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Acoustic Analysis of Inhaler Sounds from Community-Dwelling Asthmatic Patients for Automatic Assessment of Adherence

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ABSTRACT Inhalers are devices which deliver medication to the airways in the treatment of chronic respiratory diseases. When used correctly inhalers relieve and improve patients' symptoms. However, adherence to inhaler medication has been demonstrated to be poor, leading to reduced clinical outcomes, wasted medication, and higher healthcare costs. There is a clinical need for a system that can accurately monitor inhaler adherence as currently no method exists to evaluate how patients use their inhalers between clinic visits. This paper presents a method of automatically evaluating inhaler adherence through acoustic analysis of inhaler sounds. An acoustic monitoring device was employed to record the sounds patients produce while using a Diskus dry powder inhaler, in addition to the time and date patients use the inhaler. An algorithm was designed and developed to automatically detect inhaler events from the audio signals and provide feedback regarding patient adherence. The algorithm was evaluated on 407 audio files obtained from 12 community dwelling asthmatic patients. Results of the automatic classification were compared against two expert human raters. For patient data for whom the human raters Cohen's kappa agreement score was >0.81, results indicated that the algorithm's accuracy was 83% in determining the correct inhaler technique score compared with the raters. This paper has several clinical implications as it demonstrates the feasibility of using acoustics to objectively monitor patient inhaler adherence and provide real-time personalized medical care for a chronic respiratory illness.

INDEX TERMS Acoustics, adherence, algorithm, chronic respiratory diseases, inhaler.

I. INTRODUCTION

Respiratory tract diseases are those which affect the airways. Two of the most well-known chronic respiratory diseases are asthma and chronic obstructive pulmonary disease (COPD). Over 235 million people currently suffer from asthma worldwide, and it is the most common chronic disease amongst children [1]. It is estimated that 600 million people suffer some form of COPD, while nearly 3 million people die annually from this disease [2]. Although chronic respiratory diseases such as asthma and COPD are incurable, if treated with the correct medication, they can be controlled [3], [4].

Inhalers are the devices employed to deliver medication to the airways in the treatment of asthma and COPD. They are compact, portable, hand-held devices that contain medication and deliver it in exact doses so that it can be inhaled into the airways. Two types of inhalers commonly employed are metered dose inhalers (MDIs) and dry powder inhalers (DPIs). DPIs are considered advantageous over MDIs since they avoid the use of propellants, and are instead actuated during the inhalation maneuver [5]. The elimination of propellants allows patient coordination issues between the drug release and inhalation to be overcome. When used correctly, inhalers (both MDIs and DPIs) have been shown to greatly improve patients' clinical outcomes [6], [7], however many patients fail to use their inhaler as directed [7]. Consequently, adherence to inhaler medication can be poor, resulting in poor clinical responses to asthma and COPD treatment.

Nonadherence to inhaler medication is currently a major problem. For inhaled medication, adherence involves both using the inhaler at the correct time of day (temporal adherence) and in the correct manner (technique adherence). Rates of nonadherence among patients suffering from asthma alone range from 30% to 70% [8]. It is estimated that \$300 billion is spent annually in the US treating the nonadherence of chronic diseases, with asthma and COPD amongst the diseases with the highest nonadherence rates [9]. Poor inhaler adherence arises from non-use, haphazard use, excessive use or poor inhaler technique. Temporal adherence is rooted in patient perceptions of the disease, belief in the medication, medication cost and access to healthcare [6], [10], while technique adherence is related to errors in dexterity or a lack of instruction [11]. Several studies have highlighted that errors in inhaler technique may be as detrimental as a lack of temporal adherence [12], [13]. Regardless of the causes of poor adherence, the consequences are similar and include poor clinical outcomes, wasted medications, higher healthcare costs, increased morbidity, and higher mortality rates [14]–[17].

Currently there is no method for reliably monitoring patient inhaler adherence outside clinic visits in community dwelling patients. Clinicians have no objective information on how a patient uses their inhaler in-between visits to the clinic. This is a problem that needs to be acknowledged and addressed. To resolve this problem a device that can monitor patients temporal and technique adherence was developed (previously described in [18] and [19]). The inhaler compliance assessment (INCA^{TM}) device can be attached to the side of the widely used Diskus^{TM} DPI, from where it unobtrusively records the audio signal of patients using their inhaler in uncontrolled real life environments. Ambient (non-contact) microphone technology has recently been reported as a method of successfully detecting snore sounds during sleep [20]. With the aid of ambient microphone recordings, the acoustic profile of the different stages required to achieve successful inhaler drug delivery can be identified. An example of the audio signal obtained from the INCA^{TM} device and its corresponding spectrogram for Diskus^{TM} inhaler use are displayed in Fig. 1. In addition to recording the audio signal of inhaler use, the INCA^{TM} device logs the exact time and date that the inhaler was used. This provides a method of analyzing patients' temporal adherence to their medication. Visual and aural analysis of the audio files can provide information regarding a patient's inhaler technique and thus their technique adherence. However, manual analysis of the audio files obtained from the INCA^{TM} device is a tedious and time consuming process. It takes an experienced respiratory clinician 30 minutes on average to analyze a patient's audio files for one month of typical Diskus^{TM} inhaler use (60 audio files corresponding with 60 doses of medication).

