Title:

Infection Detection in Cystic Fibrosis Patients based on Tunable Q-factor Wavelet Transform of Respiratory Sound Signal and Ensemble Decision

Arezoo Karimizadeh\textsuperscript{a}, Mansour Vali\textsuperscript{b*}, Mohammadreza. Modaresi\textsuperscript{c,*}

\textsuperscript{a}Department of Biomedical Engineering, K. N. Toosi University of Technology, Tehran, Iran, Email: a.karimizadeh@ee.kntu.ac.ir
\textsuperscript{b}Department of Biomedical Engineering, K. N. Toosi University of Technology, Tehran, Iran, Email: mansour.vali@eetd.kntu.ac.ir
\textsuperscript{c}Pediatric Respiratory and Sleep Medicine Research Center, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran. Email: mr-modaresi@sina.tums.ac.ir

Corresponding Author:

Mansour Vali

Address: Faculty of Electrical Engineering, K.N. Toosi University of Technology, Seyed-Khandan Bridge, Shariati Ave., Tehran, Iran.

Postal Code: 16315-1355

Tel: +98(21)8406-2405

Mobile: +98-912-5215-783
Abstract

Most adult Cystic Fibrosis (CF) patients frequently suffer from *Pseudomonas aeruginosa* (PA) infection, which is strongly associated with inflammation, lung destruction, and increased mortality. Diagnosis of PA infection in the primary stage is essential to initiate the treatment and reduce the risk of chronic infection. Sputum culture is the gold standard for infection detection, but it is time-consuming. The objective of this study was to suggest and examine a method to decide about PA infection status in CF patients based only on their respiratory sound. Respiratory sounds were recorded from 36 CF patients. Some features which were generated from Tunable Q-factor wavelet transform (TQWT) components, were investigated. The features were fed into Support Vector Machine and also Ensemble classifier. The proposed method achieved an accuracy of 90.3% in identifying PA infection in CF patients. Furthermore, the probability of categorizing respiratory sounds as PA CF decreased significantly after the treatment of PA infection (P-value < 0.003). Moreover, the method had a satisfactory performance in the presence of noises and artifacts. The developed method represents a novel approach to the diagnosis of PA infection in CF patients based only on respiratory sound signals, which is a necessary and innovative approach for early diagnosis of PA infection.

Keywords: Cystic Fibrosis; Respiratory Sound; Tunable Q-factor wavelet transform; Support Vector Machine; Ensemble classifier
1. Introduction

Cystic Fibrosis (CF) is the most common autosomal recessive disorder in white skinned individuals that affects such organs as the lungs and pancreas. Chronic lung infections, the hallmark of CF, are the principal cause of morbidity and mortality in CF patients. Thick and sticky lung mucus is the common respiratory sign of CF. Infections of the lungs resulting in pulmonary symptoms and pulmonary exacerbation in CF [1, 2]. Infections are the key parameters considered by physicians to initiate appropriate preventive and therapeutic strategies [1].

Approximately 60–75% of adult CF patients frequently suffer from Pseudomonas aeruginosa (PA) infections[1]. The PA infection is strongly associated with inflammation, lung destruction[2], and an increased risk of mortality[3-5]. Early detection of PA is essential to initiate appropriate therapy and reduce the risk of chronic infection [6]. During the early stages, PA can be treated using inhaled or oral antibiotics (instead of intravenous antibiotics). Nevertheless, the treatment procedure must be monitored to assess its effectiveness. To diagnose infections and evaluate the treatment efficiency, airway cell culture is generally recommended once every 3 months in a stable state and with the occurrence of acute pulmonary exacerbation [7]. Although the sputum culture result is the gold standard for the detection of infection, it is time-consuming hence a real-time diagnostic method can facilitate early initiation of eradication therapy.

Evaluation of the lung sounds, which are produced during the transition of air through the respiratory tract, is a non-invasive method for investigating lung status [8]. Pulmonary diseases can alter the airways and cause variations in respiratory sounds. Identifying and categorizing information about the time and frequency of lung sounds for the diagnosis of disease and evaluation during disease follow up, are
challenging without the use of computerized analysis. Recently, computerized respiratory sound analysis has been reported as a beneficial diagnostic tool to identify lung abnormalities and disorders [9-14]. Many CF patients experience an exacerbation in the presence of PA infection. Decreased lung function, increased cough, increased sputum, and increased adventitial lung sounds are indicators of exacerbation. Even though there are evidences that infection can alter the airways by increasing mucus and sputum, few studies have investigated whether respiratory sounds are affected by infections[15-17]. Previous studies have only focused on the relations between adventitious lung sounds such as wheeze, crackles, or cough sounds, and respiratory infections[15, 17]. However, a study has investigated lung sounds originated from lungs infected by Tuberculosis to discriminate healthy subjects from Tuberculosis patients[16].

There are few studies that investigated relations between adventitious lung sounds and infection. In [15], cough sounds were analyzed to identify respiratory infection in pigs. In another study, wheeze lung sounds were detected to diagnose and monitor lower respiratory tract infection[17]. The role of respiratory physiotherapy was examined in lower respiratory tract infections in another study, which caused a significant reduction in wheeze rates and less sputum after respiratory physiotherapy[18]. In the literature, there are several uses of respiratory sound frequency analysis [19, 20] and time-frequency analysis (specially Wavelet Transform) in the automatic diagnosis of adventitious respiratory sounds [8]. Rational-dilation wavelet transform (RADWT) [21] and Tunable Q-factor wavelet transform (TQWT) [22] are kinds of wavelet transform that describe a signal as an optimum time-frequency representation by choosing an appropriate Q-factor [22]. It was shown in [23] that these features resulted in a better accuracy in comparison with Discrete Wavelet Transform, PSD, MFCC and some other features in the diagnosis of adventitious respiratory sounds. In RADWT, the Q-factor is adjusted with the combined action of three parameters, but in TQWT, it is specified directly [24]. Recently, high Q-factor and low
Q-factor features have been used in the diagnosis of adventitious respiratory sounds [23]. Altogether, these studies on the diagnosis of adventitious respiratory sounds, though not directly relevant to this study, may lead us to a hypothesis; the features extracted from the mentioned techniques may be capable of diagnosing a sound beyond the human auditory judgment which is consistent with infection in CF patients.

