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Characterization and classification of asthmatic wheeze sounds according to severity level using spectral integrated features

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A R T I C L E I N F O

Keywords:
Asthma
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Airway obstruction
Severity level

A B S T R A C T

Objective: This study aimed to investigate and classify wheeze sounds of asthmatic patients according to their severity level (mild, moderate and severe) using spectral integrated (SI) features.
Method: Segmented and validated wheeze sounds were obtained from auscultation recordings of the trachea and lower lung base of 55 asthmatic patients during tidal breathing manoeuvres. The segments were multi-labelled into 9 groups based on the auscultation location and/or breath phases. Bandwidths were selected based on the physiology, and a corresponding SI feature was computed for each segment. Univariate and multivariate statistical analyses were then performed to investigate the discriminatory behaviour of the features with respect to the severity levels in the various groups. The asthmatic severity levels in the groups were then classified using the ensemble (ENS), support vector machine (SVM) and k-nearest neighbour (KNN) methods.
Results and conclusion: All statistical comparisons exhibited a significant difference ($p < 0.05$) among the severity levels with few exceptions. In the classification experiments, the ensemble classifier exhibited better performance in terms of sensitivity, specificity and positive predictive value (PPV). The trachea inspiratory group showed the highest classification performance compared with all the other groups. Overall, the best PPV for the mild, moderate and severe samples were 95% (ENS), 88% (ENS) and 90% (SVM), respectively. With respect to location, the tracheal related wheeze sounds were most sensitive and specific predictors of asthma severity levels. In addition, the classification performances of the inspiratory and expiratory related groups were comparable, suggesting that the samples from these locations are equally informative.

1. Introduction

During breathing, acoustic signals are produced in the lungs due to oscillations in the turbulent flow at the bronchial walls, and respiratory acoustic signals provide meaningful information regarding the condition of the lungs. Specifically, normal lungs generate normal breath sounds, and pathological disorders or airway obstructions produce abnormal sounds. Asthmatic patients present some airway obstruction that results in the production of wheeze sounds. The current practice of physicians involves using a stethoscope to auscultate wheeze sounds, and this subjective process depends on the experience and hearing capability of the physician. To overcome these issues, researchers have started to intensely explore computer-based techniques.

Computerized wheeze sound analysis is an active field of research that is increasingly gaining traction. As the name suggests, computerized respiratory sound analysis has the advantage of covering a wider range of frequencies than physicians can auscultate [1]. Researchers have been investigating wheeze detection using logic-base algorithms, wheeze classification using machine learning techniques, the relationship between airway obstruction and sound spectra and wheeze sound characteristics. Several reviews on computerized breath sound analysis have also revealed that most of the researchers in the field of computerized analysis are investigating the detection or classification of adventitious sounds (including wheezes), which can be continuous or discontinuous [1–5].

2. Literature review

A previous study [6] detected wheezes in a spectrogram by identifying a set of peaks higher than a predefined threshold value. A later

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study [7] modified the threshold and smoothing technique and introduced peak grouping to enhance the wheeze duration criteria, which increased the wheeze detection accuracy. Furthermore, another study [8] developed a time-frequency wheeze detection algorithm that introduced the notion of peak coexistence, i.e., the number of peaks detected at the same interval should not be greater than a predefined constant. This wheeze detection trend then started to shift from logic-based algorithms to machine learning techniques because logic-based algorithms are dependent and susceptible to attenuation of the sound signal amplitude, which led researchers to develop methods invariant to attenuation.

Machine learning techniques then focused on the extraction of wheeze features for the classification of lung sounds into wheeze and non-wheeze sounds. The algorithm developed in a previous study [9] compared 17 systems developed using combinations of autoregression (AR), short-time Fourier transform (STFT), Mel-frequency cepstrum coefficient (MFCC), wavelet packet transform and wavelet transform feature extraction methods using Gaussian mixture model (GMM), vector quantification and artificial neural network (ANN) classifiers to classify lung sounds into wheezes and non-wheezes. The findings of the study revealed that MFCC combined with GMM performs better than all the other combinations. Another study [10] extracted MFCC features from breath sounds and introduced a two-layer coarse-to-fine support vector machine (SVM) classifier to eliminate false stridors (louder wheezes with prominent peaks at 1000 Hz) and thus classify wheeze and non-wheeze breath sounds. An earlier study conducted with children [11] had similar objectives: the researchers attempted to extract features from the power spectral density using an AR method and fed the features into an SVM classifier. Other researchers [12] introduced a temporal-spectral domain technique for feature extraction and applied the k-nearest neighbour (KNN) classifier to classify breath sounds into normal and abnormal classes. Another recent study [13] developed an empirical mode decomposition approach to obtain the Hilbert spectrum of lung sound recordings, and the features (instantaneous envelope and instantaneous frequency) obtained using this approach were then extracted and fed to an SVM classifier to classify the recordings into wheeze and normal sounds. Recently, another study [14] collected data from 30 adults and selected 200 segments of each wheeze, crackle and normal sound, and the systems obtained with various combinations of feature extraction techniques (rotational dilation wavelet transform, power spectral density (PSD), perceptual linear prediction (PLP), MFCC and stock-well transform) and classification techniques (naïve Bayes, decision trees, SVM, extreme learning machine and ensemble learning) were compared. An overall three class best accuracy was obtained with the combination of rotational dilation transform features with the ensemble (ENS) learning classifier. These studies indicate that researchers are attempting to classify breath sounds into predominantly normal and abnormal sounds.

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

In addition to computerized analysis, researchers have also examined correlations between other forms of recordings and classification. One study [18] compared the classification performance of a system between humans and an ANN classifier. Humans were shown the asthmatic patient's bar-graph spectrogram obtained during one breath cycle, whereas the ANN was developed using features of the same spectrogram. The results revealed an interesting insight – ANN classifiers perform better than humans in the analysis of a bar-graph spectrogram. Other researchers [19,20] later correlated sound spectra to 16 different lung function values, including force expiratory volume in 1 s (FEV_1). The results revealed the existence of a deterministic relationship between lung function values and sound spectra in asthmatic subjects. The researchers further claimed that the acuteness of asthmatic subjects can be identified through a computerized breath sound analysis [20] and rigidly concluded that breath sound spectra provide sufficient information to explain the acuteness of asthmatic patients [19].