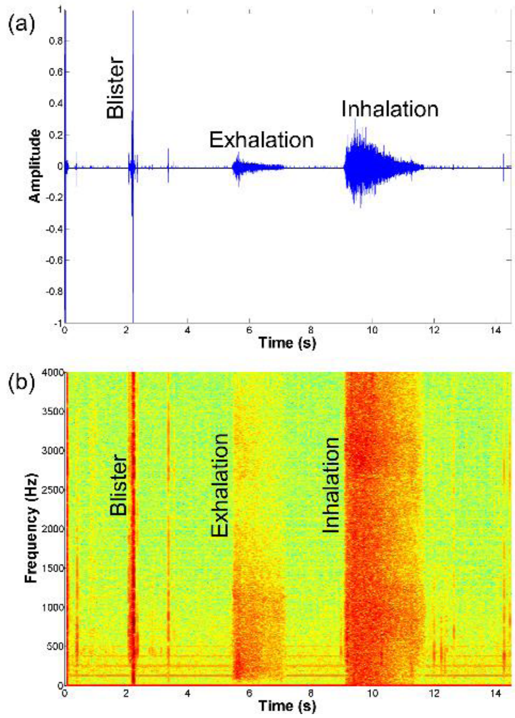

FIGURE 1. **Audio signal (a) and corresponding spectrogram (b) of Diskus^{TM} inhaler use showing the blister, exhalation and inhalation events.**

This type of labor intensive analysis would not be feasible in a large scale study. The analysis of patients' inhaler technique from audio signals may also be biased by the subjectivity of clinicians. Therefore an algorithm that could automatically analyze inhaler audio recordings and provide objective feedback on patient inhaler adherence would be of great clinical benefit.

The INCA^{TM} device is capable of detecting important critical inhaler technique errors associated with Diskus^{TM} inhaler use. Critical inhaler errors occur as a result of imperfect patient technique or lack of knowledge on correct usage and significantly impact the delivery of adequate medication [12]. Some of the critical errors associated with Diskus^{TM} inhaler use have been identified as: failure to open the inhaler device until the mouthpiece fully appears, failure to prime/blister drug foil before inhalation, failure to exhale fully before inhalation, exhalation into the inhaler before inhalation and insufficient force behind inhalation maneuver [12], [21]. Given the critical errors observed in Diskus^{TM} DPI use, the main inhaler steps to be identified by an algorithm are breaths (inhalations and exhalations) and the priming/blistering of the drug foil (henceforth referred to as blister).

The primary objective of this study was to design and develop an algorithm that could automatically analyze patient inhaler use, in order to evaluate adherence. A patient's temporal adherence to their inhaler medication can be analyzed from the time and date stamp of each audio file. Users of the Diskus^{TM} DPI are generally required to take two doses

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of medication each day, one dose in the morning, followed by a second dose in a 6–18 hour interval after the preceding dose. It was hypothesized that technique adherence can be analyzed through the detection of the breath and blister events in the audio signal, the number of each event present and the order in which the events take place. The algorithm should be able to detect the critical errors associated with Diskus™ inhaler use and provide a score on patient technique adherence. This information on inhaler use should also be compiled into an easy to understand and accessible format for both the clinician and patient. Such objective data on inhaler use can provide comprehensive information on patient inhaler use in-between clinic visits for clinicians, as well as acting as an educational aid for patients. Detailed constructive feedback from clinicians on inhaler use may encourage patients to take better control of their adherence, which in turn may improve their quality of life, prevent exacerbations and hospitalizations, and ultimately reduce mortality rates associated with chronic respiratory diseases.

II. METHODS

A. ACOUSTIC RECORDING DEVICE

An INCA™ device, manufactured by Vitalograph Ltd. [22], was employed in this study. The INCA™ device enables the acoustics of inhaler use to be recorded for analysis. The INCA™ device contains a microphone, microcontroller and battery. The microphone is a Knowles Acoustics SPM0204HE5 mini surface mount silicon microphone. The audio files are stored on the INCA™ device from where they can be subsequently uploaded to a computer via a USB connection.