Structural airway alterations may modify lung sounds by increasing mucus and sputum; Which can be used to discriminate Normal CF from PA CF patients’ lung sounds. Recent studies have demonstrated that respiratory sounds are affected by sputum conditions [25-27]. Four distinct research works have been carried out to examine the sputum condition using respiratory sounds; The first research utilized a frequency domain feature to examine the effect of increased sputum on respiratory sounds [28]. For this purpose, sound samples of three patients were used to detect sputum increasing by an accuracy of 85-97%. Two other works examined time-frequency features [25], and discrete wavelet transform features [27] to diagnose sputum accumulation in the trachea. Using sound samples of 12 patients, they achieved an accuracies of 83.5% and 84.5% employing time-frequency features and discrete wavelet transform features, respectively. Recently, another work has utilized sound samples of 14 patients to evaluate features based upon Empirical Mode Decomposition (EMD) and achieved an accuracy of 92.02% in the diagnosis of sputum condition [26]. All of these studies, however, depicted the effectiveness of time-frequency features and features from basic oscillatory portions of signal (EMD of the signal) to diagnose sputum conditions.

Mucus clusters vibrate due to air transition produced by respiration. It was mentioned in [25] that the vibration in time-frequency representation of respiratory sound signals might be created by small oscillations in the signal. Therefore, TQWT analysis can be used to obtain optimal resonance-based respiratory sound signal decomposition to detect these oscillations.
This study was done in the CF center of the children hospital; thus, the participants were only CF patients. The diagnosis of CF for the participants were confirmed based on sweet test and/or genetic test. The gold standard method for the detection of PA infection in CF patients is time-consuming (several days) hence a real-time diagnostic method can assist early initiation of eradication therapy. So far, there has been no attempt to detect PA infection in CF patients using respiratory sounds. The proposed study is, therefore, an attempt to address this issue with the aim of detecting PA infection in CF patient by analyzing only one cycle of respiratory sound instead of detecting adventitious lung sounds. For this purpose, a number of features extracted from TQWT components of respiratory sounds were evaluated in identifying PA infection in CF patients.

2. Material and Methods

The overall structure of the proposed method is illustrated in Figure 1.

After describing data acquisition part, each step in Figure 1 was described in detail.

2.1. Data acquisition

Respiratory sounds were acquired from 25 CF patients (11 females, 14 males) whom were followed-up at the Pediatric Respiratory and Sleep Medicine Research Center of Children's Medical Center. The diagnosis of CF for the participants was confirmed based on sweet test and/or genetic test. Patients were selected based on their sputum microbiology cultures according to the following category: 11 patients with normal flora culture results and 14 patients with PA infection (in this paper, ‘Normal CF subjects’ and ‘PA CF subjects’ will be used to refer to normal flora CF subjects and CF subjects with PA infection, respectively). Also, respiratory sounds of 11 patients were recorded one month after antibiotic treatment,
and they were used to investigate the effectiveness of the proposed method. Demographic data of the patients are depicted in Table 1. All procedures performed in studies involving human participants were approved (IR.TUMS.CHMC.REC.1398.094) by the ethics committee of Children’s Medical Center-Tehran University of Medical Sciences.

Table 1

Respiratory sounds were recorded with a Littman 3200 digital stethoscope in the extended mode from 20 to 2000 Hz with a sampling frequency of 4000 Hz. Sound acquisition was performed from two anatomical regions of the lungs; posterior upper right and left. Over two normal respiratory sound cycles were recorded from each volunteer in sitting position. Informed consent was obtained from all patients or their parents in case of under ages prior to respiratory sound recording.

2.2. Preprocessing

As shown in Figure 1, the first step is preprocessing, which includes noise and artifact removal and respiratory cycle separation. Recorded sounds were contaminated with the cardiac sound artifact, speaking and coughing noises, and digital stethoscope movement noise. The dominant frequency of heart sound is lower than 150 Hz [29]. To remove the cardiac sound effect, band-pass filtering was applied to the recorded respiratory sounds in the frequency range of 150-1800 Hz. Respiratory sound cycles damaged by speaking or coughing noises were excluded from the dataset. Digital stethoscope movement noises were high amplitude spikes with very low lengths which were removed from the signals based on the method in [30].

The recorded signals had good quality. Three reviewers listened to the recorded sounds, independently. All respiratory sound samples were listened precisely. Their spectrograms were investigated as well. Samples that contained speaking noises and special lines related to the speaking in their spectrogram
were omitted from the study. From 157 available respiratory sound samples, 21 samples were contaminated with noises and omitted from the study. Finally, 136 remaining sound samples were used for the study. Totally, 47, 67 and 22 respiratory sound cycles were achieved from normal CF, PA CF patients and PA CF patients after the treatment, respectively. Then, inspiration and expiration sound segments were separated from respiratory sound cycles manually.

The proposed method used preprocessed respiratory sound signals. However, noisy respiratory sound signals were utilized to evaluate the proposed method in the presence of noises and artifacts.

2.3. Feature extraction

The proposed feature extraction method includes the decomposition of respiratory sound signals into their TQWT components and the calculation of statistical parameters from the obtained components (Fig. 1). In TQWT analysis, a two-channel filter bank is applied to a signal and then the scaled version of the filter bank is iteratively applied to its low-pass parts. It is assumed that \( \alpha \) and \( \beta \) are scaling parameters of low-pass \( H_0(\omega) \) and high-pass \( H_1(\omega) \) filters, respectively, and \( 0 \leq j \leq J \) is the index of decomposition level for a J level TQWT transform.

\[
\begin{align*}
H_0(\omega) &= 1 & |\omega| &\leq (1-\beta)\pi, \\
H_0(\omega) &= 0 & \alpha\pi &\leq |\omega| \leq \pi, \\
H_1(\omega) &= 0 & |\omega| &\leq (1-\beta)\pi, \\
H_1(\omega) &= 1 & \alpha\pi &\leq |\omega| \leq \pi.
\end{align*}
\]

By analysing the cascade of several filters and scalings, the equivalent frequency response for \( \alpha \leq 1 \) and \( \beta \leq 1 \) in level \( j \) of decomposition can be calculated as \( H_1^{(j)}(\omega) \) from Equation (5)[22].
\[ H_1^{(j)}(\omega) = \begin{cases} H_1 \left( \frac{\omega}{\alpha^{j-1}} \right) \prod_{m=0}^{j-2} H_0 \left( \frac{\omega}{\alpha^m} \right), & \text{if } \alpha^{j-1} \pi \leq |\omega| \leq \alpha^{j-1} \pi, \\ 0, & \text{for other } \omega, [-\pi, \pi] \end{cases} \]  \tag{5}

where \( H_0^{(j)}(\omega) \) is calculated from equation (6).

\[ H_0^{(j)}(\omega) = \begin{cases} \prod_{m=0}^{j-1} H_0 \left( \frac{\omega}{\alpha^m} \right), & \alpha^j \pi < |\omega| \leq \pi, \\ 0, & |\omega| \leq \alpha^j \pi \end{cases} \]  \tag{6}

The major parameters in TQWT are included as Q-factor (Q), redundancy (r) and number of decomposition levels (J).

