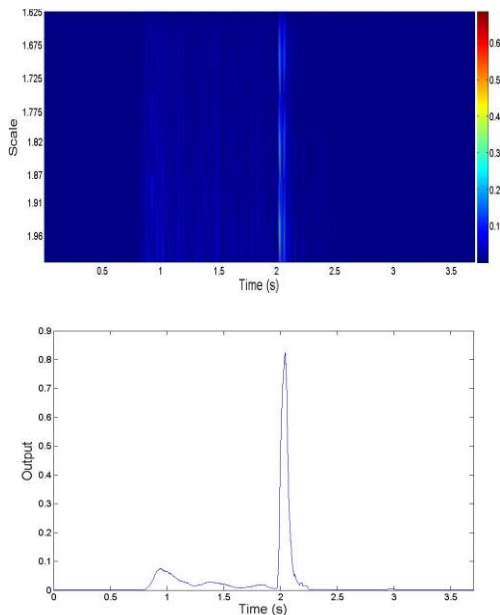

Figure 3. (Top) CWT of pMDI acoustic signal from Fig.2 using scales 2 to 1.625. (Bottom) Output of high frequency summation with peak at 2.041s.
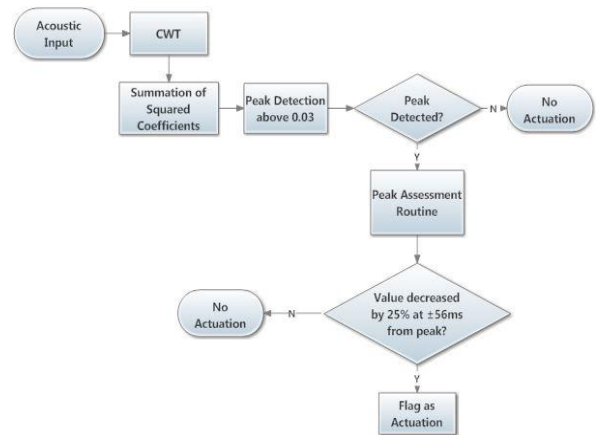

Figure 4. Flow chart of actuation sound detection.

The algorithm developed was validated against objective FSR data and visual-aural assessment. The FSR combined with expert reviewers defined 100% of the audio files for the presence of actuations before algorithmic testing. An actuation was deemed to be correctly identified if the algorithm detected the actuation within 300ms of the onset of the FSR pulse. This was to account for the delay between the canister being depressed (FSR threshold) and the actuation plume at its maximum energy point at which the algorithm detects. Fig.5 shows an example of the algorithm detection of an early actuation acoustic signal against the FSR pulse. The algorithm outputs the location of the aerosol plume peak as a result of the inhaler being actuated by the user.

Table I shows the performance of the actuation detection algorithm. Results were classified as True Positive, False Positive, True Negatives and False Negatives which were employed to assess algorithm performance. It was found that the algorithm generated a total sensitivity (Sen) of 100%, specificity (Spe) of 99.4% and accuracy (Acc) of 99.7%. Out of the 158 actuations recorded, all 158 of them were accurately detected with only one False Positive incident.

V. DISCUSSION

An algorithm employing acoustic time-frequency analysis was developed to automatically detect pMDI actuations in different real-life environments. The results, based on the acoustic method output, demonstrate that the acoustic method used can automatically identify early, correct and late actuations. An overall accuracy of 99.7% and a specificity of 99.4% for all actuation times is a promising result if this method is to be used in a fully automated system for monitoring patient pMDI technique.

If a patient incorrectly inhales too fast (PIFR > 90L/min), it can be impossible for a clinician to accurately determine if the aerosol plume was released from the canister. However placing a microphone in the vicinity of the

TABLE I

ACTUATION DETECTION PERFORMANCE TABLE

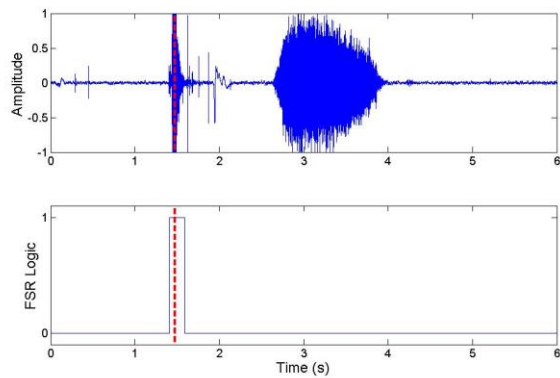| Total no. Recordings	Total no. Actuations	Sen (%)	Spe (%)	Acc (%)
159	158	100	99.4	99.7

Figure 5.   (Top) Acoustic signal showing detected early actuation peak (red) at 1.47s with an inhalation >90L/min (2.6-4s). (Bottom) FSR trigger

aerosol plume may detect the actuation even at high PIFRs as demonstrated in this study. It was noted from empirical observations that the actuation acoustic energy from a pMDI is short in duration. The CWT method was employed in this study as this approach generated high temporal resolution at high frequencies. One of the challenges in this study was detecting actuations within high PIFRs. This involves detecting a very short actuation sound within a noisy inhalation sound. Wavelet scales 2 to 1.625 frequencies contain unique acoustic information of an actuation sound which is not as prominent in inhalations. Such low scales were examined to separate actuations from that of high PIFRs. It was observed that some inhalations contained low powered frequency content even as high as 22,050Hz. It was for this reason that a summation of all squared coefficients across all selected scales at each sample point was employed to distinguish an actuation sound within inhalations containing high frequency.

It was noted upon visual-aural assessment of the patient data combined with the algorithm detection that 87% (n=13) of patients had poor actuation coordination based on the initial two recordings. However this reduced to 53% (n=8) after tuition in the third recording. This demonstrates that a monitoring device is required and would be of clinical benefit to patients and healthcare professionals. It also highlights the inability of many patients to control their illness due to persistent inhaler misuse as a result from a lack of knowledge regarding inhaler technique. It was noted that the most common technique error among patients was early actuation with 47% (n=7) of patients actuating too early before inhaling. While breath actuated pMDIs have been reported [3] which release the drug once the user reaches a PIFR of ~20L/min, their use is not mainstream. A noninvasive portable monitoring device for standard pMDI inhalers may therefore present clinically important information to patients regarding their own inhaler use.

VI.   CONCLUSIONS

To conclude, employing acoustic signal processing methods, an algorithm was developed that accurately identified actuations from a pMDI. This method provides an opportunity to enhance clinical education by providing informative feedback to patients which may contribute to improving respiratory health. Future work will consist of identifying pMDI inhalations to monitor actuation coordination technique and provide patient feedback regarding drug delivery using acoustic methods.

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