The INCA™ device can be used in conjunction with the common Diskus™ inhaler. The INCA™ device can be bonded securely to the side of the Diskus™ inhaler, from where it does not impact on the mechanics of inhaler use. The INCA™ device starts recording once the Diskus™ inhaler is opened and switches off when the Diskus™ is closed. The acoustics of inhaler use are recorded as mono WAV files, at a sampling rate of 8000 Hz and resolution of 8 bits/sample. The INCA™ device has sufficient battery life to record patient inhaler use for a period of one month.

B. STUDY BACKGROUND AND INSTRUMENTATION

To validate the performance of the algorithm data was recorded from 12 community dwelling asthmatic patients (6 female & 6 male). The age range of recruited patients was 20–83 (mean 49 ± 18) years old. All patients had previous experience using the Diskus™ DPI. It was communicated to patients before they began the study that an acoustic recording device that could monitor their temporal and technique adherence would be attached to their Diskus™ inhaler. The Diskus™ used in this study contained the combination drug Seretide™, which is comprised of both salmeterol and fluticasone propionate. In each inhaler there were 60 doses of the Seretide™ drug.

Each patient was given an INCA™ equipped Diskus™ inhaler by their clinician for a period of one month. Patients were instructed to use their inhaler as normal and they were not given any extra advice or special training. After using their INCA™ enabled inhaler for one month the patients returned to their clinic, where the INCA™ device was removed from the inhaler and the audio files were uploaded to a database for analysis.

C. CORRECT DISKUS INHALER USE

The Diskus™ inhaler was originally designed to facilitate easy use and patient acceptability [23]. When patients are given a Diskus™ inhaler they are instructed on how to use the inhaler device correctly by their clinician. In this study patients were instructed to use their inhaler twice daily. As there were 60 doses in each inhaler, this corresponds with 30 days of correct usage. The Diskus™ is opened by sliding a thumbgrip to expose the mouthpiece (see Fig. 2). When this occurs the INCA™ device switches on and begins to record audio. A lever is then pushed back which opens a blister foil containing medication inside in the mouthpiece (blister event). A sharp click noise indicates that the blister foil was pierced and that there is medication available in the mouthpiece for inhalation. The patient is then instructed to exhale gently away from the mouthpiece, taking care not to exhale into the mouthpiece. They should then seal their lips tightly around the mouthpiece, inhale steadily and deeply and hold their breath for 10 seconds. The patient should then exhale slowly after the 10 seconds. Once this is complete the patient should use the thumbgrip again to slide the Diskus™ back to its original position. When the Diskus™ is fully closed the INCA™ device will switch off and save the audio file to its internal memory storage.

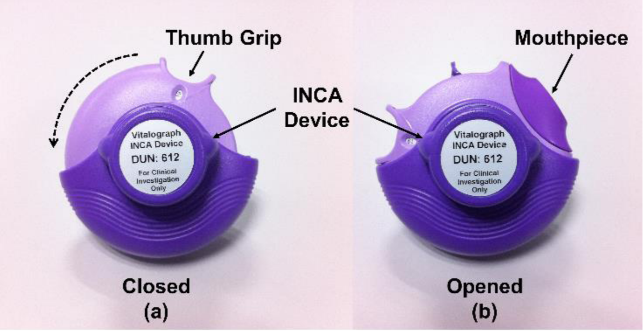

FIGURE 2. To open a closed Diskus™ DPI (a) slide thumb grip in direction of dashed arrow until mouthpiece is fully exposed as seen in (b). INCA™ device attaches onto Diskus™ inhaler to record audio signal of inhaler use.

D. TECHNIQUE ADHERENCE ALGORITHM DESIGN

The algorithm designed to detect the common inhaler events initially went through a training phase. The 12 patients recruited in this study provided 609 audio files in total. Each of these audio files represented a unique record of inhaler use. There was a great quantity of variation between subjects (inter-subject variability) and also within subjects (intra-subject variability) in terms of environment and subject technique. 202 (33% of total files available) audio files were randomly selected and employed in the training phase of the algorithm. The inhaler events to be detected specifically from the audio recordings are blisters and breaths (both inhalations and exhalations). To detect the blister events, features such as the mean power at select frequency bands, amplitude and duration are computed. A mel frequency cepstral coefficient (MFCC) approach was employed to detect breaths in this study, due to the fact that breaths have a characteristic MFCC pattern that allows them to be distinguished from other sounds [24]. Extracting MFCCs is a common parameterization method for vocalization, due to the fact that MFCCs model the known variation of the human ears critical bandwidth with frequency. An overview of the steps the algorithm takes to analyze the inhaler recordings is shown in a block diagram in Fig. 3.