Q-factor is the ratio of center frequency to bandwidth of a band-pass filter. It is a measure of number of oscillations in wavelet. Equation (7) reveals the relation between Q and \( \beta \) parameters.

\[ Q = \frac{\omega_c}{BW} = 2 - \frac{\beta}{\beta}. \]  \tag{7}

Redundancy is the total number of wavelet coefficients divided by the length of the signal. The relation between r and filter parameters \( \alpha \) and \( \beta \) is revealed in Equation (8).

\[ r = \frac{\beta}{1 - \alpha}. \]  \tag{8}

A signal can be decomposed into a collection of high Q-factor and/or low Q-factor components; the number of components is J+1.

The presence of mucus in the lung and airways due to PA infection can alter the airway structure in CF patients, subsequently causing changes in air transition and lung sounds. If any mucus is stored in a patient's airway, mucus clusters may vibrate due to air transition produced by respiration. These vibrations may create small oscillations in special parts of respiratory sound, as mentioned in [25]. Visual
evaluation of recorded respiratory sounds showed that some, but not all, of the PA infected lung had these signs. Therefore, TQWT analysis was used to obtain an appropriate resonance-based respiratory sound signal decomposition by selecting appropriate Q-factor to detect changes related to PA infection in CF patients. Hence, differences between components of respiratory sounds (which were obtained from TQWT analysis) were investigated in Normal CF and PA CF patients. In this study, both high and low Q-factor components of respiratory sounds were evaluated in the detection of PA infection. However, it can be expected that high Q-factor components of respiratory sounds have better performance than low Q-factor components in distinguishing oscillations related to infection in respiratory sounds as a result of better frequency selectivity of high Q-factor wavelet bases. The redundancy factor r controls overlapping rate between sub band frequency responses of adjacent wavelets in the TQWT method. It is often recommended to be equal to or greater than 3 in order to well localize the analysis/synthesis functions (wavelets) [24, 31]. Frequency responses of adjacent wavelets were investigated using different r values. The r was set to 3 based on some trials and for keeping a kind of balance in overlapping between wavelets of successive frequency bands. Q-factor describes the degree of resonance in a signal and affects the oscillatory behavior of the wavelet meaning that it is a measure of the number of oscillations exhibited by the wavelet. Therefore, Q-factor, which describes the degree of resonance in a signal, should be selected according to the signal type. In this study, Q-factors were selected around the values used in the previous study on adventitious respiratory sounds using high Q-factor and low Q-factor around 6 and around 2 [23]. Then, high and low Q-factor values were obtained around these values by some trial and error. Parameter J was selected based on respiratory sound signal energy distribution in different subbands. J was selected by increasing the level of decomposition until energy of the last subband was approximately less than 1 percent of the total signal energy.
Decomposition of respiratory sound cycles into high Q-factor components was done by parameters of $Q = 8$, $r = 3$ and $J = 40$ and for low Q-factor components by parameters of $Q = 1$, $r = 3$ and $J = 9$.

Energy distributions of 41 high Q-factor components of respiratory sounds in two groups of Normal CF and PA CF subjects are shown in Figure 2. They are also shown for 10 low Q-factor components in Figure 3. As it can be seen, there are some differences between energy distributions of high and low Q-factor components of Normal CF and PA CF subjects’ respiratory sounds in inspiration/expiration.

After decomposing respiratory sound signals into high and low Q-factor components, some statistical parameters were considered in order to create feature vectors from the extracted components and feed them to classifiers (Figure 1).

These parameters were maximum, minimum, mean, standard deviation, entropy and energy which were calculated as Equation (9)-(14):

$$\max(Mx_i) = \max(S_{ki}) \text{ for } k = 1, \ldots, N_i, \quad (9)$$

$$\min(Mn_i) = \min(S_{ki}) \text{ for } k = 1, \ldots, N_i, \quad (10)$$

$$\text{Mean} \left( \mu_i \right) = \frac{\sum_{k=1}^{N_i} S_{ki}}{N_i}, \quad (11)$$

$$\text{Std} \left( \sigma_i \right) = \sqrt{\frac{\sum_{k=1}^{N_i} (S_{ki} - \mu_i)^2}{N_i}}, \quad (12)$$

$$\text{Entropy} \left( \text{Ent}_i \right) = -\sum_{k=1}^{N_i} S_{ki} \ln S_{ki}, \quad (13)$$

$$\text{Energy} \left( \text{En}_i \right) = \frac{1}{N_i} \sum_{k=1}^{N_i} |S_{ki}|^2 \quad (14)$$
where ‘$S_{ki}$’ is the $i$th Q-factor component with the length of $N_i$ and $k$ is the index of samples in each component.

High Q-factor components No. 34-41 and low Q-factor components No. 7-10 contained negligible information after filtering respiratory signals in preprocessing step. Therefore, statistical parameters were calculated from high Q-factor components No. 2-33 (32 components) and low Q-factor components No. 1-6 (6 components).

In this step, 32 high Q-factor components were obtained from inspiration/expiration sounds. One feature vector was created as $FV_q (q = 1-32)$ for high Q-factor components of inspiration sound, where $q$ is the number of components.

$\begin{align*}
FV_q &= \begin{bmatrix}
Mx_q \\
Mn_q \\
\mu_q \\
\sigma_q \\
Ent_q \\
En_q
\end{bmatrix}.
\end{align*}$

In the same way, $FV_q$ was created for low Q-factor components of inspiration/expiration sounds ($q=1-6$).

As shown in Figure 1, seven feature sets were generated as a single feature vector or a combination of different feature vectors as below:

1. High Q-factor features extracted from inspiration sound signals (HQ-insp)
2. High Q-factor features extracted from expiration sound signals (HQ-exp)
3. Low Q-factor features extracted from inspiration sound signals (LQ-insp)
4. Low Q-factor features extracted from expiration sound signals (LQ-exp)
5. High Q-factor and low Q-factor features extracted from inspiration sound signals (HQ-insp & LQ-insp)

6. High Q-factor and low Q-factor features extracted from expiration sound signals (HQ-exp & LQ-exp)

7. High Q-factor and low Q-factor features extracted from inspiration and expiration sound signals together (HQ-insp & LQ-insp & HQ-exp & LQ-exp)

2.4. Feature selection

In order to reduce the number of features, a feature selection algorithm was implemented based on Genetic Algorithm (GA). GA selected the best group of features by searching possible feature combinations. It is a kind of evolutionary algorithms[32] and basic steps of the implemented algorithm can be described as below:

- Generating random initial population of chromosomes. The chromosome length was considered equal to the total number of features. Chromosome bits denoted whether or not the features were selected by assigning 1 or 0 to them, respectively.