Taken together, the previously mentioned studies indicate several important insights. First, a relationship exists between lung function values and respiratory sounds. Second, although some studies have collected data from patients with different asthma severity levels and conducted various analyses, only a few have referred their findings back to the severity levels. Third, all of the existing works focused on the identification of normal and abnormal lung sounds classes, without any reference to asthma severity levels. This cumulative gap is crucial given that according to the World Health Organization (WHO), 235 million individuals are suffering from asthma. These statistics have encouraged researchers to develop computerized devices for the self-monitoring and self-management of asthma, which are becoming increasingly more necessary and important. To this effect, several physician-assisted devices, including spirometers and peak flow metres, are currently being used. However, these devices are predominantly utilized during supervised forced respiratory manoeuvres, which could pose a problem when dealing with children, during long-term and continuous observation of patients, when assessing patients with very severe asthma conditions and in unsupervised sessions. On another note, wheezing during forced exhalation is not always correlated to the degree of airway obstruction in asthmatic patients, which reveals that the FEV_1 values obtained using spirometry might not always correlate with asthma acuteness [21].

This study attempted to observe the characteristics of wheeze sounds through a statistical analysis of spectral integrated (SI) features and to further classify wheezes into three asthma severity levels (mild, moderate and severe), which is required for deciding the medication and/or other treatments that should be administered to a patient. The management and monitoring of asthma are performed based on the asthma severity, and the administration of medications to a patient is also managed based on the severity conditions of the patient [22]. A few previous studies conducted statistical analyses of the correlations between changes in lung function values and respiratory sound spectra [23–25]. Other researchers [24] collected data from asthmatic patients during normal breathing and found a relationship between lung function values and the ratio of the wheezing duration to the total recording time (T_w/T_{tot}). Another researcher group [23] collected data from the trachea and chest of ten asthmatics patients during forced breathing, calculated the F_{50}, F_{75} and average power, and determined that only F_{50} recorded at the trachea was significantly related to the FEV_1. In another study [25], data were collected from the trachea of asthma patients during forced breathing, and the acoustic characteristics in normal, stable and nonstable asthma patients were investigated. The results revealed that the mean frequency of normal subjects is different from that of asthmatic patients. However, these studies did not perform

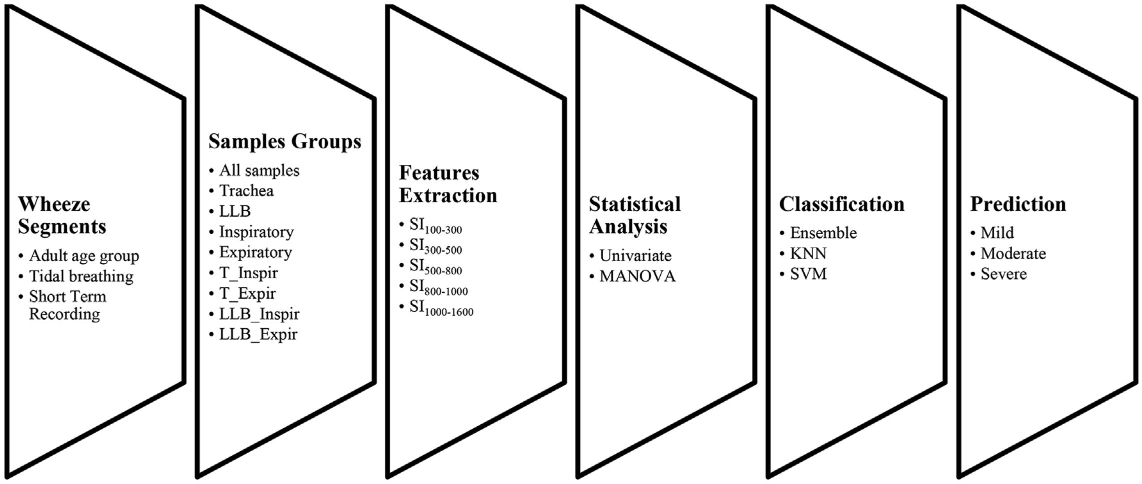

Fig. 1. Proposed methodology for the classification and investigation of wheeze sounds using SI features for asthma severity levels.

statistical analyses comparing various auscultation locations, breathing phases and severity levels. Unlike these studies, our study was inspired by issues related to the self-management and self-monitoring (unsupervised sessions) of asthma. To this effect, we were primarily concerned with tidal breathing manoeuvres.

2. Material and methods

2.1. Study protocol

The protocol used for the acquisition of respiratory sound data was designed according to CORSA standards [26] and after a detailed study of the literature [1]. The approved protocol in the proposed methodology consists of several steps, as illustrated in Fig. 1.

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 committee 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

In this study, a wireless digital stethoscope (WISE) [27] was used for data collection. The WISE used in this study 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, transmitter and receiver. In the WISE used in this study, mechanical vibrations are converted into electric signals through an air-coupled condenser. All the data were collected and saved using the VPM3000W software, which accompanies the WISE used in this study. A few previous studies have also used the same device [28–30].

2.4. Inclusion and exclusion criteria

The subjects were recruited based on suggestions from senior medical officers of both hospitals. The selected subjects were nonsmokers who were not on any drugs that could affect the outcome of the study. 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 a few hours prior to data collection.

2.5. Subject details

All the data were collected from subjects suffering from asthma. A total of 55 subjects, including 34 males and 21 females (age (mean ± SD) = 55 ± 12.2), participated. After each patient was diagnosed according to the available GINA standards [31], his/her asthma severity level (mild, moderate and severe) was identified according to the National Asthma Education and Prevention Programme – Expert Panel Report 3 [22]. This diagnosis was based on parameters such as shortness of breath, wheezes, history and condition of the patient, and each of these parameters had its own scientific and quantitative metric. A similar approach has also been used in other studies [32,33]. The severity levels of all the patients were verified by at least two physicians in both hospitals. Subjects for whom the physicians had conflicting opinions were excluded from the study. The details of the severity levels of the asthma patients included in this study are as follows: (1) mild – 17, male:female = 9:6, age (mean ± SD) = 50 ± 12.1; (2) moderate – 18, male:female = 12:6, age (mean ± SD) = 51.5 ± 13.7; and (3) severe – 20, male:female = 13:7, age (mean ± SD) = 50 ± 11.5. Our records indicate that a total of 5 subjects were excluded due to conflicting opinions.

2.6. Auscultation location and procedure

Respiratory sound recordings were obtained using a single-channel WISE. Data were collected from the trachea and the left and right LLB [34]. The exact location of the LLB was selected by ordinary auscultation with sufficient sound intensity [23] and according to a previous study [34]. In this study, the difference in breath sounds between the right and left LLB [35,36] was considered negligible, and thus, both locations were considered the LLB.