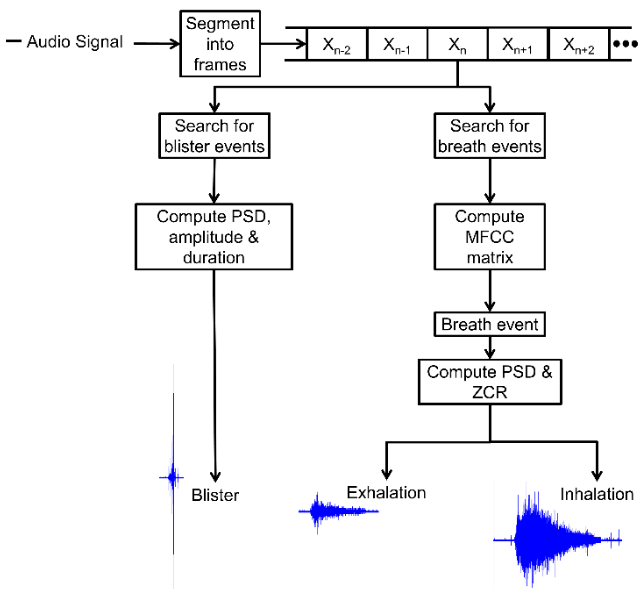

FIGURE 3. Block diagram of the basic steps the algorithm takes to analyze inhaler recordings.

Several studies have previously described algorithm's that were developed to detect breaths in speech and song signals [24] and in respiratory volume signals [25]–[27]. Acoustic analysis of breathing has also previously been employed to detect the different phases (inspiration/expiration) of breaths [28]–[31]. This study differs from previous acoustic based studies in that the acoustic signal was obtained in uncontrolled environments. Breath events occurring during inhaler use are also significantly different to those obtained during breathing.

The algorithm was developed to automatically examine each audio file in four stages. The algorithm firstly identifies the piercing of the blister containing the drug (Stage 1), before identifying breath sounds (Stage 2). It then differentiates detected breath sounds as either inhalations or exhalations (Stage 3). Lastly the algorithm calculates a score of user technique (Stage 4) for each individual audio file. A detailed explanation of each stage of the algorithm and how the technique adherence algorithm was designed will now be given.

1) STAGE 1: BLISTER DETECTION

The first stage of the algorithm involves detecting the piercing of the blister foil containing the medication. The audio signal is segmented into frames of length 100ms, with an overlap of 10ms. The mean power spectral density (PSD) is calculated for frequencies between 2–3 kHz. For this frequency band it was found from empirical observations in the training dataset that blister sounds had a mean power greater than −65dB. The reason the power in this frequency band was greater for blisters compared to nonblisters is due to the intrinsic sound associated with the blistering of the drug foil in the Diskus™ inhaler. A fixed threshold (θ_1) was set and any frames greater than the −65dB threshold are considered as potential blister sounds. The algorithm then examines the proposed blister sounds to remove false positives. Potential blister sounds with maximum normalized amplitude less than 0.7 (θ_2) are removed, in addition to potential blister sounds greater than one second (θ_3) in duration. Finally the mean PSD in the 20Hz–200Hz frequency band is calculated. It was found from the training dataset that blisters had a mean power greater than any false positives in this frequency range, due to the distinctive sound of a blister. Any potential blisters with a power less than −62dB (θ_4) are considered as false positives and removed. The selected thresholds were set as they gave the highest percentage of true positive blister events in the training dataset. A flow chart of the steps employed to detect blister events is displayed in Fig. 4.

2) STAGE 2: BREATH DETECTION

Stage 2 of the algorithm involves detecting breath sounds. The audio signal is first filtered to remove high frequency

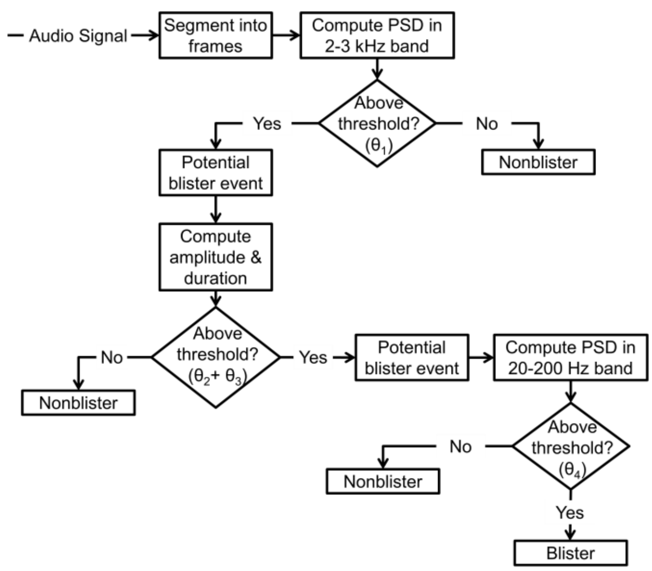

FIGURE 4. Flow chart of algorithm employed to detect blister events.