- Computing fitness for each chromosome using a defined cost function. GA cost function was proposed based on the classifier results. It also contained a term to control the number of features. More details are represented in Equation (16) in the results section.

- Selecting the best chromosomes based on the fitness (a larger fitness value corresponds to a better or lower cost) selection can be done using different methods such as stochastic uniform selection, Roulette wheel selection, etc., the latter of which was used in this study.

- Applying crossover (single point, two points, and uniform crossovers) to chromosomes, of which two points crossover was used here. In this method, parent chromosomes are split into three
fragments using two selected random points. Then, produced fragments are recombined to create new chromosomes.

- Applying mutation operators to individuals. Random bits of chromosomes were selected in the mutation. Then, new chromosomes were created by inverting selected bits (1 changed into 0 and vice versa).
- Keeping the best individual that was found for the next generation.
- Repeating crossover, mutation and selection until a stopping condition is met.

By implementing the GA algorithm, the best collection of the features was selected from a subset of possible combinations of features in a feature set.

2.5. Classification

After selecting appropriate features from each feature set, the final feature vectors were normalized in the range of [0, 1] to make an efficient classification. Then, normalized feature vectors were fed to classifiers. At first, a SVM classifier was examined to discriminate PA CF patients’ respiratory sounds from Normal CF ones. Then an Ensemble decision was proposed based on the majority voting of the class labels given by three SVM classifiers applied to three feature groups. Features were fed to classifiers by applying ‘leave-one-out’ cross-validation method to subjects meaning that the classifier was trained on all features except those of one subject. Then, remaining features were used for test to decide about the existence of PA infection based only on one respiratory cycle. This step was repeated for all the other subjects.

2.5.1. Support Vector Machine
Support Vector Machine (SVM) finds an optimal hyperplane between samples of two classes that are linearly separable (or can be separated linearly by moving to another space using a kernel function)[33].

Assume that \( x_d \) is the \( d \) th sample and \( y_d \) is its label (\( d \) is the index of samples); SVM tries to minimize

\[
L = \frac{1}{2} \sum_{d=1}^{K} a_d y_d (\bar{w} x_d + b) + \sum_{d=1}^{K} a_d .
\]

(Equation (16)) with respect to \( \bar{w} \) and \( b \), where \( a_d \geq 0 \), \( d=1, \ldots, K \) are Lagrange coefficients.

By computing \( \bar{w} \) and \( b \), optimum hyperplane will be obtained[34].

In this study, a nonlinear SVM classifier with Radial Basis (Gaussian) function kernel with radius 1 was used. Sequential Minimal Optimization (SMO) was used to find the separating hyperplane.

2.5.2. Ensemble classification:

An Ensemble classifier combines a number of simple classifiers to improve the performance of classification. This combination has been addressed by different names in the literature, including classifier fusion, the mixture of experts, dynamic classifier selection, divide-and-conquer classifiers, etc. [35]. The main reason for using Ensemble learning is to improve the generalization ability of classifier decisions.

In this study, results of applying three SVM classifiers to three feature groups were combined to decide the existence of PA infection in CF patients. Majority voting was used as a combination method, in which if more than one classifier identifies a subject as PA CF or Normal CF, the result will be categorized in that group.
3. Results

The proposed method was applied to the recorded lung sounds of CF patients with the purpose of finding appropriate feature sets to diagnose CF patients with PA infection. Seven feature sets were created and the best group of features was selected by applying GA to each feature set. GA parameters were selected as Roulette Wheel selection function, uniform mutation function, two points crossover function, and a generation number of 500. Cost function \( E \) was defined as Equation (17):

\[
E = \sqrt{(1 - Acc_1)^2 + (1 - Acc_2)^2} + 0.001 \times N_f,
\]

where \( Acc_1 \) and \( Acc_2 \) are respectively the sensitivity and specificity of PA infection detection after applying the SVM to a group of features and \( N_f \) is the number of features in that group. Some feature extraction methods assign a rank number to each feature. In those methods, a special number of features (a fix number) are selected based on their ranking from the best to the worst rank. In comparison with those methods, GA can automatically select an appropriate number of features. The constraint term in Equation (17) controls the number of selected features; this means that when two feature sets result in the same classification error, the one that has less number of features is given a lower \( E \) value. Some trial and error tests were performed to configure the GA for limiting the number of features. Then, a value of 0.001 was selected as the coefficient of the second term in Equation (17).

GA was implemented 30 times by assigning different values to crossover probability (0.6-0.8), mutation probability (0.05-0.1) and creating a different random initial population.

Figure 4 shows the percentage of selected features from each feature set No. 1 to 4 (HQ-insp, HQ-exp, LQ-insp and LQ-exp) in the feature set 5-7. GA was converged to the same kind of results using different initial populations (different or equal number of LQ and HQ features). It can be seen in the two top pies
that the percentage of selected HQ features are more than LQ features in both inspiration and expiration sounds. Therefore, they may be more effective than LQ features in the detection of PA infection. The button pie shows that HQ features are superior to LQ features, and HQ-expiration features are superior to HQ-inspiration features.

Figure 4

As mentioned before, GA feature selection was binary; hence, the length of the selected features can be different in the initial population, which can also change by crossover and mutation operators. Therefore, the length of the selected features could be different in each of the 30 implementations of GA. However, GA feature selection is usually converged to some specific feature groups. The means and standard deviations of selected feature lengths and accuracies for the seven proposed feature sets are compared in Table 2.

Table 2

As shown in Table 2, feature set 7, which is a combination of all features, results in the best average accuracy by a value of 82.0 ± 3.2%.

In comparison between HQ-insp and HQ-exp features, HQ-exp features provide a better average accuracy. As expected from Figure 4, LQ-insp and LQ-exp features (feature sets 3 and 4) provide a lower average accuracy than HQ-insp and HQ-exp. However, LQ features (feature sets 3 and 4) provide lower standard deviation compared to HQ features (feature sets 1 and 2). The lower number of features in LQ feature sets than HQ feature sets result in less variation in selected features, which can be the reason for a lower standard deviation in the accuracy of LQ features. The average accuracy of feature set 6 (HQ-exp & LQ-exp) is better than feature set 5 (HQ-insp & LQ-insp). Features that are extracted from expiration sound signals provide better accuracy than inspiration sound signals for HQ features, but it is reversed for LQ features.
The best selected features in the feature sets of 1-7 are shown in Table 3. The proposed method was applied to respiratory sounds of left and right lungs separately, which yielded similar results.