All recordings were obtained as the subjects were in a sitting position with their hands on their lap. The subjects were asked to breathe through their mouth to exert effects on the upper airway and to keep quiet and avoid any movements during the data recording. In addition, the subjects were asked to hold their breath for 10 s and then breathe normally without any targeted flow. To ensure the quality and reliability of the data, short-term recordings for 60–90 s were conducted. The data were collected in a soundproof room, and the 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 [23].

2.7. Data acquisition and pre-processing

Respiratory sound data were acquired at a sampling frequency of 8000 Hz. The respiratory sounds were filtered with a 1^{st}-order high-pass Butterworth filter at 7.5 Hz to remove the DC offset. Subsequently, an 8^{th}-order low-pass Butterworth filter with a 2500 Hz frequency was applied to remove aliasing. The dominant frequency of wheeze sounds lies between 100 and 1600 Hz. Hence, a 4^{th}-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. Wheeze sounds were segmented based on their manifestation in the spectrogram and using the following criteria – increase in intensity of 20 dB, duration longer or equal to 100 ms, and frequency greater or equal to 100 Hz [37]. Furthermore, all segments and labelling were validated by another independent physician. Segments for which the physicians had conflicting opinions were omitted from the study. Similar approaches were also used in a previous study [12,10]. The combination of these approaches produced a database of wheezes labelled according to severity level, phase and location, as shown in Table 1. The manifestation of wheeze sounds can be noted in Fig. 2, which shows the respiratory sounds recorded from the trachea of a 53-year-old woman suffering from moderate asthma.

2.9. Wheeze groups

The collected wheeze samples were split into the following nine groups – all wheeze samples regardless of location and phase (Group 1); wheeze samples divided by location, trachea (Group 2) and LLB (Group 3); wheeze samples divided by phase, inspiratory (Group 4) and expiratory (Group 5); and wheeze samples divided by combinations of location and phase, T_Inspir (Group 6), T_Expir (Group 7), LLB_Inspir (Group 8), and LLB_Expir (Group 9). Previous studies [8,9,16,17,10] have analysed all samples without discriminating their location or phase. Some researchers [7,15,21] focused only on the expiratory phase, whereas other studies [13,38,39] analysed only the inspiratory phase. Another study [40] obtained data from multiple locations and investigated them separately and/or in combination.

2.10. Feature extraction

The wheeze segments were analysed using a Fast Fourier Transform (FFT) approach. Specifically, FFT with a 512-point (64 ms) hamming window and 50% overlap was applied to obtain the power spectrum density within the range of 100–1600 Hz [41]. A hamming window is a smooth window with acceptable leakage [19,42]. Most of the studies in the literature used a 64 ms window length with an overlap of 50%. Additionally, a previous study [43] investigated the effect of wheeze sound classification using varying window lengths (10–200 ms) and concluded that the change in accuracy rates obtained with different window lengths is negligible. The amplitude of the power spectrum was normalized (the sum of the absolute power spectrum values normalized to one) based on Eqs. (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, $P(n)_{norm}$ is the normalized power spectrum, and I indicates power intensity related to the frequency.

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

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

The frequencies of all the recordings obtained using this method were comparable, regardless of the loudness of the lung sounds [19,44] and the lung capacity. The frequency range of 100–1600 Hz of each power spectrum density was divided into five unequal sub-bands, namely, 100–300, 300–500, 500–800, 800–1000 and 1000–1600 Hz. Similar spectral bands (100–1000 Hz) were also selected in a previous study [8] for the analysis of wheeze and normal breath sounds. Subsequently, the integrations of these bands and the full 100–1600-Hz band were calculated using Eq. (3), where l and h are the upper and lower limits of the band. Finally, the spectral integration of the sub-bands was normalized using the integrated value obtained from the full band. This approach yielded the five features $SI_{100\text{-}300}$, $SI_{300\text{-}500}$, $SI_{500\text{-}800}$, $SI_{800\text{-}1000}$ and $SI_{1000\text{-}1600}$.

$$SI = \int_{l}^{h} P(n)_{norm}dn \tag{3}$$

2.11. Statistical analysis

Prior to the univariate statistical analyses (individual feature), a normality test was performed, and the results showed that the data were not normally distributed. A univariate analysis using a non-parametric test (Kruskal-Wallis) was conducted to investigate the overall significant difference between the three severity levels. Subsequently, a post hoc test (Mann-Whitney) was applied to assess the significance of the differences between pairs of severity levels. A 95% confidence level was considered significant for all statistical analyses, i.e., selected groups were considered significantly different if $p < 0.05$. The strength of the statistical analysis, which depended on the test, was observed through Cohen's effect size (η_χ^2), as described previously [45]. η_χ^2 was calculated using Eq. (4), where χ^2 is the Kruskal-Wallis test statistic and N is the number of samples of the respective group, to determine the effect size as follows – 0.01 (small), 0.06 (medium) and 0.138 (large).

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

A multivariate analysis (feature vector) was then performed to investigate the discriminatory power of the combined five features among the mild, moderate and severe samples in all nine groups. Repeated MANOVA with Wilks lambda (Λ) was performed in this study. η^2 and all subsequent post hoc analyses were investigated based on a 95%

Table 1
Descriptive statistics of the nine groups of data used in this study.

Severity	Total Subjects	Male	Female	All	Trachea	LLB	Inspiratory	Expiratory	T_ Inspir	T_ Expir	LLB_ Inspir	LLB_ Expir
Mild	17	9	8	199	49	150	98	101	20	29	78	72
Moderate	18	12	6	254	85	169	127	127	32	53	95	74
Severe	20	13	7	322	123	199	158	164	54	69	104	95
Total	55	34	21	775	257	518	383	392	106	151	277	241

