



Identification of asthma severity levels through wheeze sound characterization and classification using integrated power features



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ABSTRACT

Objective: This study aimed to investigate and classify wheeze sound characteristics according to asthma severity levels (mild, moderate and severe) using integrated power (IP) features.

Method: Validated and segmented wheeze sounds were obtained from the lower lung base (LLB) and trachea recordings of 55 asthmatic patients with different severity levels during tidal breathing manoeuvres. From the segments, nine datasets were obtained based on the auscultation location, breath phases and their combination. In this study, IP features were extracted for assessing asthma severity. Subsequently, univariate and multivariate (MANOVA) statistical analyses were separately implemented to analyse behaviour of wheeze sounds according to severity levels. Furthermore, the ensemble (ENS), k-nearest-neighbour (KNN) and support vector machine (SVM) classifiers were applied to classify the asthma severity levels.

Results and conclusion: The univariate results of this study indicated that the majority of features significantly discriminated ($p < 0.05$) the severity levels in all the datasets. The MANOVA results yielded significantly ($p < 0.05$) large effect size in all datasets (including LLB-related) and almost all post hoc results were significant ($p < 0.05$). A comparison of the performance of classifiers revealed that eight of the nine datasets showed improved performance with the ENS classifier. The Trachea inspiratory (T-Inspir) dataset produced the highest performance. The overall best positive predictive rate (PPR) for the mild, moderate and severe severity levels were 100% (KNN), 92% (SVM) and 94% (ENS) respectively. Analysis related to auscultation locations revealed that tracheal wheeze sounds are more specific and sensitive predictors of asthma severity. Additionally, phase related investigations indicated that expiratory and inspiratory wheeze sounds are equally informative for the classification of asthma severity.

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1. Introduction

Computerized wheeze sound analysis is a dynamic research field. This research field has the benefits of covering an extensive range of frequencies compared to what physicians can auscultate using a stethoscope [1]. Researchers have investigated wheeze detection using logic-based algorithms, wheeze classification using machine learning methods, the association between respiratory sound spectra and airway obstruction, and wheeze sound characteristics. Recent literature reviews on the computerized respiratory sound analysis concluded that focus areas are related to the clas-

sification or detection of adventurous sounds (including wheezes), which can be discontinuous or continuous [1–5].

Early wheeze sound investigations focused on wheeze detection. Researches in [6] detected wheeze sounds by searching a set of peaks that were more than a predefined threshold. The study in [7] introduced peak grouping to define the wheeze duration criteria, which improved the wheeze sound detection accuracy. Another study [8] established a time-frequency wheeze detection algorithm that introduced the idea of peak coexistence, i.e., the number of peaks detected at the same interval should not be greater than four. A recent work applied an Hidden Markov Model wheeze detection algorithm based on the identification of instantaneous frequency [9]. This algorithm tracks the start and end of instantaneous frequency lines in the time-frequency decomposition of the recordings. However, the trend in this area has shifted from logic-based algorithms to machine learning methods as logic-based algorithms are susceptible and dependent to attenuation of

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breath sound signals, which has led researchers to develop methods invariant to attenuation.

Machine learning techniques then focused on wheeze sound feature extraction for the classification of respiratory sounds into predominantly abnormal and normal breath sounds. The algorithms developed in an earlier study [10] compared 17 systems developed using combinations of Mel-frequency cepstrum coefficients (MFCC), short-time Fourier transform, autoregression (AR), wavelet transform and wavelet packet transform feature extraction methods with vector quantization, Gaussian mixture model (GMM), and artificial neural network (ANN) classifiers to classify respiratory sounds into wheezes and non-wheezes. This research concluded that MFCC features combined with the GMM classifier performs better than all other combinations. Another group of researchers [11] extracted MFCC features from respiratory sounds and introduced a two-layer coarse-to-fine support vector machine (SVM) classifier in order to eliminate false stridors (louder wheeze sounds with prominent peaks at 1000 Hz) to classify wheeze and non-wheeze respiratory sounds. A previous study which collected data from children [12] had similar objectives: the researchers attempted to extract features from the power spectral density using the AR technique and fed the features into an SVM classifier. Another study [13] introduced a temporal spectral domain technique for feature extraction and applied the k-nearest-neighbour (KNN) classifier to classify respiratory sounds into abnormal and normal classes. Recently a group of researchers [14] employed an empirical mode decomposition technique to obtain the Hilbert spectrum of respiratory sounds recordings. The instantaneous frequency and instantaneous envelope features obtained using this technique were fed to an SVM classifier to classify the breath sounds into normal and wheeze sounds.

The literature also indicates a few studies that focused on respiratory sounds statistical analysis. In an earlier study [15], statistical analysis was performed with an average number of three expiration breathing sounds using various parameters, such as the duration of non-wheeze, the number of wheezes, monophonic wheeze sounds, polyphonic wheeze sounds and the mean frequency (MF) of wheezes. The researchers concluded that the MF of the expiration respiratory recordings was higher in normal subjects than in the patients. No significant difference was found for the other investigated parameters between the two groups [15]. In another study [16], third-order statistics of spectral features in the respiratory sounds of asthmatic subjects were analysed to observe the nonlinear behaviour of wheeze sound. The findings revealed that wheeze sound exhibit different behaviours during the inspiratory and expiratory breathing phases. Similarly, another group of researchers [17] analysed the nonlinear behaviour of wheeze sound in chronic obstructive pulmonary disease (COPD) and asthmatic patients using 23 high-order statistical spectral features calculated using continuous wavelet transform. The behaviour of monophonic and polyphonic wheezes in a breathing cycle and in the respective inspiratory and expiratory phases were analysed. The results revealed that most of the selected features indicated a significant difference between COPD and asthma for all types of wheeze sounds during the breathing cycles and individual breath phases.

Investigators have also examined associations between other forms of recordings and classification. One study [18] compared the classification performances of an ANN classifier and humans. Humans were shown the asthmatic patient's bar-graph spectrogram obtained during one breath cycle, and the ANN was developed using features of the same spectrogram. The results exposed an interesting insight: ANN classifiers perform better than humans in the analysis of a bar-graph spectrogram. Other studies [19,20] later interpolated breath sound spectra to 16 different lung function values, including force expiratory volume in one second (FEV₁). The results indicated the existence of a deterministic relation-

ship between respiratory sound spectra and lung function values in asthmatic subjects. The researchers further claimed that the severity level of asthma patients can be identified through a computerized respiratory sound analysis [20] and rigidly concluded that breath sound spectra provide sufficient information to explain the severity level of asthma patients [19].

A few previous studies also conducted statistical analysis of the correlations between respiratory sounds spectra and changes in lung function values [21–23]. Study [22] collected respiratory sounds from asthmatic patients and normal breathing sound and found a relationship between lung function values with the ratio of the wheezing duration to the total recording time (T_w/T_{tot}). Another study [21] collected respiratory sounds from the trachea and chest of 10 asthma patient with forced breathing and computed the average power, F₅₀ and F₇₅ for analysis. Only F₅₀ attained from tracheal breath sounds were found to be significantly related to FEV₁. The work in [23] collected respiratory sounds from the trachea of asthmatic patient with forced breathing and investigated the acoustic characteristics of normal subjects, non-stable and stable asthma patients. The results indicated that the MF of normal subjects is different from that of asthmatic patients. Similarly, a study working with paediatric subjects where lower lung base (LLB) sounds are louder than adults due to thinner wall thickness [24] conducted the analysis using inspiratory and expiratory peak frequency features. The results revealed that only LLB inspiratory (LLB-Inspir) breath sounds were correlated with lung function values [25].

Taken together, the previously mentioned studies indicate several important insights. First, some studies performed a detailed statistical analysis without any subsequent application such as classification and vice versa. Second, although some studies have obtained respiratory sound data from patients with different asthmatic severity and conducted various analyses, only a few have inferred back their findings to the severity levels. Given these observations, this study aims to statistically analyse the behaviour of wheeze sounds from different severity levels of asthmatic patients and perform classification using integrated power (IP) features within nine datasets with respect to auscultation location and/or breadth phases.

2. Materials and methods

2.1. Study protocol

The protocol for the acquisition of respiratory sound data was designed according to CORSA standards [26] and after a detailed study of the literature [1]. Details of the data collection are also described in [27].

2.2. Ethics statement

Data were collected from two hospitals – Al-Mustafa Chest Clinic at Wazirabad, Pakistan, and District Headquarters Teaching Hospital at Gujranwala, Pakistan. Ethical permission was obtained from the ethical committees of both hospitals separately. Clinical report forms were filled by all the subjects, and written informed consent was also obtained from the subjects that participated in this study. Prior to data collection, instructions were given to the subjects regarding the data collection procedures.

