ABSTRACT

Background and objective: Respiratory inductive plethysmography is a non-invasive technique for measuring respiratory function. However, there are challenges associated with using linear methods for calibration of respiratory inductive plethysmography. In this study, we developed two nonlinear models, artificial neural network and adaptive neuro-fuzzy inference system, to estimate respiratory volume based on thoracoabdominal movements, and compared these models with routine linear approaches, including qualitative diagnostic calibration and multiple linear regression.

Methods: Recordings of spirometry volume and respiratory inductive plethysmography were obtained for 10 normal subjects and 10 asthmatic patients, during asynchronous breathing for 7 min. The first 5 min of recording were used to develop the models; the remaining data were used for subsequent validation of the results.

Results: The results from the nonlinear models fitted the spirometry volume curve significantly better than those obtained by linear methods, particularly during asynchrony ($P < 0.05$). On a breath-by-breath analysis, estimates of tidal volume, total cycle time and sigh values using the artificial neural network model were accurate by comparison with qualitative diagnostic calibration. In contrast to the artificial neural network model, there was a significant correlation between values for thoracoabdominal asynchrony and increased error of qualitative diagnostic calibration ($P < 0.05$).

Conclusions: These results indicate that the nonlinear methods can be adapted to closely simulate variable conditions and used to study the patterns of volume changes during normal and asynchronous breathing.

Key words: artificial neural network, nonlinear model, qualitative diagnostic calibration, respiratory inductance plethysmography, respiratory volume.

INTRODUCTION

Functional studies of the respiratory system and the variability of ventilation are useful both physiologically and clinically, to classify certain respiratory abnormalities and to describe the mechanisms involved in the control of breathing. Because conventional methods requiring physical connection to the airways lead to arousal, particularly in infants, and alterations in breathing pattern, there has been recent interest in alternative methods of assessing respiratory function.

Respiratory inductance plethysmography (RIP) is a useful technique for measuring respiratory function, principally in infants, and for prolonged respiratory monitoring and assessment of some pathological
states, because it is non-invasive, does not interfere with the airways and requires minimal patient co-operation.\textsuperscript{12-14} This technique involves the subject wearing two inductance bands around the abdomen (AB) and rib cage (RC). It is assumed that tidal volume (VT) can be estimated as the weighted sum of the RC and AB inductance signals:

\[ \text{VT} = \alpha \text{RC} + \beta \text{AB}, \]  

where \( \alpha \) and \( \beta \) are the volume/motion coefficients for RC and AB, respectively.\textsuperscript{15}

Although several methods have been proposed for estimating VT using this approach, calibration of RIP remains controversial, particularly in thoracoabdominal asynchrony.

However, the most popular calibration method is qualitative diagnostic calibration (QDC),\textsuperscript{12,13,16-22} as described by Sackner et al.\textsuperscript{7} Although this method only provides information about the relative contribution of the RC and AB, the simultaneous use of a spirometer (SP) allows derivation of quantitatively calibrated values.\textsuperscript{12} Nevertheless, the validity of the QDC method has been criticized.\textsuperscript{12,18,20-23} Furthermore, the accuracy of VT predictions using a multiple linear regression (MLR) approach has been disappointing.\textsuperscript{12,21,24-27}

All these models were based on a simple linear relationship among RC, AB and VT.\textsuperscript{28-30} and it was assumed that the respiratory system moves with two degrees of freedom.\textsuperscript{32} Conversely, previous studies indicated that movement of the respiratory system was not simple and was associated with compound thoracoabdominal interactions, particularly during variable breathing.\textsuperscript{13,31-34} Therefore, a linear model can only be applied in conditions of constant or quasi-constant VT\textsuperscript{18} and is not very reliable during variable and asynchronous breathing.\textsuperscript{12,14,19,21,24,26,35-37} Therefore, the development of new models that may be adapted to this type of nonlinearity would be useful.\textsuperscript{24}

Previous investigators have used artificial neural network (ANN) and adaptive neuro-fuzzy inference systems (ANFIS), as artificial intelligence paradigms, to provide reliable outcomes from investigations of complex and nonlinear physiological and clinical problems. The usefulness of neural networks derives from their special features, including nonlinear, adaptive and parallel processing.\textsuperscript{38,39} Neuro-fuzzy inference can serve as a basis for constructing an input–output map, based on both human knowledge (in the form of fuzzy if-then rules) and stipulated input–output data pairs.\textsuperscript{40,41}

The aim of the present study was to develop ANN and ANFIS models as nonlinear approaches to estimating respiratory volume from measurements of AB and RC movements. For validation purposes, the accuracy of these nonlinear calibration approaches was compared with that of QDC and MLR during variable patterns of normal and asynchronous breathing.