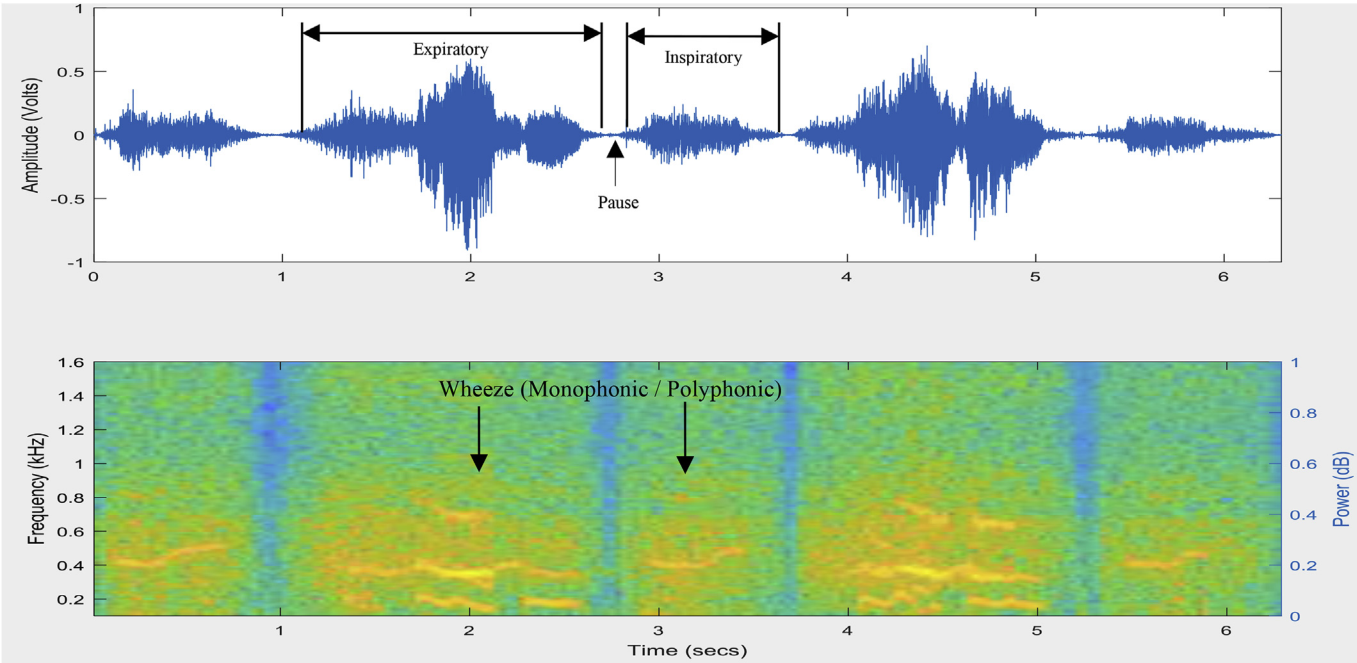

Fig. 2. Visual inspection of trachea breath sounds recording (top) of a 53-year-old woman suffering from moderate asthma and the corresponding spectrogram (bottom), indicating the presence of wheeze sounds.

confidence level to indicate significance ($p < 0.05$). In this case, η_{Λ}^2 was calculated using Eq. (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) [46].

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

2.12. Classification

Three classifiers were selected in this study – SVM, KNN and ENS. It is worth noting that the SVM and KNN classifiers have been widely used in the field of computerized wheeze classification [9,10,39,40]. Prior to the development of the classifiers, all the data was normalized between 0 and 1 with respect to their minimum and maximum values.

The SVM classifier classifies data into classes by constructing a hyperplane with the maximum margin possible. The aim of this classifier is to find the optimal separating hyperplane among the training samples. The selection of a hyperplane depends on the nature of the data, i.e., linear or non-linear. This classifier constitutes a maximum margin and kernelized approach. The optimal separating hyperplane ensures that the maximal performance is obtained through the selection of the maximal margin between the closest members of the classes to the hyperplane. The chosen kernel function (Gaussian or Cubic), which consists of the kernel scale and box constraint level, was optimized based on the classification accuracy of all available data. The optimized values for the SVM classifier were the following: Gaussian, scale of 0.6 and level 1. A one-against-one approach was selected for the multiclass SVM classification. KNN is a non-parametric approach based on the strategy of finding nearest neighbours and employs voting to determine the most likely class. The elected type of distance measurement (city block and Euclidean distance) and the number of nearest neighbours (k) were optimized based on the classification accuracy of all available data. In this study, $k = 10$ and the Euclidean distance metric were selected. In the ENS method, multiple simple learners are combined to improve the performance of the classifier. The selected learner types (bagged tree and boost tree) and the number of learners was optimized based on the classification accuracy of all available data, and a bagged decision tree with 30 learners was deemed optimal in this study.

After the optimization and learning phases, a leave-one-out subject cross-validation technique was applied to analyse the performance of the classifiers. The performances of the classifiers were monitored using the sensitivity (SEN), specificity (SPE) and PPV parameters. All computations regarding pre-processing, feature extraction and classification were performed using MATLAB® (version 2017a, Math Works, USA), and all the statistical analyses were performed using IBM SPSS Statistics (version 20, IBM Corporation, USA).

3. Results

Fig. 3 presents the μ(SD) values of $SI_{100\text{-}300}$, $SI_{300\text{-}500}$, $SI_{500\text{-}800}$, $SI_{800\text{-}1000}$ and $SI_{1000\text{-}1600}$ for mild, moderate and severe asthma patients in the nine groups. The graphs show that much of the energy in the signal is concentrated in the $SI_{100\text{-}300}$, $SI_{300\text{-}500}$ and $SI_{500\text{-}800}$ bands. Furthermore, a decreasing trend in the values was observed from the lower to the higher bands. A similar observation was also noted in the variance of the features. For the trachea related groups, the energy in the signal was better distributed among the $SI_{100\text{-}300}$, $SI_{300\text{-}500}$ and $SI_{500\text{-}800}$ bands, and better discrimination could be observed among the severity classes. In contrast, for the LLB related groups, much of the energy was contained in the $SI_{100\text{-}300}$ and $SI_{300\text{-}500}$ bands.

Table 2 presents a summary of the univariate statistical analysis of the three severity levels and the corresponding post hoc results. The results revealed that all the features exhibited statistical significance for at least 7 out of the 9 groups – $SI_{100\text{-}300}$ ($p < 0.05$, $\eta_{\chi}^2 = 0.03–0.23$), $SI_{300\text{-}500}$ ($p < 0.05$, $\eta_{\chi}^2 = 0.033–0.23$), $SI_{500\text{-}800}$ ($p < 0.05$, $\eta_{\chi}^2 = 0.02–0.361$), $SI_{800\text{-}1000}$ ($p < 0.05$, $\eta_{\chi}^2 = 0.02–0.213$) and $SI_{1000\text{-}1600}$ ($p < 0.05$, $\eta_{\chi}^2 = 0.01–0.241$). All the investigated features showed higher effect sizes for the trachea related groups ($p < 0.05$, $\eta_{\chi}^2 = 0.05–0.361$) than for the LLB related groups ($p < 0.05$, $\eta_{\chi}^2 = 0.016–0.23$). In addition, the features showed better discriminatory power in the inspiratory related groups ($p < 0.05$, $\eta_{\chi}^2 = 0.023–0.361$) than in the expiratory related groups ($p < 0.05$, $\eta_{\chi}^2 = 0.03–0.2$). The post hoc results revealed that the percentage of observations that were statistically significant between the severity level pairs were as follows – *a* (70%), *b* (81%) and *c* (54%).