2.3. Devices for data acquisition

According to CORSA respiratory sounds can be collected from air coupled microphones or contact sensors (accelerometers) [26]. In this study, a single channel wireless digital stethoscope (WISE) [28] was used for data collection. WISE is a commercially available device with dimensions of 144 × 63 × 73 mm and a weight of

270 g that is manufactured in Korea. The frequency response of this stethoscope is in the range of 20–2000 Hz. The hardware of the device comprises an air coupled microphone, a transmitter and a receiver. In WISE, mechanical vibrations are converted into electric signals through an air-coupled condenser. All data were collected using VPM3000 W software, which accompanies WISE and is saved on the computer. A few previous studies have also used the same device [29–33].

2.4. Inclusion and exclusion criteria

The subjects were recruited based on suggestions from senior medical officers of both hospitals. The selected subjects were non-smokers who were not addicted to drugs. The selected subjects were only asthmatic patients without any other lung, heart or bowel disease. In addition, the patients were not taking any medication for at least two to six hours prior to data collection.

2.5. Auscultation location and procedure

Recordings of respiratory sounds were obtained with the aid of physicians. Data were collected from the trachea and the left and right LLB as recommended by CORSA [34]. The exact location of the LLB was selected by ordinary auscultation based on a sufficient sound intensity [21] and according to a previous study [26]. Recommendations and the necessary precaution related to auscultation locations and procedures were obtained from the physicians. In this study, the difference in breath sounds between the right and left LLB [35] was considered negligible, and thus, both locations were considered as LLB.

According to CORSA, there are two types of recordings – short-term and long-term recordings. For long-term recording, the supine position is recommended while for short time recording, the sitting position is recommended [26]. To ensure the quality and reliability of the data, short-term recordings for 60–90 s were conducted. All recordings were obtained from the subjects in the sitting position with their hands on their lap. CORSA standard has suggested two breathing manoeuvres for data collection [26] – tidal breathing and forced expiratory. The subjects were asked to perform tidal breathing through their mouth to exert effects on the upper airway. The subjects were asked to keep quiet and avoid any movements during data recording. In addition, the subjects were asked to hold their breath for 10 s and then breathe normally without any targeted flow. In this study, data was collected in a sound proof room as recommended by CORSA with standard background environmental noise < 30 dB [26]. Environmental conditions and subjects' postures were identical for all the patients. Hence the ambient noise did not show any variation between patients, as described previously [21].

2.6. Subject details

All the data were collected from subjects suffering from asthma. A total of 55 subjects, including 21 females and 34 males (age ($\text{mean} \pm \text{SD}$) = 55 ± 12.2), participated. After each patient was diagnosed according to the available GINA standards [36], his/her asthma severity level (mild, moderate and severe) was identified according to the National Asthma Education and Prevention Programme – Expert Panel Report 3 [37]. This diagnosis was based on shortness of breath, wheeze, history and condition of the patient. Therefore, the decision on the severity level by physician was coupled with the patient's history and his/her present condition. Subject with conflicting opinions among the physicians were omitted from the study. A similar approach was also used in other studies [38–40]. The severity level in all the patients was verified by at least two physicians in both hospitals. The details of the patients

with different asthma severity levels are as follows: (1) mild – 17, male:female = 9:8, age ($\text{mean} \pm \text{SD}$) = 50 ± 12.1 ; (2) moderate – 18, male:female = 12:6, age ($\text{mean} \pm \text{SD}$) = 51.5 ± 13.7 ; and (3) severe – 20, male:female = 12:8, age ($\text{mean} \pm \text{SD}$) = 50 ± 11.5 .

2.7. Data acquisition and pre-processing

Respiratory sound data were acquired at an 8000 Hz sampling frequency. The respiratory sounds were filtered with a first-order high-pass Butterworth filter at 7.5 Hz to remove the DC offset. Subsequently, an eighth-order low-pass Butterworth filter with a 2500 Hz frequency was applied to remove aliasing. The dominant frequency of respiratory sounds lies between 100 and 1600 Hz. Hence, a fourth-order bandpass Butterworth filter with a bandpass of 100–1600 Hz was developed to ensure that all noise (e.g., motion artefacts and heart sounds) was filtered from the recorded respiratory sounds.

2.8. Segmentation

Wheeze sounds and the phases in the breath cycles (inspiratory and expiratory) were identified by a dedicated physician manually through an audio-visual inspection of the recordings and with the aid of spectrograms. The wheeze sounds were segmented by their manifestation in the spectrogram and using the following criteria: increase in intensity of 20 dB, duration longer than or equal to 100 ms, and frequency greater than or equal to 100 Hz [41]. Furthermore, all segments and labelling were validated by another independent physician. Similar approaches were also used in a previous study [13,11]. The combination of these approaches produced a database of wheezes labelled according to severity level, phase and location. The manifestation of wheeze sounds can be noted in Fig. 1, which shows the respiratory sounds recorded from the trachea of a 56-year-old man suffering from moderate asthma.

2.9. Wheeze datasets

In this study, the analysis was performed using nine datasets shown in Fig. 2, which were obtained as follows: (1) all wheeze samples regardless of location and phase, (2) location – trachea and LLB, (3) phase – inspiratory and expiratory and (4) combination of location and phase – trachea inspiratory (T-Inspir), trachea expiratory (T-Expir), LLB-Inspir, and LLB expiratory (LLB-Expir). Details of all data are given in Table 1. Previous studies [8,10,16,17] analysed all the samples collectively without any other discrimination. Additionally, few researchers [7,15,43] focused only on the expiratory phase, whereas other studies [14,42,44] analysed only the inspiratory phase. The researchers in another previous study [45] obtained data from four locations and investigated these locations separately and in combination. However, our study focused on all possible combinations of datasets for analysis.

2.10. Feature selection

The wheeze segments were analysed using a Fast Fourier Transform (FFT) approach with a 512-point hamming window and a 50% overlap to obtain the power spectrum density within the range of 100–1600 Hz [46]. A hamming window is a smooth window with acceptable leakage [19,47]. The amplitude of the power spectrum was normalized (the sum of the absolute power spectrum values normalized to one) based on (1) and (2), where $P(f)$ is the power spectral density at frequency f , $x(k)$ is the amplitude of the signal with respect to point k , $X(f)$ is the Fourier transform of the signal, $P(n)_{\text{norm}}$ is the normalized power spectrum, and I indicates power intensity related to the frequency. The frequencies of all record-

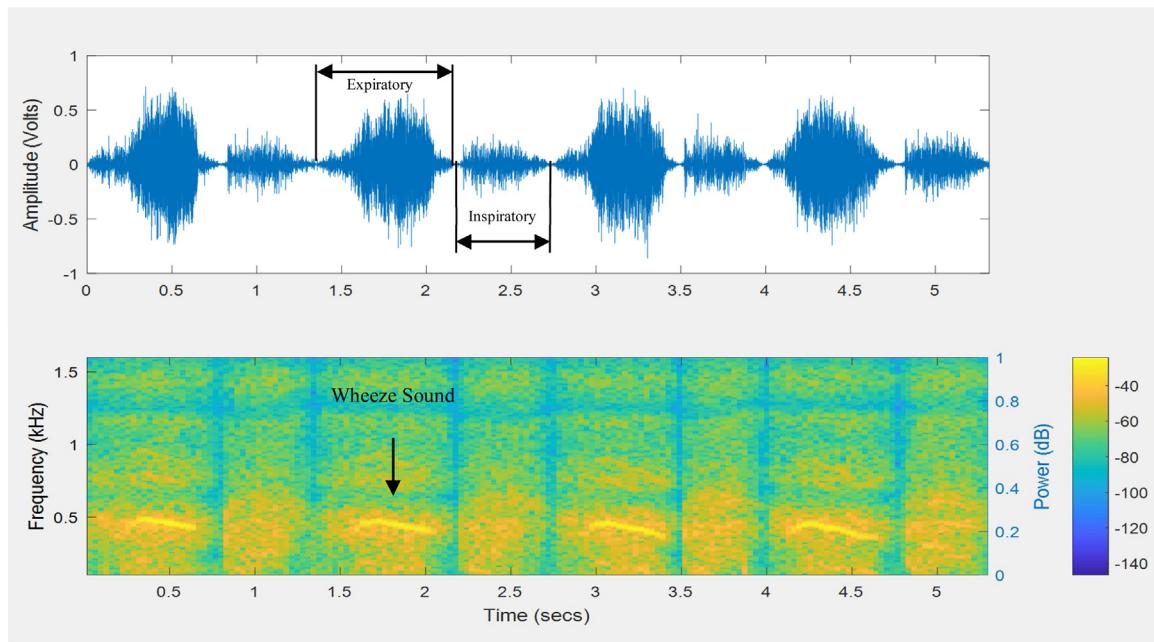


Fig. 1. Recording of respiratory sounds and spectrogram.