**METHODS**

Twenty men (10 healthy and 10 asthmatic subjects), aged 24–39, provided informed consent and were enrolled in this study, which was approved by the institutional review board and ethics committee at Tarbiat Modares University. All asthmatic patients had clinically documented asthma and reversible airflow limitation (>12% or 200 mL increase in forced expiratory volume in 1 s (FEV\textsubscript{1}) following inhalation of 200 µg of salbutamol (Aburienh Pharmaceutical Co., Tehran, Iran)).\textsuperscript{42} All the age-matched healthy subjects had normal lung function, no history of respiratory or cardiac disease and comparable tobacco use. All examinations were performed by the same pulmonologist, to ensure the reliability of diagnoses and prevent variations. Asthmatic patients were included so as to evaluate the accuracy of the models for calibrating asynchronous breathing.\textsuperscript{43}

The subjects were placed in the supine position, and two pneumotrace bands (MLT1132 Piezo Respiratory Belt Transducer, AD-Instruments, Castle Hill, Australia) were fastened at the level of the umbilicus and fourth intercostal interspace, to monitor RC and AB movements, as inputs for the models. Respiratory volume, as the output from the models, was measured using a SP (Pony Spirometer, Cosmed, Milan, Italy), which was connected to a digitizer via an interface. The signals from the pneumotrace bands and SP were digitized at a 1 KHz sampling rate (Powerlab/4, AD-Instruments). For calibration, AB and RC movement signals and spirometric respiratory volumes were simultaneously recorded for at least 7 min. Five minutes of data were used for developing the models, and the validation assessment was based on at least 40 subsequent breaths at the same period.

**ANN model**

An ANN consists of simple signal processing units or ‘neurons’. Each neuron may have multiple inputs, but only a single output. The input–output relationship is controlled by a transfer function. A complete network is built up by organizing individual neurons into a series of layers. In a feed-forward fully connected network, each neuron receives input from neurons in the preceding layer and also provides output to each neuron in the following layer. Within given topology and transfer functions, the desired behaviour of an ANN can be approximated by adjustment of the neuronal connections. This is called training of the network, and is performed using a data set for which the output from the corresponding input is available. The hypothesis is that a trained ANN can be used to estimate the output values for input data that were not used during the training. In practice, it has been demonstrated that properly trained ANNs do have this capability for generalization (see additional explanation in Appendix S1). We have designed a standard feed-forward ANN (in a MATLAB 7.4 (MathWorks Inc., Natick, MA, USA) environment with neural network toolbox) that comprises 8 input neurons, 15 neurons in a hidden layer, and 1 output neuron. The number of network layers and neurons was determined through a trial-and-error process because there is no commonly accepted theory for pre-determining the optimum number.\textsuperscript{39} The tansig and purelin functions were
used for hidden layers and the output layer, respectively. The newff function was used to create the network object for training the feed forward network, and the Levenberg-Marquardt (trainlm) algorithm was used to train the back-propagation network. To simplify the problem for the network, the input and target values were pre-processed and mapped into the interval.\(^3\) The ANN was trained 500 times (epochs).

**ANFIS model**

The basic structure of this type of fuzzy inference system is a model that maps input characteristics to input membership functions (MF), input MF to rules, rules to a set of output characteristics, output MF to rules, and the output MF to a single value output or a decision associated with the output. The neuro-adaptive learning method works similarly to that of neural networks. It is a network-type structure similar to that of a neural network, which maps inputs through input MF and associated parameters, and then through output MF and associated parameters to outputs, and can be used to interpret the input/output map (see additional explanation in Appendix S1). The ANFIS model was developed using MATLAB 7.4 software (fuzzy logic toolbox-ANFIS). The number of input MF in this model was four, for each input. The MF types for inputs and outputs were psigmf and linear, respectively. The model was trained 80 times (epochs) in the hybrid method.