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components above 1400Hz using a low-pass type I 6th order Chebyshev filter. Each signal is separated into frames of length 700ms with an overlap of 20ms. Twelve MFCCs are calculated for each frame, forming a short-time cepstrogram of the signal. Singular value decomposition (SVD) is then employed to obtain a normalized singular vector from the cepstrogram of the signal. Singular vectors have been reported to capture the most important characteristics of breath sounds obtained from MFCC calculations [24]. An adaptive threshold (θ_5) is set that is 7% higher than the lowest singular vector in the inhaler recording. Singular vectors above this adaptive threshold are marked as potential breath events. This adaptive threshold was found empirically to produce the most accurate detection of breaths in the training dataset. The mean zero crossing rate (ZCR) is then computed to reduce the number of false positive breaths detected by the algorithm.

Breaths were found to have a characteristically high ZCR compared to that of nonbreaths in the training dataset. A fixed threshold (θ_6) constant of 0.1 was therefore introduced to reflect this fact. In the training dataset, breaths consistently had a ZCR above this threshold value, while false positives were successfully removed. A flow chart of the steps employed to detect breath events can be seen in Fig. 5.

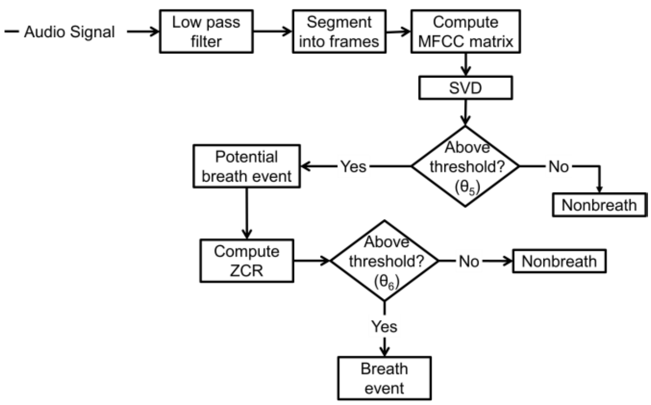

FIGURE 5. **Flow chart of algorithm employed to detect breath events.**

3) STAGE 3: INHALATION/EXHALATION DIFFERENTIATION

Stage 3 involves differentiating breaths into inhalations and exhalations. To do this the mean PSD of identified breaths is calculated for frequencies between 2.52–4 kHz in the original unfiltered signal. It was found from empirical observations in the training dataset that inhalations had a greater power in this specific frequency band compared to exhalations. Based on this fact a fixed threshold (θ_7) was put in place. Inhalations were found to have a mean power greater than -80dB in the training dataset and exhalations were found to have a mean power below this value. The standard deviation of the ZCR was also found to be higher for inhalations in comparison to exhalations in the training dataset. A fixed threshold (θ_8) of 0.045 was put in place with inhalations having a value greater than this threshold and exhalations a value below this threshold. A flow chart of the processing steps the algorithm employed to differentiate inhalations and exhalations is displayed in Fig. 6.

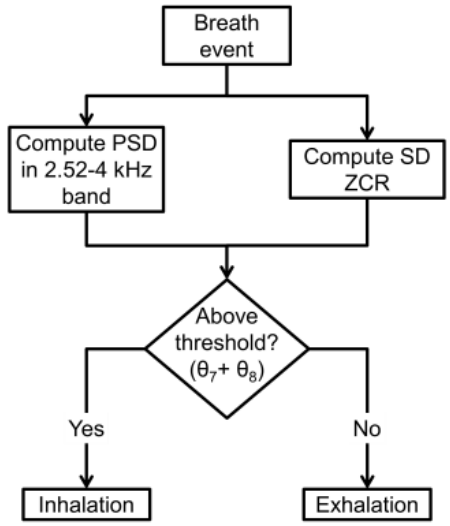

FIGURE 6. **Flow chart of algorithm employed to differentiate breaths into either inhalations or exhalations.**

4) STAGE 4: USER TECHNIQUE SCORE DECISION

The last stage of the algorithm (Stage 4) is to analyze all of the events which took place in the audio file and make a decision regarding the quality of a patient's inhaler technique. This information is outputted as a score which can be one of three possibilities; (1) used correctly, (2) technique error or (3) not used. To decide a technique score the algorithm checks to see what events have taken place, the frequency of each type of inhaler event and the order in which these events have taken place (Fig. 7).

The Diskus$^{\mathrm{TM}}$ inhaler is deemed to have been used correctly if a patient first blisters the foil and secondly inhales the medication. Exhalations can take place before the blister or after the inhalation, still leading to a 'used correctly' score from the algorithm. However, if the patient exhales in the time between the blister and inhalation then they are judged to have committed a 'technique error' as they may have exhaled into the mouthpiece of the inhaler and dispersed some of the medication. Such a scenario is viewed as a critical error. Although instructions for Diskus$^{\mathrm{TM}}$ inhaler use specify that patients should exhale between the blister and inhalation steps, this should be in a direction away from the mouthpiece.