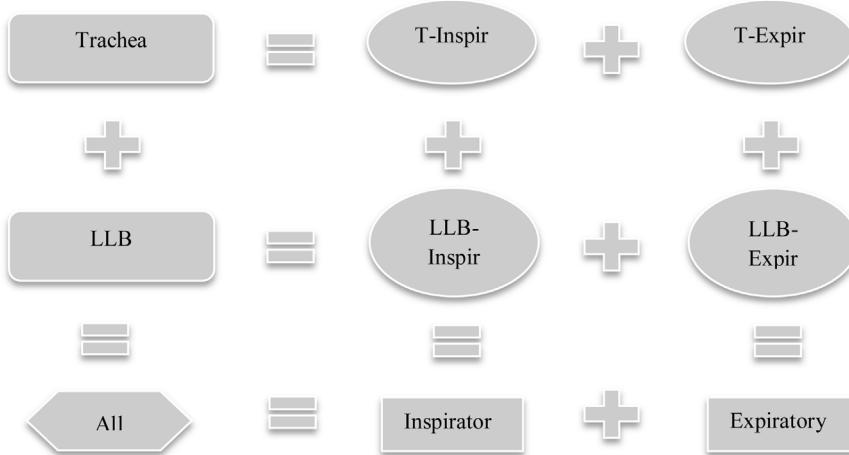


Fig. 2. Subdivision of the collected data into nine datasets.

Table 1
Summary of data related to each dataset.

Severity Level	Total Subjects	Trachea	T-Inspir	T-Expir	LLB	LLB-Inspir	LLB-Expir	Inspiratory	Expiratory	All
Mild	17	49	20	29	150	78	72	98	101	199
Moderate	18	85	32	53	169	95	74	127	127	254
Severe	20	123	54	69	199	104	95	158	164	322
Total	55	257	106	151	518	277	241	383	392	775

ings obtained using this method were comparable, regardless of the loudness of the lung sounds [19,48] and the lung capacity.

$$P(f) = \frac{1}{k} \left| \sum_{n=0}^{k-1} \left(x(k)e^{-j2\pi fk} \right) \right|^2 = \frac{1}{k} |X(f)|^2 \quad (1)$$

$$P(n)_{norm} = \frac{P(f, I)}{\max(I)} \quad (2)$$

The frequency range of 100–1600 Hz of each wheeze segment power spectrum density was divided into 20 equal sub-bands with a bandwidth of 75 Hz. This bandwidth was selected based on the findings of a previous study [19], which defined FFT with a resolu-

tion of 15–75 Hz as suitable for the analysis of asthmatic severity. Subsequently, integrations of the sub-bands were calculated using (3), and this approach yielded the features IP₁ until IP₂₀.

$$IP_i = \int_{100+75(i-1)}^{100+75(i)} P(n)_{norm} dn, \quad i = 1, \dots, 20 \quad (3)$$

Our decision to split the frequency range is not baseless. The literature reveals that airway obstruction causes the change in airway thickness (wall area) [49] due to which high-pitch sounds manifest [50]. Hence, airway obstruction causes the change in frequencies of breath sounds which varies the velocity and energy of sounds. IP

features potentially indicate the energy of breath sounds, which are not affected by the air flow rate and have shown to be of substantial clinical utility [51]. The selection of power bands, from which the IP features are computed from, is based on the natural resonance generated by lungs. Multiple small IP bands have been selected because breath sounds are produced by a very complex human respiratory system. Breath sounds originate from a complicated breathing system, which consists of a branching system up to 23 generations with a total of almost 17 million tubes [20]. Such an approach is not entirely alien in previous works. Previous detailed power spectrum analysis have computed various other power statistical features such as average [19,20], skewness, kurtosis variance [45] and, energy, entropy, minimum, maximum and standard deviation [52].

2.11. Statistical analysis

For the univariate statistical analyses, a normality test was performed, and the data were found to be not normally distributed. A non-parametric test (Kruskal-Wallis) was used to investigate the overall significant difference between the three severity levels through a univariate analysis. Subsequently, a post hoc test (Mann-Whitney test) was applied to assess the significance of the differences between pairs of severity levels, and the 95% confidence level was considered significant for all statistical analyses, i.e., selected datasets were considered to be significantly different if $p < 0.05$. Cohen's effect size (η^2_{χ}) has been calculated as described previously [53]. Eta squared (η^2_{χ}) was calculated with (4) where, Chi-square (χ^2) is the Kruskal-Wallis test statistic and N is the number of samples of the respective dataset, to determine the effect size as follows: 0.01, small; 0.06, medium; and 0.138, large.

$$\eta^2_{\chi} = \frac{\chi^2}{N - 1} \quad (4)$$

A multivariate analysis was performed to investigate the combined effect of five features and thus identify significant differences between mild, moderate and severe samples by considering nine datasets. MANOVA with Wilks lambda (Λ) was performed in this study. Cohen's effect size (η^2_{Λ}) and all subsequent post hoc analyses were also investigated, and a 95% confidence level was considered to indicate significance ($p < 0.05$) in all statistical analyses. Eta squared (η^2_{Λ}) was calculated with (5) where Λ is the Wilks lambda statistic, to determine the effect size as follows: 0.02, small; 0.13, medium; and 0.26, large [54].

$$\eta^2_{\Lambda} = 1 - \Lambda \quad (5)$$

2.12. Classifier

In this study, the SVM KNN and ENS classifiers were implemented. As detailed in the literature, SVM [55,12,52] and KNN [13,19,20,52] are widely used in the field of computerized wheeze classification. Few studies also implemented ENS classifier [32,52]. The SVM classifier, works based on the principle of constructing hyperplanes with the maximal possible margins within the classes. The aim of this classifier is to find the optimal separating hyperplane among the training samples to classify data in classes [56]. The selection of a hyperplane depends on the nature of the data, i.e., linear or non-linear. This classifier establishes a maximal margin and kernelized approach. The optimal separating hyperplane ensures the maximal performance with the selection of the maximal margin between the closest members of the classes to the hyperplane. In this study the selected kernel function (Cubic or Gaussian), which consists of the box constraint and level kernel scale, was optimized based on the classification accuracy of all available data. Our data produced best optimized classification

accuracy with the Gaussian kernel at level 1 and scale 0.6. In addition, one against one approach has been selected for multiclass SVM classification. KNN is a non-parametric approach based on the strategy of finding nearest neighbours, and voting is employed to determine the most possible class [57]. The adopted type of distance measurement (Euclidean distance and city block) and number of nearest number (k), was optimized based on the classification accuracy of all available data. As previously, when we tested with our total data, best results were obtained with the Euclidean distance metric and $k = 10$. The bagged tree learning is a type of ENS classification. In this learning method, multiple simple learners are combined to improve the performance of the classification [58]. The selected learner types (boost tree and bagged tree) and the number of learners was optimized based on the classification accuracy of all available data. In this study, the bagged tree approach with 30 learners produced the best results. In all classification methods, ten-fold cross validation was selected to analyse the performance of the models. The sensitivity (SENS), specificity (SPEC) and positive predictive rate (PPR) were calculated to observe the performance of the classifiers. SENS is defined as the probability at which class 1 is correctly classified as class 1, SPEC is defined as the probability at which classes other than class 1 are correctly classified and PPR is defined as the ratio of true detection of classes to the total number of subjects,

$$\text{SENS} = \text{TP}/(\text{TP} + \text{FN}) \quad (6)$$

$$\text{SPEC} = \text{TN}/(\text{TN} + \text{FP}) \quad (7)$$

$$\text{PPR} = (\text{TP} + \text{TN})/(\text{TP} + \text{TN} + \text{FP} + \text{FN}) \quad (8)$$

where, TP = true positive, TN = true negative, FP = false positive and FN = false negative. All computations regarding pre-processing, feature extraction and classification were performed using MATLAB® (version 2017a, Math Works, USA) and all the statistical analysis was performed using IBM SPSS Statistics (version 20, IBM Corporation, USA).