Table 3 presents the results of the statistical analysis of the

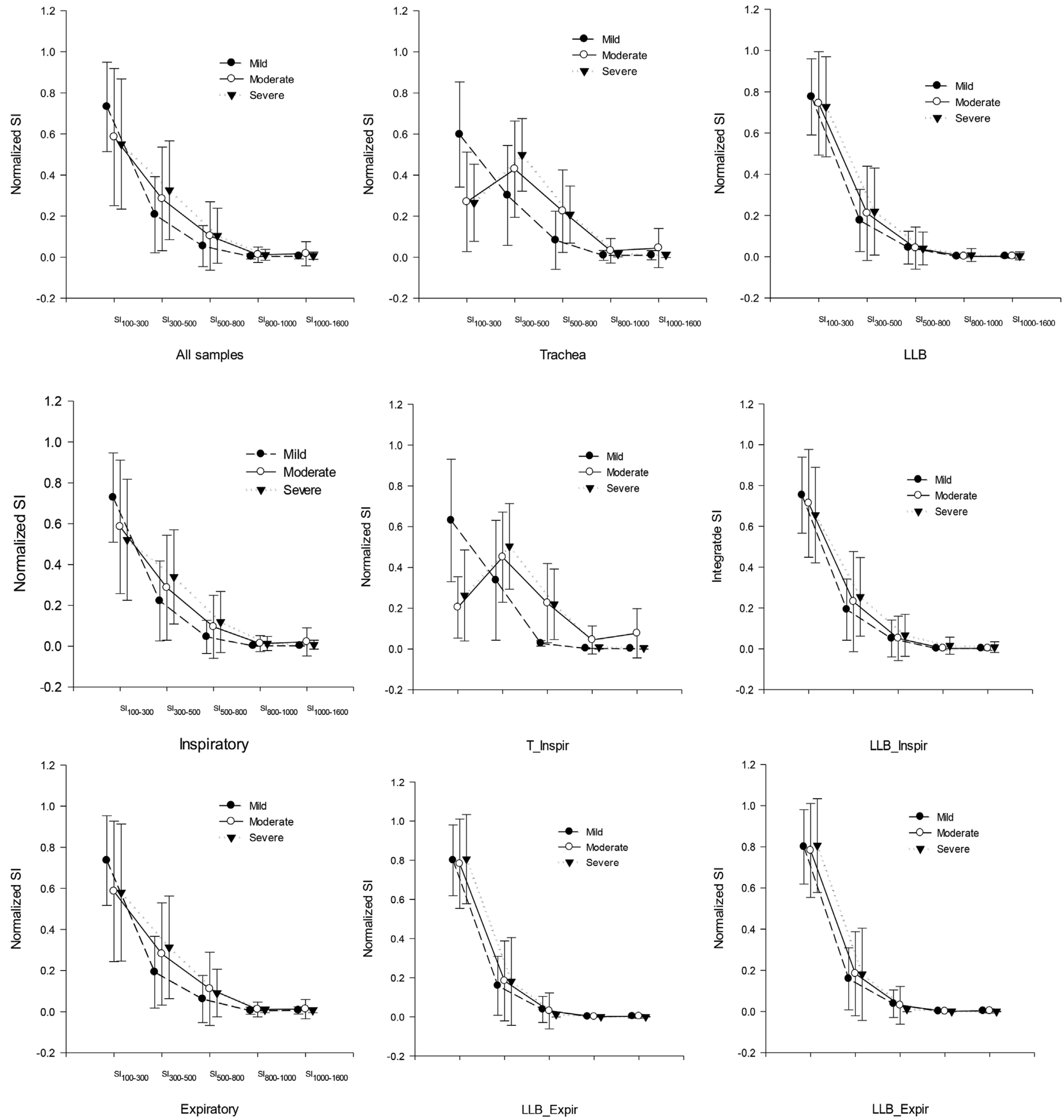

Fig. 3. μ(SD) values of $SI_{100\text{-}300}$, $SI_{300\text{-}500}$, $SI_{500\text{-}800}$, $SI_{800\text{-}1000}$ and $SI_{1000\text{-}1600}$ features for the mild, moderate and severe asthma patients in the nine groups.

combined effects of five features (MANOVA) and the corresponding post hoc test results. The values revealed that the combined feature vector exhibited statistical significance for all the sample groups ($p < 0.05$, $\eta_\Lambda{}^2 = 0.044$–0.523). All the comparisons of the investigated groups yielded a higher effect size for the trachea related groups ($p < 0.05$, $\eta_\Lambda{}^2 = 0.257$–0.523) than for the LLB related groups ($p < 0.05$, $\eta_\Lambda{}^2 = 0.044$–0.09). In addition, the features showed better discriminatory power in the inspiratory related groups ($p < 0.05$, $\eta_\Lambda{}^2 = 0.09$–0.523) than in the expiratory related groups ($p < 0.05$, $\eta_\Lambda{}^2 = 0.05$–0.257). The post hoc results revealed that the percentage of observations that were statistically significant between pairs of severity levels were as follows: *a* (78%), *b* (100%) and *c* (44%).

The classification results for the three classifiers using the nine groups as the input data is given in Table 4. The performance of the classifiers was evaluated using the SEN, SPE and PPV performance measures. In general, all the tested classifiers performed well – ENS (SEN = 78 ± 8%, SPE = 79 ± 9%, PPV = 79 ± 7%), KNN (SEN = 72 ± 13%, SPE = 72 ± 14%, PPV = 73 ± 10%) and SVM (SEN = 73 ± 11%, SPE = 74 ± 12%, PPV = 75 ± 8%).