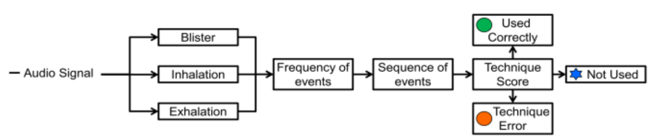

FIGURE 7. **Flow chart demonstrating how algorithm decides inhaler technique score for each audio file.**

Such exhalations will not be detected by the algorithm, however, those in the direction of the mouthpiece will be detected and classified as errors in inhaler technique. Any other sequence of inhaler events is deemed to be a technique error. For example: An inhalation event followed by a blister event, a blister event but no inhalation present, exhalation event but no inhalation event etc. If the algorithm detects multiple inhalations or multiple blisters then a technique error will also be judged to have taken place.

E. TECHNIQUE ADHERENCE ALGORITHM VALIDATION

To test the algorithm's performance 407 new audio files were selected from the 12 asthmatic patients recruited in this study (67% of total audio files obtained). Two human raters, trained by an experienced respiratory clinician to identify correct/incorrect Diskus™ inhaler use, independently classified each of the 407 audio files using the audio tool Audacity®. Each human rater manually examined the audio files using visual and aural methods and scored each individual audio file as one of the three possible outcomes: (1) used correctly, (2) technique error or (3) not used.

F. TEMPORAL ADHERENCE ANALYSIS

As previously mentioned the INCA™ device also provides information regarding the exact time and date that the Diskus™ DPI was employed. Using this data the algorithm automatically computed the number of doses that were taken each day and represented this information in bar chart format. Audio files less than one second in duration are discarded for this analysis due to the fact that this is not a sufficient time period to use the inhaler adequately.

III. RESULTS

The algorithm designed in this study aimed to detect blister, inhalation and exhalation events, analyze the frequency of each event, in addition to the order they took place and output a score on user technique each time the inhaler was employed. The patient user technique score for each inhaler audio file, as computed by the algorithm, was designed to be stored in a text file. However, for the purposes of presenting the specific user technique score to both clinicians and patients, it was decided that a more interpretable output would be needed. Previous research has suggested that people perceive visual cues most accurately from information positioned along a common scale [32]. Based on this information the best method of visualizing data is with the use of scatterplots and bar charts [33]. Bar charts and scatterplot graphs were thus used to display adherence data to clinicians and patients. The algorithm analyzed the time and date stamps from the INCA™ device in order to generate feedback on a patient's temporal adherence. Fig. 8 presents a bar chart output from the algorithm that can be employed to illustrate patient temporal adherence. In this bar chart graph one can observe if a patient overdoses, underdoses or takes the correct amount of doses of their medication (red dashed line) for each single day that they should be using their inhaler.

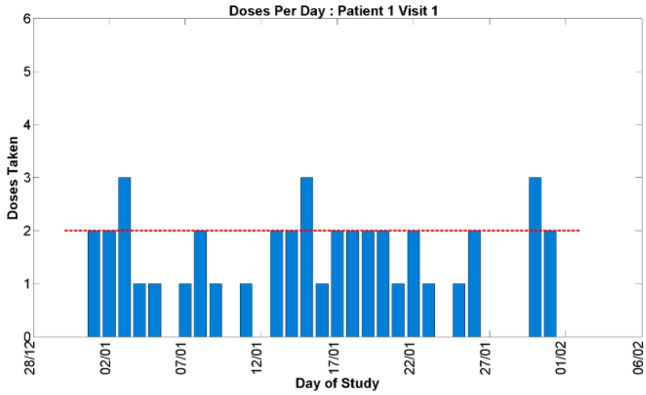

FIGURE 8. Algorithm output on the number of doses taken per day. Red dashed line represents the number of doses prescribed by clinician.

Colors are also widely used in data visualization to indicate appropriate levels of risk (i.e. green=safe, red=danger). A traffic light scatterplot was created to display the algorithms score on technique adherence. An example of such a graph is displayed in Fig. 9. This output graph displays information on the time and date the inhaler was used, in addition to how the inhaler was used. The color green indicates that the inhaler was used correctly while the color orange indicates that there was a technique error. This allows clinicians to examine a patient's adherence to their inhaler medication, while it also provides a method for patients to easily understand when and how they are using their inhaler.