3. Results

Fig. 3 presents the $\mu(\text{SD})$ values of 20 IP features for mild, moderate and severe asthma patients in the nine datasets. From the graphs, it can be seen that much of the energy in the signal is concentrated in the IP₁ - IP₁₀ bands. Further, we also observed a decreasing trend in the values from the lower to higher bands. A similar observation was also noticed in the variance of the features. It was also observed that for the trachea-related datasets, the energy in the signal was better distributed among the IP₁ - IP₁₀ bands and better discrimination can be observed among the severity classes. In contrast, for the LLB-related datasets, much of the energy was contained in the IP₁ - IP₈ bands.

Table 2 presents a summary of the univariate statistical analysis of three severity levels and the corresponding post hoc results. The results reveal that all features exhibited statistical significant for at least 4 out of the 9 datasets ($p < 0.05$, $\eta^2_{\chi} = 0.01 - 0.36$) except IP₃. All investigated features performed with higher effect size for trachea-related datasets ($p < 0.05$, $\eta^2_{\chi} = 0.04 - 0.36$) as compared to LLB-related datasets ($p < 0.05$, $\eta^2_{\chi} = 0.02 - 0.12$). It was also noticed that the features showed almost similar discriminatory power in the inspiratory-related datasets ($p < 0.05$, $\eta^2_{\chi} = 0.02 - 0.32$) and expiratory related datasets ($p < 0.05$, $\eta^2_{\chi} = 0.02 - 0.36$). The post hoc results reveal that the percentage of observations that were statistically significant between the severity level pairs were as follows – a (75%), b (79%) and c (47%).

Table 3 presents the results of the statistical analysis using the combined effect of 20 features (MANOVA) and the corresponding post hoc test results. The values reveal that the combined

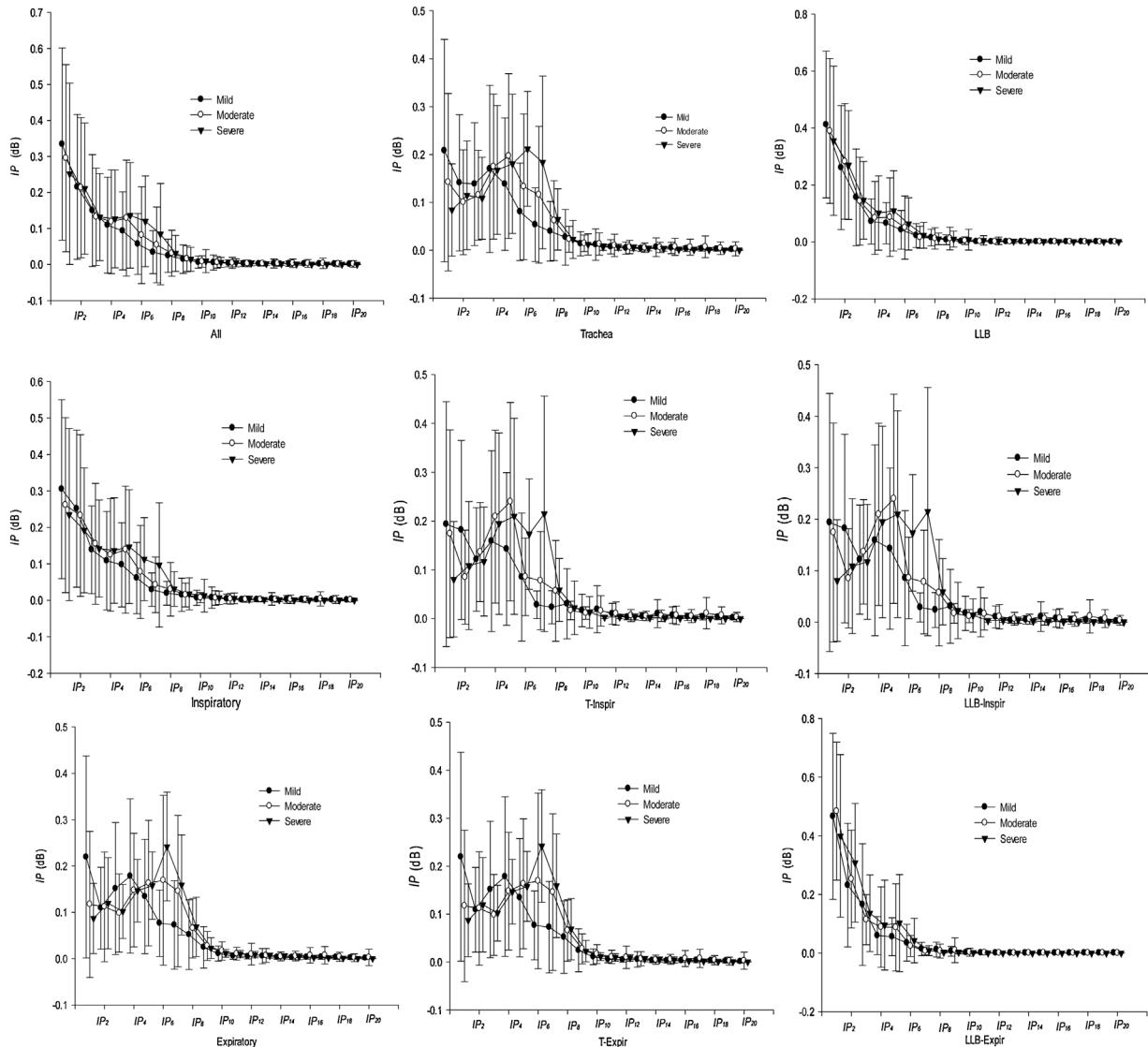


Fig. 3. μ (SD) values of 20 IP features for mild, moderate and severe asthma patients in the nine datasets.

feature vector exhibited statistical significance for all sample datasets ($p < 0.05$, $\eta^2_\Delta = 0.137 - 0.76$). All investigated datasets produced comparison results with high effect size for trachea-related datasets ($p < 0.05$, $\eta^2_\Delta = 0.506 - 0.76$) as compared to LLB-related datasets ($p < 0.05$, $\eta^2_\Delta = 0.137 - 0.319$). It was also noticed that the features showed almost similar discriminatory power in the inspiratory-related datasets ($p < 0.05$, $\eta^2_\Delta = 0.208 - 0.76$) as compared to the expiratory related datasets ($p < 0.05$, $\eta^2_\Delta = 0.253 - 0.592$). The post hoc results reveal that the percentage of observations that were statistical significant between the severity level pairs were as follows – a (100%), b (89%) and c (89%).

The classification results for the three classifiers using the 20 IP features as input data on the nine datasets is given in Table 4. The performance of the classifiers was evaluated using the SENS, SPEC and PPR performance measures. In general, all tested classifiers indicated powerful results – ENS (SENS = 82 ± 7%, SPEC = 83 ± 6%, PPR = 83 ± 6%), KNN (SENS = 68 ± 19%, SPEC = 73 ± 16%, PPR = 77 ± 7%) and SVM (SENS = 73 ± 11%, SPEC = 74 ± 9%, PPR = 75 ± 7%).

In terms of location, with trachea-related datasets, the classifiers performed as follows – ENS (SENS = 86 ± 6%, SPEC = 89 ± 7%, PPR = 91 ± 3%), KNN (SENS = 75 ± 22%, SPEC = 75 ± 21%, PPR = 86 ± 7%) and SVM (SENS = 83 ± 13%, SPEC = 84 ± 12%,

PPR = 88 ± 5%), while with LLB-related datasets as input data – ENS (SENS = 78 ± 5%, SPEC = 79 ± 4%, PPR = 79 ± 3%), KNN (SENS = 67 ± 11%, SPEC = 72 ± 11%, PPR = 71 ± 4%) and SVM (SENS = 68 ± 7%, SPEC = 70 ± 9%, PPR = 69 ± 4%).

When the results were analysed in terms of breathing phases, we observed the following for inspiratory-related dataset – ENS (SENS = 81 ± 8%, SPEC = 82 ± 10%, PPR = 83 ± 7%), KNN (SENS = 69 ± 16%, SPEC = 74 ± 17%, PPR = 77 ± 10%) and SVM (SENS = 77 ± 11%, SPEC = 78 ± 11%, PPR = 78 ± 12%), while with the expiratory- related datasets – ENS (SENS = 84 ± 7%, SPEC = 84 ± 6%, PPR = 85 ± 4%), KNN (SENS = 72 ± 17%, SPEC = 72 ± 16%, PPR = 78 ± 7%) and SVM (SENS = 76 ± 11%, SPEC = 76 ± 10%, PPR = 78 ± 6%).

When the results were analysed in terms of all datasets, T-Inspir performed better than all other datasets with the following measures – ENS (SENS = 90 ± 5%, SPEC = 90 ± 11%, PPR = 92 ± 3%), KNN (SENS = 76 ± 21%, SPEC = 76 ± 28%, PPR = 88 ± 11%) and SVM (SENS = 90 ± 6%, SPEC = 90 ± 11%, PPR = 93 ± 4%).