**QDC model**

The QDC method uses Equation 2:

\[
VT = MKRC + AB
\]  

(2)

\(K\) can be calculated as the ratio of the standard deviations of the AB and RC signals. The calculated value of \(K\) was then re-applied to Equation 2 and \(M\), which is the slope of the regression line between the output of this equation and SP volume, was obtained.

**MLR model**

MLR was performed using the volume obtained from the SP as the dependent variable, and RC and AB changes with each breath, to obtain the regression equation containing \(\alpha\) and \(\beta\) (Eqn 1).

**Statistical analysis**

To compare the accuracy of the models to fit with reference SP volume, mean absolute error (MAE), root mean square error (RMSE) and \(R^2\) were calculated. The accuracy of each model for estimating VT, total cycle time (TT), and sigh, on a breath-by-breath basis, using mean differences (95% confidence interval); MAE and RMSE were also evaluated. Individual breath results were compared by estimating the relative differences between VT, TT, and sigh obtained from the models and by SP, using the method described by Bland and Altman.\(^41\) For example, the differences between output of the models (\(VT_{\text{model}}\)) and \(VT_{\text{SP}}\) were calculated from the following equation:

\[
VT_{\text{DIF}, \%} = (VT_{\text{model}} - VT_{\text{SP}}) / (VT_{\text{model}} + VT_{\text{SP}}) / 2 \times 100.
\]  

(3)

Thoracoabdominal asynchrony was assessed by calculating the percentage of the time during inspiration that the RC and AB signals were not moving in the same direction, and is presented as paradox percentage.

ANOVA was used to compare the accuracy of the models. The Bonferroni test was performed for post-hoc analysis. Correlations between error values for the models and degrees of asynchrony were assessed using Pearson correlation coefficients. Student’s t-test was used for comparison of parameters between healthy volunteers and asthmatic patients. SPSS 11.0

### Table 1  Comparison between nonlinear (ANN and ANFIS) and (QDC and MLR) linear models of fit with reference spirometric volume

<table>
<thead>
<tr>
<th></th>
<th>ANN</th>
<th>ANFIS</th>
<th>QDC</th>
<th>MLR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>0.006 ± 0.001(^1)</td>
<td>0.011 ± 0.003(^1)</td>
<td>0.034 ± 0.005(^2)</td>
<td>0.038 ± 0.006(^2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A</td>
<td>0.010 ± 0.002</td>
<td>0.030 ± 0.002</td>
<td>0.070 ± 0.004</td>
<td>0.080 ± 0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RMSE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>0.008 ± 0.000</td>
<td>0.016 ± 0.002</td>
<td>0.039 ± 0.003</td>
<td>0.045 ± 0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A</td>
<td>0.012 ± 0.003</td>
<td>0.044 ± 0.003</td>
<td>0.092 ± 0.004</td>
<td>0.120 ± 0.022</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(R^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>0.997 ± 0.001</td>
<td>0.987 ± 0.002</td>
<td>0.942 ± 0.003(^1)</td>
<td>0.941 ± 0.004(^4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A</td>
<td>0.993 ± 0.002</td>
<td>0.962 ± 0.002</td>
<td>0.705 ± 0.017(^6)</td>
<td>0.698 ± 0.021(^6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± standard deviation. All differences between the models were statistically significant (except \(^{1, 4, 6}\), \(^{P > 0.05}\)).

A, asthmatic patients; ANFIS, adaptive neuro-fuzzy inference system; ANN, artificial neural network; H, healthy subjects; MAE, mean absolute error; MLR, multiple linear regression; QDC, qualitative diagnostic calibration; \(R^2\), \(R^2\)-squared; RMSE, root mean square error.
(SPSS Inc., Chicago, IL, USA) was used for statistical analyses. A P-value <0.05 was considered statistically significant.

RESULTS
Ten healthy and 10 asthmatic males were enrolled in the study; the mean paradox percentages were 9.7 ± 3.2 (range 5–15) and 36.2 ± 8.6 (range 21–47), respectively.

The relationship between thoracoabdominal movements and respiratory volume is shown in Figure 1. This figure illustrates the relationship between AB and RC movements, and SP volume in a healthy subject and an asthmatic patient. The oblique plane in this figure shows a linear relationship between the parameters. As shown, some points are out of the oblique plane, and a linear model cannot fit all the real data points, even in a healthy subject breathing synchronously.