In terms of location, the classifiers performed as follows in the trachea related groups – ENS (SEN = 86 ± 6%, SPE = 86 ± 9%, PPV = 87 ± 3%), KNN (SEN = 81 ± 14%, SPE = 81 ± 15%,

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

Group	$SI_{100\text{-}300}$	$SI_{300\text{-}500}$	$SI_{500\text{-}800}$	$SI_{800\text{-}1000}$	$SI_{1000\text{-}1600}$
All	**2.E^{-08}(0.046)^{a,b}**	**1.E^{-07}(0.041)^{a,b,c}**	**4.E^{-04}(0.02)^{b,c}**	**1.E^{-04}(0.02)^{b,c}**	**5.E^{-02}(0.01)^{c}**
Trachea	**2.E^{-12}(0.21)^{a,b}**	**2.E^{-07}(0.122)^{a,b,c}**	**5.E^{-11}(0.19)^{a,b}**	**1.E^{-07}(0.13)^{a,b}**	**1.E^{-04}(0.07)^{a,b}**
LLB	5.E^{-01}(0.002)	4.E^{-01}(0.003)	**1.E^{-02}(0.016)^{a,c}**	**2.E^{-08}(0.041)^{a,c}**	**7.E^{-09}(0.045)^{a,b}**
Inspiratory	**6.E^{-07}(0.074)^{a,b,c}**	**5.E^{-05}(0.052)^{b,c}**	**6.E^{-04}(0.038)^{b,c}**	**5.E^{-03}(0.028)^{b,c}**	2.E^{-01}(0.008)
Expiratory	**3.E^{-03}(0.03)^{a,b}**	**1.E^{-03}(0.033)^{a,b}**	2.E^{-01}(0.008)	3.E^{-03}(0.013)	7.E^{-02}(0.000)
T_Inspir	**6.E^{-06}(0.23)^{a,b}**	**3.E^{-02}(0.066)^{b}**	**6.E^{-09}(0.361)^{a,b}**	**1.E^{-05}(0.213)^{a,b,c}**	**3.E^{-06}(0.241)^{a,b,c}**
T_Expir	**2.E^{-07}(0.2)^{a,b}**	**1.E^{-06}(0.18)^{a,b,c}**	**3.E^{-04}(0.11)^{a,b}**	**1.E^{-06}(0.18)^{a,b,c}**	**3.E^{-02}(0.05)^{b}**
LLB_Inspir	**1.E^{-02}(0.033)^{b,c}**	**4.E^{-02}(0.23)^{b,c}**	**4.E^{-02}(0.023)^{c}**	**2.E^{-03}(0.05)^{a,c}**	**6.E^{-03}(0.04)^{a,c}**
LLB_Expir	4.E^{-01}(0.007)	6.E^{-01}(0.004)	**2.E^{-02}(0.032)^{a}**	**1.E^{-10}(0.1)^{a,b}**	**8.E^{-10}(0.1)^{a,b}**

**bold font indicates statistical significance, $p < 0.05$.*

Table 3
Summary of the MANOVA statistical analysis for the features in the various groups – p-value, η_{Λ}^{2} and details of the post hoc tests – a (mild and moderate), b (mild and severe), and c (moderate and severe).

Groups	Wilks' Lambda (Λ)	F	df	Error	p-value	Effect Size (η_{Λ}^{2})	Post Hoc
All	0.919	6.631	10	1536	**2.E^{-17}**	0.08	***a,b,c***
Trachea	0.67	11.1	10	500	**3.E^{-17}**	0.33	***a,b,c***
LLB	0.96	2.3	10	1024	**1.E^{-02}**	0.044	***b***
Inspiratory	0.877	5.09	10	752	**3.E^{-07}**	0.123	***a,b,c***
Expiratory	0.936	2.59	10	770	**4.E^{-03}**	0.064	***a,b***
T_Inspir	0.477	8.69	10	198	**5.E^{-12}**	0.523	***a,b,c***
T_Expir	0.74	4.6	10	288	**4.E^{-06}**	0.257	***a,b***
LLB_Inspir	0.91	2.62	10	540	**4.E^{-03}**	0.09	***a,b***
LLB_Expir	0.94	1.38	10	468	**4.E^{-02}**	0.05	***b***

**bold font indicates statistical significance, $p < 0.05$.*

PPV = 85 ± 4%) and SVM (SEN = 82 ± 10%, SPE = 82 ± 13%, PPV = 85 ± 4%). In contrast, if the LLB related groups were used the input data, the following performances were obtained – ENS (SEN = 73 ± 6%, SPE = 75 ± 7%, PPV = 74 ± 5%), KNN (SEN = 66 ± 8%, SPE = 68 ± 10%, PPV = 67 ± 3%) and SVM (SEN = 68 ± 9%, SPE = 70 ± 11%, PPV = 70 ± 5%).

The results were then analysed in terms of breathing phases, and the results showed that the classifiers exhibited the following performances in the inspiratory related groups – ENS (SEN = 77 ± 10%, SPE = 79 ± 11%, PPV = 79 ± 9%), KNN (SEN = 72 ± 15%, SPE = 73 ± 14%, PPV = 73 ± 13%) and SVM (SEN = 73 ± 12%, SPE = 75 ± 10%, PPV = 74 ± 10%). In contrast, the performances with the expiratory related groups were as follows ENS (SEN = 80 ± 7%, SPE = 80 ± 6%, PPV = 81 ± 5%), KNN (SEN = 72 ± 14%, SPE = 72 ± 15%, PPV = 75 ± 9%) and SVM (SEN = 75 ± 11%, SPE = 76 ± 12%, PPV = 78 ± 6%).

The analysis of the results in terms of the 9 individual groups revealed that T_Inspir exhibited better performance than all other groups – ENS (SEN = 88 ± 9%, SPE = 88 ± 12%, PPV = 89 ± 5%), KNN (SEN = 87 ± 13%, SPE = 87 ± 12%, PPV = 89 ± 6%) and SVM (SEN = 86 ± 9%, SPE = 86 ± 7%, PPV = 86 ± 4%).

Finally, from the point of view of severity levels, the behaviour of the classifiers were as follows: mild samples – ENS (SEN = 75 ± 9%, SPE = 86 ± 7%, PPV = 79 ± 8%), KNN (SEN = 63 ± 14%, SPE = 84 ± 10%, PPV = 74 ± 13%) and SVM (SEN = 66 ± 13%, SPE = 84 ± 8%, PPV = 75 ± 10%), moderate samples – ENS (SEN = 76 ± 6%, SPE = 79 ± 8%, PPV = 78 ± 7%), KNN (SEN = 71 ± 6%, SPE = 72 ± 11%, PPV = 72 ± 8%) and SVM (SEN = 73 ± 5%, SPE = 75 ± 8%, PPV = 74 ± 8%), and severe samples – ENS (SEN = 84 ± 7%, SPE = 71 ± 5%, PPV = 81 ± 6%), KNN (SEN = 81 ± 12%, SPE = 60 ± 9%, PPV = 74 ± 7%) and SVM (SEN = 81 ± 7%, SPE = 62 ± 9%, PPV = 75 ± 7%).