Table 3

As it can be seen, the existence of PA infection in CF patients can be detected based on only one cycle of their respiratory sound samples recorded from the right or left side. Therefore, both sound samples were used together to increase the number of samples. Sensitivity, specificity, and accuracy of detecting PA infection for all the sound samples are reported in percentage in Table 4.

Table 4

As shown in Table 4, the best result for the detection of infection is obtained from feature set 7 by sensitivity, specificity, and accuracy of 88.0%, 87.2% and 87.7%, respectively. The second best accuracy is obtained from features set 6.

PA infection detection is vital for early initiation of eradication therapy, and also it is essential to reduce the wrong detection to prevent antibiotic overuse. To increase sensitivity (PA infection detection) and specificity (reduce the wrong detection), an Ensemble classification was applied to feature sets No. 1-7.

The proposed Ensemble classifier was a combination of three SVM classifiers that were applied to the best three selected feature groups of each feature set. Table 5 presents the parameters of sensitivity, specificity, and accuracy after applying the Ensemble classifier to the seven feature sets. Besides, the Ensemble classifier was applied to three selected feature groups of different feature sets (feature sets 1, 6, & 7, feature sets 2, 6, & 7, and feature sets 5, 6, & 7).

Table 5

Table 5 shows that combining the three SVM increases accuracies in some cases. The increased accuracies after applying the Ensemble classifier are shown in bold in the last column of Table 5. Errors
of the three SVM classifiers are correlated in other cases, and the Ensemble classifier does not change efficiently by combining these classifiers. The highest accuracy is obtained from a combination of feature sets 5 & 6 & 7 and feature sets 1 & 6 & 7 by an accuracy of 90.3%. The two mentioned Ensemble classifiers (items 8 and 10 in Table 5) result in sensitivities of 95.5% and 94.0% and specificities of 82.9% and 85.1%, respectively. Results show that TQWT features are capable of diagnosing respiratory cycles with PA infection.

To show the effectiveness of the proposed method, Respiratory sounds of PA CF patients, which were recorded one month after treatment, were investigated. For these respiratory sounds, the probability of being classified as PA CF was computed by the best selected feature groups in Table 5. These probabilities were compared with that of classifying PA CF patients into PA CF class before treatment. To this end, after training SVM, the posterior probability of assigning a sample to a class was obtained using the method in [34]. After that, the existence of significant differences was investigated between the probabilities of these two groups (CF patients before and after the treatment of PA infection) using a two-sample t-test with a P-value of 0.05. The probabilities for assigning respiratory sounds to PA CF class before and after treatment are shown in Table 6 for the best ensemble classifiers of Table 5.

<table>
<thead>
<tr>
<th>Table 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>As it can be seen in Table 6, the probability of identifying respiratory sounds of PA CF subjects as PA infection after the treatment decreased significantly by the proposed method.</td>
</tr>
</tbody>
</table>

Feature/parameter selection and training steps were done using noise-free signals. The performance of the proposed method was investigated in the presence of noises and artifacts using noisy respiratory sound signals. Three noisy conditions were examined as follow:
- Raw noisy signals: respiratory sound signals after discarding speaking and coughing segments without applying any additional noise removal technique (raw noisy signals contaminated with digital stethoscope movement noises and cardiac sounds).
- Digital stethoscope movement noises: Raw noisy signals after cardiac sound effect removal.
- Cardiac sound effect: Raw noisy signals after removing digital stethoscope movement noises.

The best features in Table 5 were extracted from these three noisy signals. Then, the accuracy of PA infection detection was computed. The results are shown in Table 7.

Table 7

As shown in Table 7, the presence of digital stethoscope movement noises and cardiac sounds reduced the accuracy about 10% in comparison with noise-removed signals. In noisy conditions, the accuracy was reduced no more than 14%. The results show that the proposed features are appropriate for this study and that the performance of the method is satisfactory in the presence of noise.

The following are the final obtained results:

- High Q-factor features are superior to low Q-factor features in terms of PA detection accuracy since the former are selected more than the latter in feature sets, which contain both types of features and result in better accuracies.
- In comparison between inspiration and expiration sound features, none of the two is superior to the other in terms of PA detection accuracy. Accuracies for HQ expiration features are better than HQ inspiration features and they are reversed for LQ features.
- The best groups of features are a combination of high Q-factor and low Q-factor features in inspiration and expiration (feature set 7).
- Using Ensemble decision increased the average accuracy of detecting PA infection. The best result of detecting PA infection is obtained from combining the three best feature sets by the Ensemble classifier. Results indicate that Normal CF and PA CF patients’ respiratory sound signals are distinguishable with an accuracy of 90.3%.
• The probability of classifying respiratory sounds as PA CF is reduced significantly after the treatment of PA CF subjects by the proposed groups of features.

• Results show that the performance of the proposed method is satisfactory in the presence of noises and artifacts.

4. Discussion

As mentioned above, the diagnosis of PA infection in the primary stage is essential to initiate the treatment and reduce the risk of chronic infection. The gold standard method for detecting PA infection is time-consuming; therefore, a rapid diagnostic method can facilitate eradication therapy. For the first time, this research examined the capability of respiratory sound in diagnosing PA infection in CF patients.

Although there are some studies on the topic of the relationship between increasing sputum and respiratory sound samples (as summarized in Table 8), there has been no research on the detection of PA infection in CF patients using respiratory sounds.