Finally, if we look at the results from the point of view of severity levels, the behaviour of the classifiers were as follows; mild samples – ENS (SENS = 78 ± 7%, SPEC = 89 ± 6%, PPR = 84 ± 7%), KNN (SENS = 55 ± 9%, SPEC = 89 ± 8%, PPR = 81 ± 10%) and SVM (SENS = 67 ± 8%, SPEC = 85 ± 9%, PPR = 78 ± 611%), moderate

Table 2

Summary of the univariate statistical analysis of the IP features in the various datasets – p-value, η_{χ^2} and details of the post hoc test for pairs *a* (mild and moderate), *b* (mild and severe), and *c* (moderate and severe).

Dataset	IP ₁	IP ₂	IP ₃	IP ₄	IP ₅	IP ₆	IP ₇	IP ₈	IP ₉	IP ₁₀	IP ₁₁	IP ₁₂	IP ₁₃	IP ₁₄	IP ₁₅	IP ₁₆	IP ₁₇	IP ₁₈	IP ₁₉	IP ₂₀	
ALL	4.E⁻¹³	8.E ⁻⁰¹	6.E ⁻⁰¹	1.E⁻⁰³	8.E⁻¹⁰	4.E⁻⁰⁵	3.E ⁻⁰¹	4.E⁻⁰²	2.E⁻⁰⁶	2.E⁻⁰³	2.E⁻⁰³	9.E⁻⁰³	2.E ⁻⁰¹	7.E ⁻⁰¹	4.E ⁻⁰¹	4.E ⁻⁰¹	1.E ⁻⁰¹	3.E⁻⁰²	1.E⁻⁰²		
	0.07	0.00	0.00	0.02	0.05	0.03	0.00	0.01	0.03	0.02	0.02	0.01	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	
	a,b,c	a,b	b,c	b,c	b,c	b	b,c	a	a,b												
Trachea	7.E⁻¹²	7.E⁻⁰³	6.E⁻⁰¹	1.E⁻⁰²	2.E⁻¹⁵	4.E⁻¹³	8.E⁻⁰⁷	1.E⁻⁰⁵	2.E⁻⁰⁷	2.E⁻⁰⁹	7.E⁻⁰⁷	1.E⁻⁰⁷	1.E⁻⁰⁵	8.E⁻⁰⁶	3.E⁻⁰⁴	5.E⁻⁰⁴	7.E⁻⁰³	1.E ⁻⁰¹	3.E ⁻⁰¹	1.E ⁺⁰⁰	
	0.20	0.04	0.00	0.04	0.26	0.22	0.11	0.09	0.12	0.16	0.11	0.12	0.09	0.09	0.06	0.06	0.04	0.02	0.01	0.00	
	a,b	a,b	a,b	a,b,c	a,b,c	a,b,c	a,b	a,b,c	a,b,c	a,b,c	a,b	a	a,b								
LLB	1.E⁻⁰²	2.E⁻⁰²	5.E⁻⁰¹	5.E⁻⁰¹	2.E⁻⁰¹	5.E⁻⁰²	1.E⁻⁰²	6.E⁻⁰³	9.E⁻⁰⁵	1.E⁻⁰⁴	3.E⁻⁰⁵	1.E⁻⁰⁵	2.E⁻⁰⁵	4.E⁻⁰⁵	5.E⁻⁰⁵	4.E⁻⁰⁶	2.E⁻⁰⁶	2.E⁻⁰⁶	1.E⁻⁰⁶	1.E⁻⁰⁵	
	0.02	0.02	0.00	0.00	0.01	0.01	0.03	0.02	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.05	0.05	0.05	0.04	
	a,b	a,b	a,b	a,c	a,b,c	a,b															
Inspiratory	6.E⁻⁰⁶	2.E⁻⁰²	7.E⁻⁰¹	3.E⁻⁰²	1.E⁻⁰⁶	1.E⁻⁰⁴	2.E⁻⁰¹	2.E⁻⁰¹	5.E⁻⁰⁵	2.E⁻⁰²	4.E⁻⁰³	1.E⁻⁰²	2.E⁻⁰¹	4.E⁻⁰¹	4.E⁻⁰¹	2.E⁻⁰¹	2.E⁻⁰¹	3.E⁻⁰¹	2.E⁻⁰¹	3.E⁻⁰¹	
	0.06	0.02	0.00	0.02	0.07	0.05	0.01	0.01	0.05	0.02	0.03	0.02	0.01	0.00	0.00	0.01	0.01	0.01	0.01	0.01	
	a,b	b	b	b,c	b,c	a,b	b	b	b,c	a	a,b										
Expiratory	6.E⁻⁰⁸	1.E ⁻⁰¹	7.E ⁻⁰¹	3.E⁻⁰²	3.E⁻⁰⁴	4.E⁻⁰²	8.E ⁻⁰¹	2.E ⁻⁰¹	7.E⁻⁰³	9.E ⁻⁰²	2.E ⁻⁰¹	3.E ⁻⁰¹	6.E ⁻⁰¹	1.E ⁺⁰⁰	1.E ⁺⁰⁰	9.E ⁻⁰¹	5.E ⁻⁰¹	3.E ⁻⁰¹	8.E ⁻⁰²	4.E⁻⁰²	
	0.08	0.01	0.00	0.02	0.04	0.02	0.00	0.01	0.03	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.02	
	a,b	a,b	b	a																	
T-Inspir	2.E⁻⁰⁴	8.E⁻⁰⁴	6.E ⁻⁰¹	9.E⁻⁰³	2.E⁻⁰⁵	3.E⁻⁰⁵	1.E⁻⁰⁷	5.E⁻⁰⁸	7.E⁻⁰⁷	2.E⁻⁰⁷	4.E⁻⁰⁵	3.E⁻⁰⁵	1.E⁻⁰⁷	3.E⁻⁰⁶	7.E⁻⁰⁵	2.E⁻⁰⁴	5.E⁻⁰⁴	9.E⁻⁰⁴	2.E⁻⁰³		
	0.16	0.13	0.01	0.09	0.21	0.20	0.30	0.32	0.27	0.29	0.19	0.20	0.20	0.30	0.24	0.18	0.16	0.14	0.13	0.12	
	a,b	a,b	a	b,c	a,b	a,b,c	a,b,c	a,b,c	a,b,c	a,b,c	a,b	a,b,c	a,b,c	a,b,c	a,b,c	a,b,c	a,c	a,c	a,c		
T-Expir	5.E⁻⁰⁹	9.E ⁻⁰¹	2.E ⁻⁰¹	8.E ⁻⁰²	2.E⁻¹²	1.E⁻⁰⁸	3.E⁻⁰²	5.E⁻⁰²	8.E⁻⁰³	4.E⁻⁰⁶	4.E⁻⁰⁶	2.E⁻⁰⁵	3.E⁻⁰⁴	6.E⁻⁰³	6.E⁻⁰²	5.E⁻⁰²	3.E⁻⁰¹	3.E⁻⁰¹	4.E⁻⁰²	2.E⁻⁰²	
	0.26	0.00	0.02	0.03	0.36	0.24	0.05	0.04	0.06	0.17	0.16	0.14	0.11	0.07	0.04	0.04	0.02	0.02	0.04	0.05	
	a,b	a,b,c	a,b,c	a,b,c	b	b	b	b	b	a,b	b,c	a,b,c	b,c	b	b	b	c	c	c		
LLB-Inspir	5.E⁻⁰²	7.E ⁻⁰²	3.E ⁻⁰¹	4.E⁻⁰²	1.E⁻⁰²	1.E⁻⁰²	8.E ⁻⁰²	4.E⁻⁰²	8.E⁻⁰⁴	2.E⁻⁰³	1.E⁻⁰³	8.E⁻⁰³	9.E⁻⁰³	1.E⁻⁰²	9.E⁻⁰³	5.E⁻⁰³	5.E⁻⁰³	8.E⁻⁰³	4.E⁻⁰³	2.E⁻⁰²	
	0.02	0.02	0.01	0.02	0.03	0.03	0.02	0.02	0.05	0.05	0.05	0.04	0.03	0.03	0.03	0.04	0.04	0.04	0.04	0.03	
	a,b	c	b,c	c	c	c	b,c	c	a,c	a	a	a,c	a								
LLB-Expir	1.E⁻⁰¹	4.E⁻⁰⁴	4.E ⁻⁰¹	3.E ⁻⁰¹	8.E ⁻⁰¹	1.E ⁻⁰¹	1.E⁻⁰³	1.E⁻⁰²	3.E⁻⁰⁴	4.E⁻⁰⁵	8.E⁻⁰⁶	3.E⁻⁰⁶	2.E⁻⁰⁵	2.E⁻⁰⁵	3.E⁻⁰⁵	4.E⁻⁰⁶	2.E⁻⁰⁶	4.E⁻⁰⁶	7.E⁻⁰⁷	3.E⁻⁰⁶	
	0.02	0.06	0.01	0.01	0.00	0.02	0.05	0.04	0.07	0.08	0.10	0.11	0.09	0.09	0.09	0.10	0.11	0.10	0.12	0.10	
	a,b	a,b	a,c	a,c	a,b																

*Bold font indicates statistical significance ($p < 0.05$). a, b and c indicate significance, as determined through the post hoc test.