The accuracy of linear (QDC and MLR) and nonlinear (ANN and ANFIS) models for fit with reference SP volume are compared in Table 1. The nonlinear models had significantly lower errors for predicting real volume than linear models (P < 0.05). In addition, the accuracy of all models was superior in healthy subjects, compared with asthmatic patients with variable breathing patterns. Subsequently, ANN and QDC were used for analysis of data, as better nonlinear and linear models, respectively.

As shown in Figure 2, the output of ANN was a better fit with SP volume (as a reference) than the QDC output. During asynchronous breathing (Fig. 2b), the error of QDC was marked; however, the ANN model was adaptable to the asynchronous condition and simulated the real volume more accurately. In contrast to the ANN model, there was significant correlation between values for thoracoabdominal asynchrony and increased error of QDC (P < 0.05).

Figure 1 Three-dimensional illustration of the relationship between abdomen (AB) and rib cage (RC) movements, and spirometer (SP) volume in a healthy (a) and an asthmatic (b) subject. The oblique plane shows the linear relationship between the parameters.

Figure 2 Comparison of the artificial neural network (ANN) and qualitative diagnostic calibration (QDC) models for prediction of spirometer (SP) volume based on abdomen (AB) and rib cage (RC) signals in a healthy subject (a) and an asthmatic patient with thoracoabdominal asynchrony (b).
On a breath-by-breath analysis, the performance of the ANN model for calculating VT, TT and the sigh values was significantly better than that of QDC (Table 2). In particular, ANN outperformed the QDC model in estimating sigh, which differs markedly from constant breathing. Similar results were obtained for evaluation of individual breaths by determining the relative differences for VT, TT and sigh, between the outputs of the models and SP (Fig. 3). A Bland–Altman plot showed wide ranges of relative differences between parameters obtained by QDC and SP, in contrast to ANN, particularly for estimation of sigh.

**DISCUSSION**

Nonlinear models (ANN and ANFIS) were developed to estimate respiratory volume from measurements of AB and RC movements during normal and asynchronous breathing. To our knowledge, this is the first study in which nonlinear methods for calibration of RIP have been developed. In contrast to linear models (QDC and MLR), respiratory volume as determined by nonlinear models was a closer fit with the reference volume, even in the presence of thoracoabdominal asynchrony. From the present results, the accuracy of the ANN model for estimation of VT, TT and sigh was significantly better than that of QDC.

It is evident from Figure 1 that the relationship between AB and RC movements, and the reference volume is not linear even in healthy patients. Linear models are satisfactory for signals near the oblique plane, but they are inadequate for signals that are far from it. In patients with asynchronous and variable breathing patterns, this nonlinearity is more noticeable, and the use of linear models is not reliable, as reported previously. Previous models of the relationship among RC/AB movements and VT were based on analogies such as connected cylinders. It was assumed that the RC and AB move independently and that the respiratory system moves with two degrees of freedom. However, these assumptions are not physiologically realistic. More recent studies indicate that even during normal breathing, RC and AB movements are in proportion to each other, and the normal respiratory system moves with at least three to four degrees of freedom of motion. Therefore, it is not possible to accurately describe respiratory volume using a linear model. In this study, we developed two nonlinear models, thereby improving the accuracy of estimation of respiratory volume.

The main outcome of this study was the determination of the reference volume pattern, not just VT, as sometimes reported. In contrast to the linear methods, the nonlinear models resulted in a better fit among RC and AB movements, and SP volumes, particularly in patients with thoracoabdominal asynchrony. As reported previously, the accuracy of breath-by-breath volume quantification of RIP was poor. In this study, the relative breath-by-breath differences between VT obtained by the ANN model or SP in healthy patients were significantly lower (<5%), comparable with those obtained by QDC (<10%), and in agreement with the results from other studies. The neural network model predicted significantly lower VT and TT differences with the reference volume, and it showed narrower limits of agreement. Therefore, this is a good approach to quantifying breath-by-breath variability of ventilation and studying its complexity. Although the relative differences under conditions of acute changes in breathing pattern, such as sigh, exceeded 10% when using QDC, as reported previously, the ANN model predicted reference volume similarly to other situations, with relative differences of <5% (Fig. 3c). Thoracoabdominal breathing patterns, this nonlinearity is more noticeable, and the use of linear models is not reliable, as reported previously.
Nonlinear model for RIP calibration