To assess the performance of the algorithm, one month's data from 12 community dwelling asthma patients using their inhalers in real world environments was analyzed. The validation dataset consisted of 407 audio files in total (mean 34 $\pm$ 11 per patient). Each file was scored as either (1) used correctly, (2) technique error or (3) not used, by two trained independent human raters. Cohen's kappa statistic is a measure of interrater agreement and takes into account the prior probability of a specific class occurring [34]. The overall kappa agreement (Cohen's Kappa Statistic) between Rater 1 and Rater 2 was found to be 0.58, indicating moderate agreement between the two human raters. Patients were divided

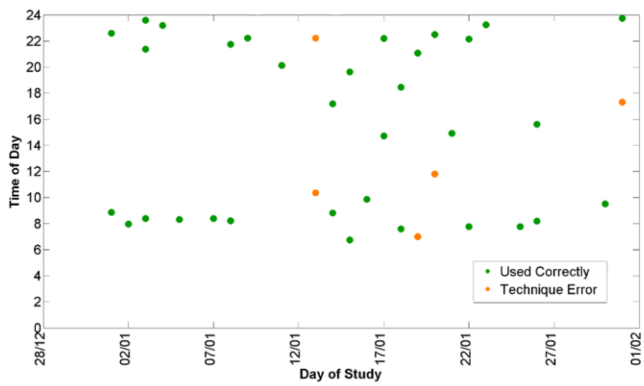

FIGURE 9. Traffic light graph showing the time and day inhaler was used, in addition to how it was used.

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into two subgroups based on the kappa agreement scores between the human raters; Group A consisted of patients for whom the raters had almost perfect agreement (kappa > 0.81) and Group B consisted of patients for whom the kappa agreement was below this score (kappa < 0.81). For Group A (n=8), the overall accuracy of the algorithm in deciding the correct user technique score compared to the human raters was found to be 83%. For Group B (n=4), the algorithms accuracy compared to the human raters was found to be 58%. The accuracy of the algorithm in deciding the correct user technique score in comparison to the human raters for each of the eight patients in Group A is displayed in Fig. 10. Table 1 details the classification performances of the algorithm, in comparison to the human raters, for the various types of inhaler technique scores in Group A. Table 2 demonstrates the classification performance of the algorithm in detecting blister, inhalation and exhalation events for Group A in comparison to the human raters. A Cohen's kappa statistic was calculated to compare the agreement between the algorithm and the expert human raters. For this measure of system performance the algorithm was designated as one rater and one of the expert human raters was randomly selected as the other rater. The user technique score between the two classification approaches was investigated for Group A and it was found that the kappa agreement statistic was 0.49. This indicates moderate agreement between the two classification methods employed in this study.

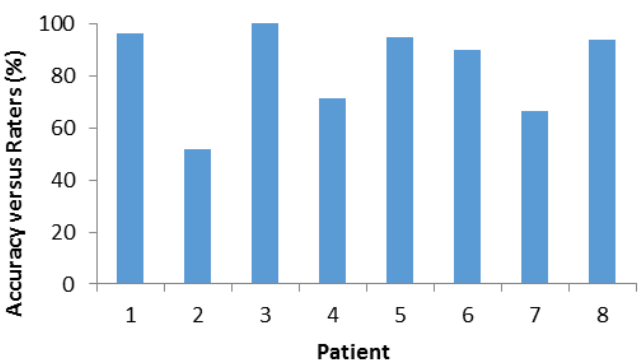

FIGURE 10. Accuracy of algorithm versus human raters for patients in Group A.

TABLE 1. Algorithm accuracy compared to human raters in correctly deciding inhaler technique score for each audio file from Group A.

Inhaler Technique Score	Files Correctly Classified by Algorithm	Total Number of Audio Files	Algorithm Accuracy (%)
Used Correctly	124	150	83
Technique Error	54	58	93
Not Used	15	27	56

TABLE 2. Algorithm classification performance compared to human raters in correctly classifying blister, inhalation and exhalation events in Group A.

Inhaler Event	Sensitivity (%)	Specificity (%)	Accuracy (%)
Blister	98.3	86.8	92.1
Inhalation	84.8	98.4	91.7
Exhalation	81.3	94.5	93.7

IV. DISCUSSION

This study presents a method of automatically analyzing patient inhaler adherence through the use of acoustics. This is the first known method of automatically analyzing both the temporal and technique adherence of a patient to their inhaler medication. The algorithm was designed to identify the critical steps associated with Diskus^{TM} inhaler use and the operations that lead to critical errors in user technique. For the patients that the two human raters had almost perfect agreement upon (Kappa > 0.81) the algorithms accuracy was 83% in deciding the correct user technique score. When the algorithm was taken as one rater and the human raters as another rater, the kappa agreement statistic was found to be 0.49, indicating moderate agreement between the two classification techniques. This is an encouraging initial result if this algorithm is to be used in a fully automated system that actively evaluates patient inhaler adherence.