Table 3

Summary of MANOVA statistics for the various datasets – details of post hoc test for pairs *a* (mild and moderate), *b* (mild and severe), and *c* (moderate and severe).

Dataset	Wilks's Lambda (Λ)	F	df	Error	p-value	Effect Size (η_{Λ}^2)	Post hoc
All	0.842	3.568	38	1508	3.E⁻¹²	0.158	a,b,c
Trachea	0.494	5.253	38	472	5.E⁻¹⁹	0.506	a,b,c
LLB	0.863	1.996	38	994	4.E⁻⁰⁴	0.137	a,b
Inspiratory	0.775	2.595	38	724	1.E⁻⁰⁶	0.225	a,b,c
Expiratory	0.747	3.065	38	742	5.E⁻⁰⁹	0.253	a,b,c
T-Inspir	0.240	4.649	38	170	2.E⁻¹²	0.760	a,b,c
T-Expir	0.408	3.868	38	260	4.E⁻¹¹	0.592	a,b,c
LLB-Inspir	0.792	1.66	38	512	9.E⁻⁰³	0.208	a,c
LLB-Expir	0.681	2.457	38	440	8.E⁻⁰⁶	0.319	a,b,c

*Bold font indicates statistical significance ($p < 0.05$).

Table 4

Performance of the ENS, KNN and SVM classifiers with the nine datasets as input using ten-fold cross validation.

Dataset	Classes	ENS			KNN			SVM		
		SENS(%)	SPEC(%)	PPR(%)	SENS(%)	SPEC(%)	PPR(%)	SENS(%)	SPEC(%)	PPR(%)
All	Mild	74	88	80	60	85	74	67	83	73
	Moderate	80	78	80	73	67	68	74	74	74
	Severe	88	76	84	79	59	73	81	65	77
Trachea	Mild	85	97	93	53	97	90	63	95	86
	Moderate	88	89	90	82	78	85	85	77	86
	Severe	95	83	91	96	57	82	93	78	86
LLB	Mild	73	81	76	66	77	71	56	79	69
	Moderate	75	78	77	70	64	65	64	63	63
	Severe	84	74	80	71	65	72	74	51	65
Inspiratory	Mild	69	88	82	59	85	74	69	76	67
	Moderate	76	76	77	70	71	72	67	73	73
	Severe	87	68	79	84	56	73	80	67	77
Expiratory	Mild	79	89	84	60	89	78	69	89	81
	Moderate	81	87	86	78	71	73	81	74	75
	Severe	92	75	84	82	60	75	82	68	79
T-Inspir	Mild	90	97	96	55	100	100	85	99	98
	Moderate	85	95	90	75	82	84	89	94	92
	Severe	95	78	90	97	45	79	97	78	91
T-Expir	Mild	80	95	88	38	98	92	61	96	88
	Moderate	91	81	89	83	63	80	80	75	83
	Severe	96	90	94	96	56	84	95	65	83
LLB-Inspir	Mild	73	85	78	44	89	76	64	76	67
	Moderate	78	77	76	63	75	70	69	71	69
	Severe	77	78	79	75	63	69	71	69	72
LLB-Expir	Mild	81	81	79	62	85	77	69	78	73
	Moderate	77	85	82	73	78	74	82	70	70
	Severe	86	78	84	81	54	70	67	71	75

samples – ENS (SENS = 81 ± 6%, SPEC = 83 ± 6%, PPR = 83 ± 6%), KNN (SENS = 74 ± 6%, SPEC = 72 ± 7%, PPR = 74 ± 7%) and SVM (SENS = 77 ± 9%, SPEC = 74 ± 8%, PPR = 76 ± 9%) and severe samples – ENS (SENS = 89 ± 6%, SPEC = 78 ± 6%, PPR = 85 ± 5%), KNN (SENS = 84 ± 10%, SPEC = 57 ± 6%, PPR = 75 ± 5%) and SVM (SENS = 82 ± 11%, SPEC = 68 ± 8%, PPR = 78 ± 8%).

4. Discussion

This study has obtained satisfactory results with the implementation of 20 IP features that are directly related to the physiology of airway obstruction, and is computationally less expensive compared to other studies. Furthermore, previous studies [15,45,17] selected bands from a lower frequency to a maximum of 800 or 1000 Hz, whereas our study selected a higher bandwidth (100–1600 Hz) for the analysis and found satisfactory results within the 1000–1600 Hz band. Fig. 3 reveals that the 20 features have μ (SD) values that do not indicate any specific and consistent trend, but they (individually or combined) exhibit significant differences ($p < 0.05$) to discriminate the severity levels in most of the datasets. The conducted MANOVA statistical analysis indicates that the combined IP feature vector improved the discriminatory power for the severity levels ($p < 0.05$), produced improved (η_{Λ}^2) and resulted in a higher percentage of significant ($p < 0.05$) post hoc tests.

The results of univariate and MANOVA produced higher effect size (η_x^2 and η_{Λ}^2) for trachea-related datasets compared to LLB related datasets. Coupled with the difference in variance observed in the trachea and LLB datasets shown in Fig. 3, these findings indicate that tracheal wheeze sounds are more sensitive and specific predictors of severity level of asthma patients, similar to [21,59]. This could be due to the physiology of the LLB, which behaves as a stronger filter [60,61]. Our findings reveal that wheeze sounds from the trachea and LLB related datasets behave differently within the different band of IP features, which provides evidence that sounds from the trachea and LLB have different characteristics [35,61,62]. Nevertheless, our study finds that IP features can discriminate ($p < 0.05$) among the severity levels of asthma when applied to both locations and/or phases. Specifically, for the challenging LLB-related datasets in adults, our MANOVA test indicated a significant difference ($p < 0.05$) with a large effect size (η_{Λ}^2) and the post hoc test also yielded significant results for all corresponding pairs.

We also observe that inspiratory and expiratory related datasets behave differently [16,17,62]. This could be due to the variation in the physiology of the airway passage (i.e., long and short airways) experienced by the airflow during the inspiratory and expiratory phases [61]. Interestingly, while the phases produce sounds of different behaviour, we note that both phases are equally informative to identify the severity level of asthma patients, as observed in [59].

If we look at the combined location and phase datasets, the univariate analysis of T-Inspir indicated more discriminating power ($p < 0.05$) than that of T-Expir. Similarly, MANOVA results illustrated higher effect size (η_A^2) for the T-Inspir. On the other hand, LLB-Inspir and LLB-Expir performed almost equally. These findings contradict those of [25], which concluded that LLB-Inspir performs better than LLB-Expir for correlating lung function values with peak frequency features, suggesting that IP features are more sensitive and suitable for LLB-Expir than frequency based features. An interesting point to note is that the statistical results reveal that combined location and phase datasets (e.g. T-Inspir or T-Expir) perform better than its related datasets (e.g. Trachea).

Using the combined feature vector of 20 IP values, we found that the performance of ENS, KNN and SVM classifiers produced above than average results. Nevertheless, the performance of the classifiers indicated different behaviours according to auscultation location and breaths phase, similar to that of [45]. Detailed comparisons in our study among the three classifiers reveal improved performance in the ENS classifier when eight of the nine datasets were used as input. The reason for this could be its working principle which combines multiple learners to obtain better performance. Such improved performance was also observed in [52] which had implemented KNN, SVM, naïve bayes, decision tree and ENS classifiers for the classification of normal, wheeze and crackles. While [10–12,14] indicated better performance with the SVM classifier, these studies were not benchmarked with the ENS classifier and none used IP features for the classification of wheeze sound according to severity levels of asthma patients.