Healthy cases: ANN

Individual breaths

Healthy cases: QDC

Individual breaths

Asthmatic cases: ANN

Individual breaths

Asthmatic cases: QDC

Individual breaths
dominal asynchrony, which is a problematic factor in calibration of RIP \cite{13,14,36} is often observed in neonates and in many respiratory disorders. Previous studies indicated that changes in the degree of asynchrony may have contributed to an increased error in calibration.\cite{37} The present QDC results confirmed this. The error of the QDC method for determining respiratory volume increased significantly with greater asynchrony, particularly during sigh. However, this correlation was not significant for the ANN model, which could be adapted to different conditions. This nonlinear and adaptive capability of the neural network model makes it a satisfactory tool for providing reliable outcomes from investigation of complex, nonlinear physiological and clinical problems.

It is not difficult to understand why QDC is not satisfactory and has been criticized, especially when used to investigate asynchrony.\cite{12,21,23} In Equation 2, $K$ was calculated as the ratio of the standard deviations of the AB and RC signals. However, even during normal breathing, $K$ varies from breath to breath so that constant values of $K$ cannot be used to accurately determine respiratory volume.\cite{24} During asynchronous breathing, the quality of fit with reference volume deteriorates further.\cite{21,26} However, QDC provides good calibration in subjects with constant or quasi-constant VT.\cite{18}

The if-then rules of the ANFIS model are used to formulate the conditional statements that comprise fuzzy logic. Although these rules are powerful for distinguishing categorical variables with good accuracy, they cannot accurately predict continuous variables.\cite{47} Neural networks, which were derived from studies of the nervous systems, process information in parallel and are useful for pattern recognition. The nonlinear, adaptive and parallel processing features of ANN models have been used to obtain greater performance accuracy in outcome prediction, as compared with conventional statistical methods.\cite{48,49} Because of the ambiguous relationship among RC/AB movements and respiratory volume, particularly during variable breathing, it is not surprising that linear methods are relatively inappropriate for investigating this type of problem. ANN models can be used to anticipate arbitrary nonlinear relationships between independent and dependent variables.\cite{38,39} These advantages make

**Figure 3** Individual breath-to-breath variation in tidal volume (VT) (a); total cycle time (TT) (b); and sigh (c) between output from the models and spirometer (SP) measurements. For example, VT$_{\text{DIF}}$% was calculated as $\text{VT}_{\text{DIF}}$% $= (\text{VT}_{\text{model}} - \text{VT}_{\text{SP}})/(\text{VT}_{\text{model}} + \text{VT}_{\text{SP}})/2 \times 100$, for seven consecutive breaths and four sighs during spontaneous ventilation in five healthy subjects and five asthmatic patients. The mean difference (----) and 95% limits of agreement (- - -) are indicated. ANN, artificial neural network; QDC, qualitative diagnostic calibration.
the ANN model a more robust paradigm for application in the real-world setting.30,31 The real-time use of the ANN model is not difficult. The number of hospitals that have electronic medical records is increasing rapidly. Once trained, the ANN model can reside in the background of clinical information systems. We suggest that implementation of this ANN software on databases at pulmonary centres will help physicians to calibrate the respiratory volume for each patient more accurately. However, it should be noted that a new training process must be completed before the ANN model can be used for this purpose. It should also be noted that although we designed new program codes for ANN and ANFIS in this study, simple tools for designing models are available in MATLAB, and these may be useful for investigators who are not expert in programming.

In conclusion, the output of the nonlinear models, which were used in this study, predicted reference volume, and VT, TT and sigh with accuracy that was comparable with that of classical linear methods. Although thoracoabdominal asynchrony and variable breathing patterns are always factors that have adverse effects on calibration of RIP, their effects on the accuracy of the ANN model were not significant. The nonlinear methods provide adequate models, which can be used to study the pattern of changes in respiratory volumes during normal and asynchronous breathing (as in asthma), and to accurately quantify the variability in ventilation, particularly during prolonged respiratory monitoring, and when assessing some pathological states.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Additional explanation on artificial neural network (ANN) and adaptive neuro-fuzzy inference systems (ANFIS) models.