The gold standard used to evaluate the algorithm in this study was the subjective classification of inhaler audio files by two independent human raters. These raters were trained by an experienced respiratory clinician to assess the Diskus^{TM} inhaler audio files and classify user technique. Overall the two raters agreed with each other at a moderate level (Kappa = 0.58). The fact that the agreement between the human raters, who independently classified the dataset, was moderate demonstrates the subjective nature of analyzing patient inhaler user technique. The identification of common Diskus^{TM} inhaler events from acoustic signals, namely blisters, inhalations and exhalations, can be challenging. Oftentimes it can be difficult to distinguish blister events as they can have similar characteristics to other background artifacts in the audio signal. The human raters also found it problematic to differentiate inhalations from exhalations when using visual and aural analysis methods. It was for these reasons that patients were subsequently divided into two subgroups for analysis, Group A (kappa > 0.81) and Group B (kappa < 0.81). For Group A, the algorithm was able to correctly identify blister, inhalation and exhalation events with an accuracy greater than 90%.

Given the level of disagreement between the two human raters, it is clear that a better method of classifying inhaler technique will be needed for future studies. Device specific checklists are currently used as the gold standard to assess inhaler technique in clinical settings, and provide a method of assessing the accuracy of inhaler technique algorithms.

However, such checklist methods are subjective in nature and are limited in that they can only be performed in controlled environments. In addition to this, clinicians have no information on the total emitted dose from the inhaler or drug deposition in the airways. We believe that experiments that provide empirical evidence on inhaler use are required to remove the subjectivity of these checklists. Using acoustic algorithms, such as the one presented in this study, will allow the objective analysis of inhaler technique. Such acoustic algorithms can provide all of the existing information that checklists currently provide and improve them furthermore by being objective. In addition, a number of supplementary objective metrics concerning inhaler use may be obtained such as inspiratory flow rate, inspiratory capacity, total emitted dose and drug deposition in the airways. Recent studies have reported that acoustics may be used to obtain such objective metrics [18], [35].

The accuracy of the algorithm in predicting the user technique score for certain patients in this study was slightly lower than others, for example patients 2, 4 and 7. The primary reason for this was due to these patients consistently fumbling with their inhaler, creating a large number of blister-like sounding events. These patients also had a number of conversations while using their inhaler and their general inhaler technique was poor and erratic. Future developments will focus on the orientation and number of microphones in the INCA™ device, coupled with adaptive noise cancelling. The robustness of the algorithm to a wide variety of real world environmental noises will also be investigated in future studies. Such modifications to the INCA™ device and testing of the algorithm in noisy environments may improve the accuracy of the algorithm in analyzing future patients' audio files.

One of the major benefits of the algorithm described in this study is that it is able to detect critical errors associated with inhaler use. Analysis of the audio files revealed that many patients unintentionally exhaled into the mouthpiece of the Diskus™ inhaler, dispersing some or even all of the medication. Such detrimental exhalations can only take place after a patient has first carried out the blister step and released medication into the mouthpiece of the inhaler. The algorithm designed in this study is capable of detecting this critical error and will give a 'technique error' score if such an exhalation is detected. A previous study demonstrated that acoustics can also be employed to determine if there is a sufficient force behind the inhalation maneuver [18]. Another critical error that was detected during this study was that many patients blister their Diskus*™* DPI multiple times or inhale multiple times. The algorithm is capable of automatically detecting these types of critical errors and reporting them to clinicians. As clinicians presently have no method of analyzing patients' inhaler use in-between clinic visits, the use of acoustics and the algorithm to detect such critical errors would be highly beneficial.

The algorithm designed in this study has many advantages for both inhaler users and clinicians alike. Currently there is no way for clinicians to know how a patient is using their inhaler once they take the inhaler device home with them. Many patients often show no improvement in their respiratory condition despite receiving an appropriate inhaler and medication regime. Clinicians are often left confused as to why these patients show no improvement in their condition. The system described in this study addresses this problem. It provides a record of inhaler use that can be interrogated in order to assess when and how an inhaler was used over a period of days or weeks in uncontrolled environments. For a clinician to manually evaluate a potentially large quantity of audio files would not be very feasible. Thus, an automatic algorithm such as the one described in this study may allow clinicians to efficiently and objectively monitor patients' inhaler adherence. Such information may be used as an educational tool to provide objective feedback to patients in the hope of them improving their adherence. For patients, improved inhaler adherence may lead to increased levels of medication efficacy. An improvement in adherence rates will lead to a decrease in the number of exacerbations and subsequently hospital admissions.

V. CONCLUSION

In conclusion, an algorithm has been designed and developed that can automatically evaluate patient adherence in a common dry powder inhaler. This algorithm creates the opportunity for clinicians to monitor inhaler users in order to understand if they are consistently using their inhaler device with the correct user adherence technique and at the correct time. Active feedback may encourage patients to improve their adherence and take better control of their disease.

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