Table 8

As shown in Table 8, 12 frequency features were used in [28] to discriminate sputum from non-sputum respiratory sounds with an accuracy of 85%-97%. In [25], 16 features of respiratory sounds in the time-frequency domain and 14 features in [27] derived from Discrete Wavelet Transform of respiratory sounds achieved accuracies of 83.5% and 84.53% in discriminating sputum from non-sputum states, respectively. In another study, 46 features derived from the EMD method achieved an accuracy of 92.02% in classifying sputum from non-sputum states. In this study, TQWT analysis was used. The result of TQWT analysis are consistent with previous studies that revealed the effectiveness of time-frequency features in detecting sputum increase. In comparison with other investigations [25-28], the proposed method achieved an acceptable accuracy (90.3%) with less number of features (15 features).
Furthermore, the proposed method was examined after the infection treatment and it was effective in the investigation of PA infection treatment. Two methods (EMD features and center of gravity in frequency domain features) which had better accuracies than the other methods, were selected from Table 8. These features were extracted from recorded respiratory sounds of CF patients. The numbers of EMD features and center of gravity features are 46 and 12. GA feature selection was applied to these two feature sets to select the best features of each feature set. Results of these two methods were compared with the proposed method. TQWT features resulted in better accuracies (7\textsuperscript{th} row in Table 4: sensitivity: 87.2\%, specificity: 88.0\% and accuracy: 87.7\%) than EMD (sensitivity: 79.1\%, specificity: 72.3\% and accuracy: 76.3\%) and center of gravity features (sensitivity: 55.2\%, specificity: 70.2\% and accuracy: 61.4\%). Results show that differences between spectral properties of lung sounds in PA CF and Normal CF are emphasized when the pulmonary sounds are decomposed with TQWT filters. This effect may be a result of better localization of the small vibrations caused by increasing sputum.

Since infection increases mucus and thickens airways, it was expected that high Q-factor components could result in better accuracies than low Q-factor components in differentiating between Normal CF and PA CF respiratory sound cycles; this is due to their higher resolution in comparison with low Q-factor. Consistently, results demonstrated the expectation and the best accuracies were obtained from features of high Q-factor components. Features extracted from both high Q-factor components of inspiration and expiration sounds resulted in the best accuracy. Moreover, the Ensemble classifier increased the accuracy.

The results of this study showed that the respiratory sounds of CF patients were affected by PA infection. Furthermore, the proposed features, extracted by the TQWT analysis of respiratory sounds, were able to detect the changes. Although the proposed approach was able to detect PA infection in CF patients, the
present study was limited by its small number of participants. Clinical use of this method needs further studies with more number of patients involving other infections in CF patients. The aim of this research was to find whether PA infection had an effect on lung sounds of CF patients which could be identified based on the lung sound analysis. Recorded respiratory sound samples had good quality. Due to the presence of some noises in the recorded sound signals and noise removal in the preprocessing step, the effects of different noises were investigated in this study. Results show that the proposed method can detect PA infection, even in the presence of noise. In the future, results of this project will be used to design an automatic system to detect PA infection in CF patients for the clinical use. Therefore, all the preprocessing steps for respiratory sound preparation will be implemented as a package to be used for all respiratory sound signals, which makes this work fully reproducible.

In future work, the proposed method can be used for monitoring the treatment in CF patients by recording respiratory sounds in different time intervals after initiating the treatment. Subsequently, physicians can follow-up a patient's status using the proposed approach. As another work, the effect of other infections such as *Staphylococcus aureus*, can be investigated on respiratory sound. Additionally, the results of the proposed method of detecting PA infection were only validated for CF patients. One suggestion is to apply the proposed method to respiratory sound signals of other lung diseases such as other lung infections in non-CF patients. Structural airway alterations in obstructive disease (such as chronic obstructive pulmonary disease) may be different from increasing mucus and sputum in CF patients. Different structural changes in airways cause different changes in respiratory sounds. Therefore, the effectiveness of the proposed features can be investigated in the detection of these changes and discrimination of respiratory disease with obstructive airway structures from those related to mucus airway structures.

5. **Conclusion**
This study proposes an innovative method to detect PA infection in respiratory sounds. For the first time, some lung sound features were introduced for the detection of PA infection in CF patients. The proposed TQWT-related features successfully discriminated respiratory sound signals of PA CF patients from normal CF ones. The findings also revealed that the probability of classifying respiratory sound signals of CF patients as PA CF was reduced after the treatment of PA infection. The proposed method utilized lung sound, which is a fast, low-priced, and accessible procedure. Furthermore, it can be helpful in deciding on both preventive and therapeutic strategies.

Acknowledgments

We thank the team of physicians, pharmacologists and microbiologists for collaboration to collect data in Pediatric Respiratory and Sleep Medicine Research Center of Children's Medical Center.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
References


Arezoo Karimizadeh received bachelor and master’s degree in Biomedical Engineering in University of Isfahan in 2010 and 2012, respectively. She is currently PhD student in K.N. Toosi university of Technology. Her research interests are in the fields of medical signal and image processing and also medical sound processing.

Dr. Mansour Vali is an Assistant Professor in Biomedical Engineering group of K.N. Toosi University of Technology. He received his B.Sc. degree in 1997 from Isfahan University of Technology in Electrical Engineering, M.Sc. degree in 2000 from Sharif University of Technology in Bioelectric Engineering and Ph.D. degree in 2006 from Amirkabir University of Technology in Biomedical Engineering, Tehran, Iran.. He was a faculty member of Biomedical Engineering group at Shahed University from 2007 to 2012. On February 2013, he joined K.N. Toosi University of Technology. His main research interests are “sound and speech processing in medical and psychological assessments”. He has developed a new course with the same title at Electrical Engineering department of K.N. Toosi University for supplementary students. Also he is working on Big Data processing in medical application.
**Dr. Mohammad Reza Modaresi** has practiced pediatric pulmonary at Children’s Medical Center, Pediatric Center of Excellence, since 2010. He is the founder and current chief of the Pediatric Pulmonary Division at Children's Medical Center. He is also the founder of a large and active program in the state for diagnostic and Interventional Flexible Bronchoscopy. It is available for the patients of any age and size including neonate, infant, children, and adolescent. He also designed Pediatric Sleep Lab and a modern full-service facility Infant and Pediatric Pulmonary Function Laboratory which performs various lung function tests for infant, preschool and school-age patients. Dr. Modaresi is the president of Iran Cystic Fibrosis Foundation and also he is Director of CF Center at Children’s Medical Center which provides care for over 1000 patients with cystic fibrosis.
Figures:

Figure 5: The overall structure of the proposed method
Figure 6: Energy distribution of 41 high Q-factor components of inspiration and expiration sounds in two groups of Normal CF and PA CF subjects with median and IQR calculated across all patients.
Figure 7: Energy distribution of 10 low Q-factor components of inspiration and expiration sounds in two groups of Normal CF and PA CF subjects with median and IQR calculated across all patients.
Figure 8: The percent of selected features from feature set 1-4 (HQ-insp, HQ-exp, LQ-insp and LQ-exp) in the feature set 5-7

Tables:

Table 9: CF Participant's information
Table 10: mean and standard deviation of feature lengths and (train/test) accuracies for selected features after applying GA.
Table 11: Performance results of the best selected features for feature sets 1-7 for respiratory sounds of left and right lungs.
Table 12: Performance results of the best selected features for feature sets 1-7 in percentage.
Table 13: Sensitivity, specificity and accuracy of applying Ensemble classifier to 7 features sets in percentage
Table 14: The probability of being classified as PA CF for features of PA CF patients before and after treatment.
Table 15: results of the proposed method in the presence of noises and artifacts
Table 16: Some related studies which were investigated respiratory sounds to diagnose sputum condition
Figure 1

Respiratory Sound

Preprocessing

Inspiration Sound

Expiration Sound

High Q-factor components (22)

Low Q-factor components (6)

High Q-factor components (22)

Low Q-factor components (6)

Statistical parameters: Max, Min, Mean, Std, Entropy, Energy

HQ-imp Features (192)

LQ-imp Features (36)

HQ-exp Features (192)

LQ-exp Features (36)

Add features

Add features

Add features

GA

GA

GA

GA

GA

GA

GA

GA

Selected groups of features from each feature set

SVM

Preprocessing

TQWT

Statistical

Extraction

Analysis

Parameter

Selection

Classification
Figure 2
### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Normal CF (n = 11)</th>
<th>PA CF (n = 14)</th>
<th>PA CF after treatment (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Female/Male)</td>
<td>5/6</td>
<td>6/8</td>
<td>5/6</td>
</tr>
<tr>
<td>Age (mean ± std)</td>
<td>12.18 ± 3.9</td>
<td>15.1 ± 5.3</td>
<td>15.5 ± 5.7</td>
</tr>
<tr>
<td>Height (mean ± std)</td>
<td>147.2 ± 20.1</td>
<td>149.5 ± 17.4</td>
<td>153.7 ± 12.3</td>
</tr>
<tr>
<td>Weight (mean ± std)</td>
<td>36.1 ± 12.1</td>
<td>37.3 ± 11.6</td>
<td>40.4 ± 12.5</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Feature</th>
<th>HQ-insp</th>
<th>HQ-exp</th>
<th>LQ-insp</th>
<th>LQ-exp</th>
<th>HQ-insp &amp; LQ-insp</th>
<th>HQ-exp &amp; LQ-exp</th>
<th>HQ-insp &amp; LQ-exp &amp; HQ-exp &amp; LQ-exp</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of features</td>
<td>5.05 ± 0.7</td>
<td>4.2 ± 1.1</td>
<td>4.7 ± 0.6</td>
<td>3.2 ± 0.6</td>
<td>4.4 ± 1.1</td>
<td>5.2 ± 1.1</td>
<td>4.6 ± 0.9</td>
</tr>
<tr>
<td>Accuracy (Train)</td>
<td>(87.2 ± 2.5)</td>
<td>(84.6 ± 2.5)</td>
<td>(76.8 ± 1.9)</td>
<td>(76.9 ± 3.6)</td>
<td>(84.4 ± 2.5)</td>
<td>(87.8 ± 4.3)</td>
<td>(89.3 ± 3.2)</td>
</tr>
<tr>
<td>Accuracy (Test)</td>
<td>(72.1 ± 4.6)</td>
<td>(73.9 ± 4.2)</td>
<td>(72.1 ± 0.5)</td>
<td>(69.8 ± 0.8)</td>
<td>(72.3 ± 3.5)</td>
<td>(74.3 ± 5.4)</td>
<td>(82.0 ± 3.2)</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Feature Set</th>
<th>SVM Left+Right (Train/Test)</th>
<th>SVM Right (Train/Test)</th>
<th>SVM Left (Train/Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HQ-insp</td>
<td>(87.7/79.8)</td>
<td>(87.7/80.4)</td>
<td>(87.8/79.4)</td>
</tr>
<tr>
<td>2 HQ-exp</td>
<td>(86.7/78.9)</td>
<td>(85.9/76.1)</td>
<td>(85.7/79.4)</td>
</tr>
<tr>
<td>3 LQ-insp</td>
<td>(77.8/72.8)</td>
<td>(78.2/78.6)</td>
<td>(77.7/66.2)</td>
</tr>
<tr>
<td>4 LQ-exp</td>
<td>(75.9/71.0)</td>
<td>(74.7/65.3)</td>
<td>(74.4/69.1)</td>
</tr>
<tr>
<td>5 HQ-insp &amp; LQ-insp</td>
<td>(82.3/78.9)</td>
<td>(82.2/84.7)</td>
<td>(82.6/73.5)</td>
</tr>
<tr>
<td>6 HQ-exp &amp; LQ-exp</td>
<td>(98.1/81.5)</td>
<td>(98.2/80.4)</td>
<td>(98.2/85.3)</td>
</tr>
<tr>
<td>7 HQ-insp &amp; LQ-insp &amp; HQ-exp &amp; LQ-exp</td>
<td>(92.1/87.7)</td>
<td>(92.2/84.7)</td>
<td>(92.7/89.3)</td>
</tr>
</tbody>
</table>
Table 4

<table>
<thead>
<tr>
<th>Feature Set</th>
<th>SVM Spec. N (Train/Test)</th>
<th>SVM Sens. PA (Train/Test)</th>
<th>SVM Acc. (Train/Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HQ-insp</td>
<td>(76.7/65.9)</td>
<td>(95.4/89.5)</td>
<td>(87.7/79.8)</td>
</tr>
<tr>
<td>2 HQ-exp</td>
<td>(82.9/74.4)</td>
<td>(89.4/82.0)</td>
<td>(86.7/78.9)</td>
</tr>
<tr>
<td>3 LQ-insp</td>
<td>(72.4/70.2)</td>
<td>(81.8/74.6)</td>
<td>(77.8/72.8)</td>
</tr>
<tr>
<td>4 LQ-exp</td>
<td>(72.1/61.7)</td>
<td>(78.6/77.6)</td>
<td>(95.9/71.0)</td>
</tr>
<tr>
<td>5 HQ-insp &amp; LQ-insp</td>
<td>(78.8/72.3)</td>
<td>(84.8/83.5)</td>
<td>(82.3/78.9)</td>
</tr>
<tr>
<td>6 HQ-exp &amp; LQ-exp</td>
<td>(97.8/70.2)</td>
<td>(98.4/89.5)</td>
<td>(98.1/81.5)</td>
</tr>
<tr>
<td>7 HQ-insp &amp; LQ-insp &amp; HQ-exp &amp; LQ-exp</td>
<td>(93.6/87.2)</td>
<td>(90.9/88.0)</td>
<td>(92.1/87.7)</td>
</tr>
</tbody>
</table>