4. Discussion

SI features are dependent on the energy of breath sounds, which varies with changes in the obstruction severity. The airway thickness (wall area) changes in response to airway obstruction [47]. Similarly, a previous study [48] noted that high-pitch sounds are produced when the air calibre becomes narrow, which leads to the fluttering of airway walls and fluids and thus the production of wheeze sounds. These studies indicate that changes in lung airways inevitably cause changes in the frequency of breath sounds, which varies the velocity and energy of the breath sounds. This finding is particularly obvious in patients with severe asthma, who produce wheezes that are louder than the underlying breath sounds and can be clearly heard through the patient's open mouth. The findings obtained in this study agree with those obtained in previous studies [24,47,48], which revealed that obstructions in lung airways affects the frequencies of breath sounds from which wheezes manifest.

Breath sound analysis has potential to be used for the non-invasive detection of the asthma severity level of adults. Importantly, breath sounds are affected by the flow rate of breaths. New breath sound parameters are not affected by the air flow rate, and these will be of considerable clinical utility [49]. Furthermore, selection of the spectral band is based on the natural resonance generated by lung organs. A study conducted in 1991 investigated the spectral characteristics of the upper and central airway using plastic pipers of varying length [50]. The study predicted that the natural resonance of shorter tubes was higher than that of longer tubes. A tube length of 8 cm creased the highest natural resonance of 1031 Hz consecutive harmonics at 5155 and 3093 Hz, whereas a 16 cm tube had resonances of 516, 2580 and 3612 Hz, and a 32 cm tube had a natural resonance of 258 Hz with successive higher resonances at 774 and 1290 Hz, etc. These findings led some researchers [8] to select the spectral bands 100–300, 300–500, 500–800 and 800–1000 for the detection of wheeze sounds. Another study used the bands 0–250, 250–500 and 500–1000 for wheeze detection [51]. However, in this study, the frequency band 100–1600 and the sub-bands 100–300, 300–500, 500–800, 800–1000 and 1000–1600 were selected for the analysis.

The findings related to μ(SD) values (Fig. 3) do not indicate any specific and consistent trend with respect to asthma severity levels. However, significant differences ($p < 0.05$) between severity levels were observed for all features in most of the groups. These findings concur with the findings of a previous study [52], which indicated that wheeze sound spectra do not follow any specific pattern with respect to the asthma severity level but can be used for the detection of airway obstruction. The graphs further provide an indication of the variations in the distribution of energy in the signal according to the asthma severity level, phase and location.

Some recent literature reviews [1–5] concluded that most studies have classified breath sounds into two classes, namely, normal and abnormal, using different features and classification techniques. Our

Table 4
Performance of the three classifiers with the nine groups as input data using a leave one out subject cross validation technique.

Groups	Classes	ENS			KNN			SVM		
		SEN (%)	SPE(%)	PPV(%)	SEN(%)	SPE(%)	PPV(%)	SEN(%)	SPE(%)	PPV(%)
All	Mild	69	82	73	50	83	68	61	79	67
	Moderate	74	74	74	70	66	67	68	70	69
	Severe	82	69	79	80	51	71	78	58	73
Trachea	Mild	83	93	85	74	91	82	80	95	88
	Moderate	80	89	88	71	85	83	76	86	84
	Severe	92	72	85	93	61	81	86	60	76
LLB	Mild	69	78	73	61	75	66	51	81	71
	Moderate	73	72	72	69	69	68	66	65	64
	Severe	79	70	77	73	59	69	76	47	64
Inspiratory	Mild	68	83	75	53	75	60	59	76	64
	Moderate	73	71	72	69	62	65	68	65	67
	Severe	81	68	78	72	56	70	78	63	75
Expiratory	Mild	72	83	74	55	89	71	59	84	73
	Moderate	79	82	82	74	66	69	74	74	74
	Severe	86	72	82	84	57	69	82	58	74
T_Inspir	Mild	93	98	95	95	97	95	95	92	85
	Moderate	78	91	85	72	91	84	77	88	82
	Severe	93	75	87	94	73	87	87	79	90
T_Expir	Mild	81	93	85	54	99	94	64	96	88
	Moderate	85	81	84	81	72	82	80	78	85
	Severe	89	81	88	95	60	81	95	66	83
LLB_Inspir	Mild	73	86	79	58	74	63	58	73	62
	Moderate	65	70	67	76	57	62	67	71	68
	Severe	70	65	69	57	76	72	71	67	70
LLB_Expir	Mild	69	79	74	64	76	69	67	83	76
	Moderate	76	81	79	61	76	69	78	80	77
	Severe	85	71	80	78	51	67	80	62	74

*Sensitivity (SEN) is defined as the probability at which class 1 is correctly classified as class 1 = TP/(TP + FN). Specificity (SPE) is defined as the probability at which classes other than class 1 are correctly classified respective to their class = TN/(TN + FP). Positive predictive values (PPV) is defined as the ratio of true detection of classes to the total number of subjects = (TP + TN)/(TP + TN + FP + FN) where, TP = true positive, TN = true negative, FN = false negative, FP = false positive.

study further classified wheeze sounds into classes according to the severity level (mild, moderate and severe) of asthma patients using SI features. This study differs from previous investigations that used a large number of features to classify lung sounds as either normal or wheeze sounds [9,10,40] because this study only used five features to achieve the satisfactory classification of wheeze sounds according to asthma severity levels. To this effect, although previous studies selected bands from a lower frequency range to a maximum of 800 or 1000 Hz [15,40,17], our study selected a higher band (100–1600) for the analysis and found satisfactory results with the 1000–1600 Hz band. In fact, six of the nine groups showed significant results for $SI_{1000\text{-}1600}$. The MANOVA performed in this study indicated that the combined SI feature vector improved the discriminatory power among the severity levels in most of the groups. Furthermore, we found that the combined feature vector showed statistical significance for all the groups, yielded improved values of η_{Λ}^2 and resulted in a higher percentage of significant findings from post hoc tests. Taken together, these findings provide the sufficient and necessary background information for the interpretation of the results from a physiological point of view.

Previous studies have investigated the correlation of lung function values with respiratory sounds using data collected only from the trachea [18–20,25]. Another study collected data from the trachea and LLB but found that only the mean frequency from the trachea was correlated to lung function values [23]. However, auscultation at the trachea is not practised by physicians because it does not provide information regarding the location of the obstruction. Thus, one of the major obstacles in respiratory sound analysis is the challenge of auscultation at the LLB. In infants, LLB sounds are louder and clearer because the chest wall of infants is thinner than that of adults [53]. A study on paediatric patients analysed LLB sounds with respect to the correlation of lung function values with inspiratory and expiratory peak frequency features. The results only revealed a significant difference in the LLB_Inspir samples [54]. However, in our study, even though the LLB sounds were recorded from adults with thicker chest walls, the SI features obtained from sounds recorded at the LLB location were able to discriminate various levels of asthma severity, regardless of the phase.