The classification results of this study were compared using other feature extraction techniques available in the literature – 7th-order wavelet transform [63] (6 class normal and abnormal) and 6th-order AR [10] (2 class normal and wheeze). Interestingly, the comparison results showed that IP features performed better than wavelet transform and AR. The overall comparison on all datasets indicated the following improvements in classifier performance measures; IP vs. wavelet transform – ENS ($\Delta SENS = 17 \pm 8\%$, $\Delta SPEC = 16 \pm 9\%$, $\Delta PPR = 16 \pm 6\%$), KNN ($\Delta SENS = 13 \pm 12\%$, $\Delta SPEC = 13 \pm 13\%$, $\Delta PPR = 15 \pm 8\%$) and SVM ($\Delta SENS = 16 \pm 15\%$, $\Delta SPEC = 16 \pm 16\%$, $\Delta PPR = 17 \pm 6\%$) and IP vs. AR – ENS ($\Delta SENS = 7 \pm 8\%$, $\Delta SPEC = 8 \pm 8\%$, $\Delta PPR = 8 \pm 4\%$), KNN ($\Delta SENS = 2 \pm 10\%$, $\Delta SPEC = 3 \pm 10\%$, $\Delta PPR = 4 \pm 7\%$) and SVM ($\Delta SENS = 5 \pm 10\%$, $\Delta SPEC = 6 \pm 12\%$, $\Delta PPR = 6 \pm 6\%$). Furthermore, these methods also rely on the selection of frequency bands to obtain the features. In view of this, the comparisons results indicate that the selected set of bands in our work appear to be more suitable for the classification and identification of asthma severity levels.

5. Conclusion

The identification of asthmatic patients as mild, moderate and severe during tidal breathing can be achieved through an analysis of integrated power (IP) features. The findings prove that wheeze sounds have different power spectral distributions in different bands according to severity levels (mild, moderate and severe), location (trachea and LLB) and phase (inspiratory and expiratory). The IP μ (SD) values of mild, moderate and severe wheeze sound samples do not follow any specific and consistent pattern with respect to severity level, but these behaviours show significant differences ($p < 0.05$) among asthmatic patients. The MANOVA results revealed significance differences ($p < 0.05$) with large effect size in all datasets, including the LLB dataset. Furthermore, in the post hoc test, most of the pairs were found to be significant in all datasets. The performance of the ENS, KNN and SVM classifiers was found to be above average. Overall comparisons exhibited improved classification results for ENS. Among the nine datasets, trachea inspiratory

(T-Inspir) indicated highest performance. The best PPR obtained for the mild, moderate and severe classifications were 100% (KNN), 92% (SVM) and 94% (ENS), respectively. The analysis of IP features indicated that tracheal wheeze sounds are more responsive and precise predictors of severity levels. Phase related observations indicated that inspiratory and expiratory wheeze sounds are almost equally informative for the identification of severity levels. In the future, acoustic features, deep learning classification techniques and feature optimization can be implemented and analysed.

Conflict of interest

The authors declare that they have no conflict of interest. This study was not supported by any funding sources.

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References

- [1] F.G. Nabi, K. Sundaraj, C.K. Lam, S. Sundaraj, R. Palaniappan, Wheeze sound analysis using computer-based techniques: a systematic review, *Biomed. Eng.-Biomed. Technol.* 64 (2019) 1–28.
- [2] R.X.A. Pramono, S. Bowyer, E. Rodriguez- Villegas, Automatic adventitious respiratory sound analysis: a systematic review, *PLoS One* 12 (2017), p. e0177926.
- [3] R. Palaniappan, K. Sundaraj, S. Sundaraj, Artificial intelligence techniques used in respiratory sound analysis—a systematic review, *Biomed. Eng.-Biomed. Technol.* 59 (2014) 7–18.
- [4] A. Gurung, C.G. Scrafford, J.M. Tielsch, O.S. Levine, W. Checkley, Computerized lung sound analysis as diagnostic aid for the detection of abnormal lung sounds: a systematic review and meta-analysis, *Respir. Med.* 105 (2011) 1396–1403.
- [5] R. Palaniappan, K. Sundaraj, N.U. Ahamed, A. Arjunan, S. Sundaraj, Computer-based respiratory sound analysis: a systematic review, *IETE Tech. Rev.* 30 (2013) 248–256.
- [6] Y. Shabtai-Musih, J.B. Grotberg, N. Gavriely, Spectral content of forced expiratory wheezes during air, He, and SF6 breathing in normal humans, *J. Appl. Physiol.* 72 (February) (1992) 629–635.
- [7] A. Homs-Corbera, J.A. Fiz, J. Morera, R. Jane, Time-frequency detection and analysis of wheezes during forced exhalation, *IEEE Trans. Inf. Technol. Biomed.* 51 (January) (2004) 182–186.
- [8] S.A. Taplidou, L.J. Hadjileontiadis, Wheeze detection based on time-frequency analysis of breath sounds, *Comput. Biol. Med.* 37 (August) (2007) 1073–1083.
- [9] D. Oletic, V. Bilas, Asthmatic wheeze detection from compressively sensed respiratory sound spectra, *IEEE J. Biomed. Health Inform.* 22 (2018) 1406–1414.
- [10] M. Bahoura, Pattern recognition methods applied to respiratory sounds classification into normal and wheeze classes, *Comput. Biol. Med.* 39 (September) (2009) 824–843.
- [11] I. Mazić, M. Bonković, B. Džaja, Two-level coarse-to-fine classification algorithm for asthma wheezingrecognition in children's respiratory sounds, *Biomed. Signal Process Control* 21 (2015) 105–118.
- [12] P. Bokov, B. Mahut, P. Flaud, C. Delclaux, Wheezing recognition algorithm using recordings of respiratory sounds at the mouth in a pediatric population, *Comput. Biol. Med.* 70 (2016) 40–50.
- [13] F. Jin, S. Krishnan, F. Sattar, Adventitious sounds identification and extraction using temporal-spectral dominance-based features, *IEEE Trans. Inf. Technol. Biomed.* 58 (2011) 3078–3087.
- [14] M. Lozano, J.A. Fiz, R. Jane, Performance evaluation of the Hilbert-Huang transform for respiratory sound analysis and its application to continuous adventitious sound characterization, *Signal Process* 120 (2016) 99–116.
- [15] J.A. Fiz, R. Jane, A. Homs, J. Izquierdo, M.A. Garcia, J. Morera, Detection of wheezing during maximal forced exhalation in patients with obstructed airways, *Chest* 122 (July) (2002) 186–191.
- [16] S.A. Taplidou, L.J. Hadjileontiadis, Nonlinear analysis of wheezes using wavelet bicoherence, *Comput. Biol. Med.* 37 (2007) 563–570.
- [17] S.A. Taplidou, L.J. Hadjileontiadis, Analysis of wheezes using wavelet higher order spectral features, *IEEE Trans. Biomed. Eng.* 57 (July) (2010) 1596–1610.