Table 5

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HQ-insp</td>
<td>Train</td>
<td>87.7</td>
<td>86.2</td>
<td>86.5</td>
<td>84.9</td>
<td>92.9</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>79.8</td>
<td>77.1</td>
<td>77.1</td>
<td>74.4</td>
<td>86.5</td>
</tr>
<tr>
<td>2 HQ-exp</td>
<td>Train</td>
<td>86.7</td>
<td>85.7</td>
<td>83.7</td>
<td>87.3</td>
<td>90.2</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>78.9</td>
<td>78.9</td>
<td>78.9</td>
<td>80.8</td>
<td>82.0</td>
</tr>
<tr>
<td>3 LQ-insp</td>
<td>Train</td>
<td>77.8</td>
<td>76.3</td>
<td>76.3</td>
<td>75.9</td>
<td>76.6</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>72.8</td>
<td>72.8</td>
<td>72.8</td>
<td>70.2</td>
<td>74.6</td>
</tr>
<tr>
<td>4 LQ-exp</td>
<td>Train</td>
<td>75.9</td>
<td>75.9</td>
<td>75.2</td>
<td>74.7</td>
<td>76.7</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>71.0</td>
<td>70.1</td>
<td>70.1</td>
<td>70.1</td>
<td>70.1</td>
</tr>
<tr>
<td>5 HQ-insp &amp; LQ-insp</td>
<td>Train</td>
<td>82.3</td>
<td>82.3</td>
<td>89.3</td>
<td>78.6</td>
<td>85.1</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>78.9</td>
<td>78.9</td>
<td>72.8</td>
<td>72.3</td>
<td>83.5</td>
</tr>
<tr>
<td>6 HQ-exp &amp; LQ-exp</td>
<td>Train</td>
<td>98.1</td>
<td>94.6</td>
<td>88.7</td>
<td>97.8</td>
<td>99.8</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>81.5</td>
<td>80.7</td>
<td>79.8</td>
<td>76.5</td>
<td>89.5</td>
</tr>
<tr>
<td>7 HQ-insp &amp; LQ-insp &amp; HQ-exp &amp; LQ-exp</td>
<td>Train</td>
<td>92.1</td>
<td>82.4</td>
<td>98.1</td>
<td>93.5</td>
<td>98.1</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>87.7</td>
<td>86.8</td>
<td>85.9</td>
<td>87.2</td>
<td>88.0</td>
</tr>
<tr>
<td>8 Feature sets 1 &amp; 6 &amp; 7</td>
<td>Train</td>
<td>87.7</td>
<td>98.1</td>
<td>92.1</td>
<td>96.7</td>
<td>98.7</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>79.8</td>
<td>81.5</td>
<td>87.7</td>
<td>82.9</td>
<td>95.5</td>
</tr>
<tr>
<td>9 Feature sets 2 &amp; 6 &amp; 7</td>
<td>Train</td>
<td>86.7</td>
<td>98.1</td>
<td>92.1</td>
<td>96.7</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>78.9</td>
<td>81.5</td>
<td>87.7</td>
<td>78.7</td>
<td>94.0</td>
</tr>
<tr>
<td>10 Feature sets 5 &amp; 6 &amp; 7</td>
<td>Train</td>
<td>82.3</td>
<td>98.1</td>
<td>92.1</td>
<td>96.7</td>
<td>95.5</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>78.9</td>
<td>81.5</td>
<td>87.7</td>
<td>85.1</td>
<td>94.0</td>
</tr>
</tbody>
</table>
### Table 6

<table>
<thead>
<tr>
<th>Feature set</th>
<th>Before treatment (mean ± std )</th>
<th>1 month after treatment (mean ± std )</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HQ-insp &amp; LQ-insp &amp; HQ-exp &amp; LQ-exp</td>
<td>0.75 ± 0.20</td>
<td>0.62 ± 0.24</td>
<td>0.003 *</td>
</tr>
<tr>
<td>Feature sets 1 &amp; 6 &amp; 7</td>
<td>0.87 ± 0.09</td>
<td>0.55 ± 0.09</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>Feature sets 2 &amp; 6 &amp; 7</td>
<td>0.81 ± 0.11</td>
<td>0.64 ± 0.09</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>Feature sets 5 &amp; 6 &amp; 7</td>
<td>0.84 ± 0.09</td>
<td>0.57 ± 0.11</td>
<td>&lt;0.001 *</td>
</tr>
</tbody>
</table>

### Table 7

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Feature sets 1 &amp; 6 &amp; 7</td>
<td>82.9</td>
<td>70.2</td>
<td><strong>90.3</strong></td>
<td>68.1</td>
<td>82.1</td>
<td><strong>76.3</strong></td>
<td>70.2</td>
<td>86.5</td>
<td><strong>79.8</strong></td>
<td>72.3</td>
<td>88.0</td>
<td><strong>81.5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature sets 5 &amp; 6 &amp; 7</td>
<td>85.1</td>
<td>74.4</td>
<td><strong>90.3</strong></td>
<td>63.8</td>
<td>88.0</td>
<td><strong>78.1</strong></td>
<td>74.4</td>
<td>85.1</td>
<td><strong>80.7</strong></td>
<td>74.4</td>
<td>86.5</td>
<td><strong>81.5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 8

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Features</th>
<th># Features</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TQWT features (Proposed method)</td>
<td>25 patients &amp; 114 respiratory sound cycle &amp; 11 patients after treatment (22 respiratory sound cycle)</td>
<td>Features from TQWT analysis of respiratory sound signals</td>
<td>15</td>
<td>90.2%</td>
</tr>
<tr>
<td>Center of gravity features [28]</td>
<td>3 patients. 128 respiratory sound samples.</td>
<td>Center of gravity in a frequency domain.</td>
<td>12</td>
<td>85%-97%</td>
</tr>
<tr>
<td>Time-frequency image features[25]</td>
<td>12 patients. 272 respiratory sound samples</td>
<td>Features from time-frequency distribution of respiratory sound signals</td>
<td>16</td>
<td>83.5%</td>
</tr>
<tr>
<td>Discrete Wavelet Transform features [27]</td>
<td>595 sound samples</td>
<td>Features extracted from Discrete Wavelet Transform</td>
<td>14</td>
<td>84.53%</td>
</tr>
<tr>
<td>EMD features[26]</td>
<td>14 patients. 803 sound samples</td>
<td>Features based upon Empirical Mode Decomposition.</td>
<td>46</td>
<td>92.02%</td>
</tr>
</tbody>
</table>