This work also investigated the correlation of wheeze sounds obtained from two auscultation locations, namely, the trachea and LLB, to severity levels. Both the univariate and multivariate analysis revealed that the SI features were statistically significant ($p < 0.05$) in the trachea related groups with a large effect size (η_{χ}^2, η_{Λ}^2). This finding could be attributed to the difference in the mean values observed in the trachea and LLB related groups, as shown in Fig. 3. These findings indicate that tracheal wheeze sounds are more sensitive and specific predictors of airway obstruction, which is similar to the findings obtained in a previous study [23,52]. This result could be due to the physiology of the LLB, which behaves as a stronger filter. Previous studies [36,55] also found that the trachea is a better location for recording wheeze sounds, even though it does not allow physical identification of the pathological location. Other researchers [35,36,56] also concluded that the respiratory sounds from various auscultation locations of the body show different behaviours. Taken together, these results provide evidence that sounds from the trachea and LLB have different characteristics.

The correlation between severity levels and SI features was also investigated within different breath phases. The results of most of the univariate analyses and MANOVAs indicated that the inspiratory related groups exhibited better discrimination ($p < 0.05$) than the expiratory related groups. For example, although the univariate analysis obtained similar behaviour for the T_Inspir and T_Expir groups, LLB_Inspir performed better than LLB_Expir. A similar finding was also obtained from the multivariate analysis: all that inspiratory related groups exhibited a better effect size (η_Λ^2) than the expiratory related groups. The findings of our study concur with those obtained in another study [54], which found that LLB_Inspir exhibits better performance than LLB_Expir in correlating lung function values with peak frequency features. However, care should be exercised when interpreting these results because inspiratory and expiratory wheeze sounds are considered to be almost equally informative for characterizing asthma severity levels [52]. These results provide evidence that tidal breathing in normal subjects produces inspiratory and expiratory sounds in the trachea hat exhibit almost equal intensity, whereas at the LLB, inspiratory sounds are louder than expiratory sounds [36,56]. This finding demonstrates that sounds obtained during the inspiratory and expiratory phases exhibit different behaviour [16,17,56], which could be due to variations in the physiology of the airway passage (i.e., short and long airways) experienced by the airflow during the inspiratory and expiratory phases at different locations [36].

The overall comparison of the classifier results with respect to location indicated that the trachea related groups performed better than the LLB related groups. A similar behaviour was noted in the results of a previous study [40] that collected data from four different locations for wheeze and normal sound classification, analysed the data using combinations of different locations, and concluded that the classifier performance was dependent on the location. In terms of phase, the classification results obtained in our study point to the previous conclusion that although the inspiratory and expiratory related groups behave differently because they are equally informative, the performance of the classifiers was almost similar.

The overall comparison of the three classifiers indicated that every type of input yielded better-than-average results. However, a detailed comparison revealed that the ENS classifier obtained improved results in seven of the nine investigated groups. The reason for this subtle dominance of the ENS could be its working principle, which combines multiple learners to obtain a better classification performance. This finding is no novel. Another study [14] previously implemented the KNN, SVM, naïve Bayes, decision tree and ENS classifiers for the classification of normal, wheeze and crackles and found that the highest performance was obtained with the ENS classifier. In contrast, other studies [9–11,13] indicated that the SVM classifier showed the best performance, but these studies did not investigate the ENS classifier. In addition, in all these aforementioned works, SI features were not implemented for the classification of wheeze sounds according to severity levels of asthma patients.

The classification results of this study were compared with those obtained using methods described in the literature, including 7^{th}-order wavelet transform [57] (2 class – normal and abnormal sounds) and 6^{th}-order AR [9] (2 class – normal and wheeze sounds). In these studies, the selected numbers of features for wavelet transform and AR were 19 and 7, respectively, which are definitely higher than the SI features investigated in our work. Interestingly, even though the present study included a reduced feature vector size, the comparison results showed that the SI features performed better than wavelet transform and AR. The overall comparison of all the groups indicated the following improvements in classifier performance measures; SI vs. Wavelet transform – ENS (ΔSEN = 17 ± 8%, ΔSPE = 16 ± 9%, ΔPPV = 16 ± 6%), KNN (ΔSEN = 13 ± 12%, ΔSPE = 13 ± 13%, ΔPPV = 15 ± 8%) and SVM (ΔSEN = 16 ± 15%, ΔSPE = 16 ± 16%, ΔPPV = 17 ± 6%); and SI vs. AR – ENS (ΔSEN = 7 ± 8%, ΔSPE = 8 ± 8%, ΔPPV = 8 ± 4%), KNN (ΔSEN = 2 ± 10%, ΔSPE = 3 ± 10%, ΔPPV = 4 ± 7%) and SVM (ΔSEN = 5 ± 10%, ΔSPE = 6 ± 12%, ΔPPV = 6 ± 6%). Because these methods also rely on the selection of frequency bands to obtain the features, the comparisons results indicated that the set of bands selected in our work appear to be more suitable for the classification and identification of asthma severity levels.

5. Conclusion

This study reveals that classification of asthmatic subjects during tidal breathing as mild, moderate and severe can be performed using SI features. The findings also illustrate that the distribution of spectral energy in the recorded signals varies depending on the auscultation location (trachea and LLB), phase (inspiratory and expiratory) and severity levels (mild, moderate and severe). The results also show that the μ(SD) of the SI values in the wheeze sound spectra does not follow any specific and consistent pattern with respect to severity level, but this behaviour nevertheless exhibits significant differences among the mild, moderate and severe asthmatic patients. The statistical and classification results obtained with the SI features indicate that tracheal wheeze sounds are more sensitive and specific predictors of airway obstruction. In addition, the Phase related observations indicated that the SI features obtained during the inspiratory and expiratory phases are equally informative for the identification of severity levels. The performance measures of the SVM, KNN and ENS classifiers produced better-than-average results in the classification of wheeze sounds according to severity levels. Nevertheless, the ENS classifier showed better classification performance in most of the investigated groups, although the best performance was obtained with the T_Inspir group. Among the tested classifiers, the best PPV obtained for the mild, moderate and severe classifications were 95% (ENS), 88% (ENS) and 90% (SVM) respectively. Regardless, our findings reveal that the approach does not appropriately address the LLB related groups, and thus, future work should focus on achieving a better representation of the frequency and phase responses using the adopted methods.

Conflicts 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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