- [18] S. Rietveld, M. Oud, E.H. Dooijes, Classification of asthmatic breath sounds: preliminary results of the classifying capacity of human examiners versus artificial neural networks, *Comput. Biomed. Res.* 32 (1999) 440–448.
- [19] M. Oud, E.H. Dooijes, J.S. van der Zee, Asthmatic airways obstruction assessment based on detailed analysis of respiratory sound spectra, *IEEE Trans. Inf. Technol. Biomed.* 47 (2000) 1450–1455.
- [20] M. Oud, Lung function interpolation by means of neural-network-supported analysis of respiration sounds, *Med. Eng. Phys.* 25 (2003) 309–316.
- [21] L.P. Malmberg, L. Pesu, A. Sovijärvi, Significant differences in flow standardised breath sound spectra in patients with chronic obstructive pulmonary disease, stable asthma, and healthy lungs, *Thorax* 50 (1995) 1285–1291.
- [22] R.P. Baughman, R.G. Loudon, Lung sound analysis for continuous evaluation of airflow obstruction in asthma, *Chest* 88 (1985) 364–368.
- [23] J. Fiz, R. Jane, J. Izquierdo, A. Homs, M. Garcia, R. Gomez, E. Monso, J. Morera, Analysis of forced wheezes in asthma patients, *Respiration* 73 (2006) 55–60.
- [24] G.R. Manecke, J.P. Dilger, L.J. Kutner, P.J. Poppers, Auscultation revisited: The waveform and spectral characteristics of breath sounds during general anesthesia, *Int. J. Clin. Monit. Comput.* 14 (1997) 231–240.
- [25] C. Habukawa, Y. Nagasaka, K. Murakami, T. Takemura, High-pitched breath sounds indicate airflow limitation in asymptomatic asthmatic children, *Respirology* 14 (2009) 399–403.
- [26] M. Rossi, A.R.A. Sovijärvi, P. Piirilä, L. Vannuccini, F. Dalmaso, J. Vanderschoot, Environmental and subject conditions and breathing manoeuvres for respiratory sound recordings, *Eur. Respir. Rev.* 10 (2000) 611–615.
- [27] F. Nabi, K. Sundaraj, C.K. Lam, R. Palaniappan, J. Hussain, Recommendations related to wheeze sound data acquisition, *J. Telecommun. Electron. Comput. Eng. (JTEC)* 10 (2018) 117–120.
- [28] Wireless Digital Stethoscope 2019; Available: <http://www.summeditec.com> accessed date (01 March 2018).
- [29] R. Palaniappan, K. Sundaraj, S. Sundaraj, Adaptive neuro-fuzzy inference system for breath phase detection and breath cycle segmentation, *Comput. Meth. Prog. Bio.* (2017).
- [30] R. Palaniappan, K. Sundaraj, S. Sundaraj, N. Huliraj, S. Revadi, Classification of pulmonary pathology from breath sounds using the wavelet packet transform and an extreme learning machine, *Biomed. Eng.-Biomed. Technol.* (2017).
- [31] R. Palaniappan, K. Sundaraj, S. Sundaraj, N. Huliraj, S. Revadi, A telemedicine tool to detect pulmonary pathology using computerized pulmonary acoustic signal analysis, *Appl. Soft Comput.* 37 (2015) 952–959.
- [32] F.G. Nabi, K. Sundaraj, C.K. Lam, R. Palaniappan, Characterization and classification of asthmatic wheeze sounds according to severity level using spectral integrated features, *Comput. Biol. Med.* 104 (2019) 52–61.
- [33] F.G. Nabi, K. Sundaraj, C.K. Lam, R. Palaniappan, Analysis of wheeze sounds during tidal breathing according to severity levels in asthma patients, *J. Asthma* (2019), <http://dx.doi.org/10.1080/02770903.2019.1576193>.
- [34] G. Charbonneau, E. Ademovic, B.M.G. Cheetham, L.P. Malmberg, J. Vanderschoot, A.R.A. Sovijärvi, Basic techniques for respiratory sound analysis, *Eur. Respir. Rev.* 10 (2000) 625–635.
- [35] Z.K. Moussavi, M.T. Leopando, H. Pasterkamp, G. Rempel, Computerised acoustical respiratory phase detection without airflow measurement, *Med. Biol. Eng. Comput.* 38 (2000) 198–203.
- [36] J. Bousquet, T. Clark, S. Hurd, N. Khaltaev, C. Lenfant, P. O'byrne, A. Sheffer, GINA guidelines on asthma and beyond, *Allergy* 62 (2007) 102–112.
- [37] A. Education, National Asthma Education and Prevention Program? Guidelines for the Diagnosis and Management of Asthma (NAEPP National Asthma Education and Prevention Program) Available: <http://www.nhlbi.nih.gov/guidelines/asthma/asthdln.pdf> accessed date (01 March 2018), 2007.
- [38] M. Wisniewski, T.P. Zielinski, Joint application of audio spectral envelope and tonality index in an e-asthma monitoring system, *IEEE J. Biomed. Health Inform.* 19 (May) (2015) 1009–1018.
- [39] C. Yu, T.-H. Tsai, S.-I. Huang, C.-W. Lin, Soft stethoscope for detecting asthma wheeze in young children, *Sensors* 13 (2013) 7399–7413.
- [40] C.S. Shim, M.H. Williams, Relationship of wheezing to the severity of obstruction in asthma, *Arch. Intern. Med.* 143 (1983) 890–892.
- [41] A. Saarinen, H. Riihkanen, L. Malmberg, L. Pekkanen, A.R. Sovijärvi, Tracheal sounds and airflow dynamics in surgically treated unilateral vocal fold paralysis, *Clin. Physiol. Funct.* 1 21 (2001) 223–228.
- [42] J.A. Fiz, R. Jané, M. Lozano, R. Gómez, J. Ruiz, Detecting unilateral phrenic paralysis by acoustic respiratory analysis, *PLoS One* 9 (2014), p. e93595.
- [43] J.A. Fiz, R. Jane, D. Salvatella, J. Izquierdo, L. Lores, P. Caminal, J. Morera, Analysis of tracheal sounds during forced exhalation in asthma patients and normal subjects: bronchodilator response effect, *Chest* 116 (1999) 633–638.
- [44] M. Lozano, J. Fiz, R. Jané, Automatic differentiation of normal and continuous adventitious respiratory sounds using ensemble empirical mode decomposition and instantaneous frequency, *IEEE J. Biomed. Health Inform.* 20 (2016) 486–497.
- [45] M.A. Islam, I. Bandyopadhyaya, P. Bhattacharyya, G. Saha, Multichannel lung sound analysis for asthma detection, *Comput. Meth. Prog. Biomed.* 104 (2018) 52–61.
- [46] P. Welch, The use of fast Fourier transform for the estimation of power spectra: a method based on time averaging over short, modified periodograms, *Ieee Trans. Audio Electroacoust.* 15 (1967) 70–73.
- [47] F.J. Harris, On the use of windows for harmonic analysis with the discrete Fourier transform, *Proc. Ieee* 66 (1978) 51–83.
- [48] V. Gross, A. Dittmar, T. Penzel, F. Schuttler, P. Von Wichert, The relationship between normal lung sounds, age, and gender, *Am. J. Respir. Crit. Care Med.* 162 (2000) 905–909.
- [49] A. Niimi, H. Matsumoto, R. Amitani, Y. Nakano, M. Mishima, M. Minakuchi, K. Nishimura, H. Itoh, T. Izumi, Airway wall thickness in asthma assessed by computed tomography: relation to clinical indices, *Am. J. Respir. Crit. Care Med.* 162 (2000) 1518–1523.
- [50] N. Meslier, G. Charbonneau, J.L. Racineux, Wheezes, *Eur. Respir. J.* 8 (November) (1995) 1942–1948.
- [51] H. Tabata, M. Enseki, M. Nukaga, K. Hirai, S. Matsuda, H. Furuya, M. Kato, H. Mochizuki, Changes in the breath sound spectrum during methacholine inhalation in children with asthma, *Respirology* 23 (2018) 168–175.
- [52] S. Ulukaya, G. Serbes, Y.P. Kahya, Overcomplete discrete wavelet transform based respiratory sound discrimination with feature and decision level fusion, *Biomed. Signal Process. Control* 38 (2017) 322–336.
- [53] A. Field, Non-Parametric Tests in Discovering Statistics Using SPSS, 3rd ed, Sage publications, 2009.
- [54] H. Steyn Jr., S. Ellis, Estimating an effect size in one-way multivariate analysis of variance (MANOVA), *Multivar. Behav. Res.* 44 (2009) 106–129.
- [55] C.-H. Chen, W.-T. Huang, T.-H. Tan, C.-C. Chang, Y.-J. Chang, Using k-nearest neighbor classification to diagnose abnormal lung sounds, *Sensors* 15 (2015) 13132–13158.
- [56] C. Cortes, V. Vapnik, Support-vector networks, *Mach. Learn.* 20 (1995) 273–297.
- [57] I. Hmeidi, B. Hawashin, E. El-Qawasmeh, Performance of KNN and SVM classifiers on full word Arabic articles, *Int. J. Adv. Sci. Eng. Inf. Technol.* 22 (2008) 106–111.
- [58] I. Barandiaran, The random subspace method for constructing decision forests, *IEEE Trans. Pattern Anal. vol.* 20 (1998).
- [59] S. Rietveld, E. Dooijes, L. Rijssenbeek-Nouwens, F. Smit, P. Prins, A. Kolk, W.A. Everaerd, Characteristics of wheeze during histamine-induced airways obstruction in children with asthma, *Thorax* 50 (1995) 143–148.
- [60] T.R. Fenton, H. Pasterkamp, A. Tal, V. Chernick, Automated spectral characterization of wheezing in asthmatic children, *IEEE Trans. Inf. Technol. Biomed.* 32 (January) (1985) 50–55.
- [61] H. Pasterkamp, S.S. Kraman, G.R. Wodicka, Respiratory sounds: advances beyond the stethoscope, *Am. J. Respir. Crit. Care Med.* 156 (1997) 974–987.
- [62] A. Yadollahi, Z.M. Moussavi, Acoustical respiratory flow, *Ieee Eng. Med. Biol. Mag.* 1 (2007) 56–61.
- [63] A. Kandaswamy, C.S. Kumar, R.P. Ramanathan, S. Jayaraman, N. Malmurugan, Neural classification of lung sounds using wavelet coefficients, *Comput. Biol. Med.* 34 (2004) 523–537.