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(54) Title: METHOD AND SYSTEM FOR QUANTITATION OF RESPIRATORY TRACT SOUNDS

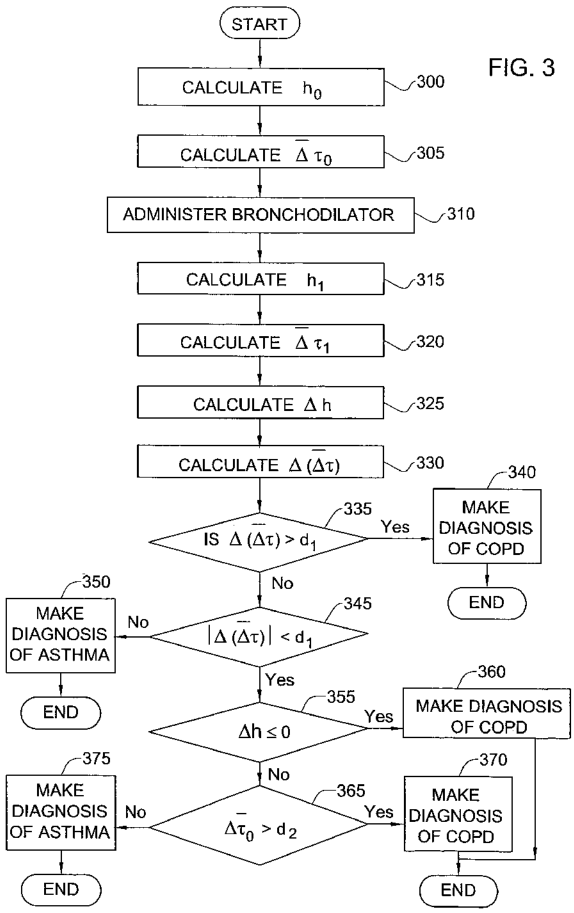

FIG. 3

(57) Abstract: The invention provides a system and method for analyzing respiratory tract sounds. Sound transducers are fixed on the skin over the thorax that generate signals indicative of pressure waves at the location of the transducer. Processing of the signals involves performing an event search in the signals and determining event parameters for events detected in the search.

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METHOD AND SYSTEM FOR QUANTITATION OF RESPIRATORY TRACT SOUNDS

FIELD OF THE INVENTION

This invention relates to medical devices and methods, and more particularly to such devices and methods for analyzing body sounds.

BACKGROUND OF THE INVENTION

Body sounds are routinely used by physicians in the diagnosis of various disorders. A physician may place a stethoscope on a person's chest or back and monitor the patient's breathing in order to detect abnormal or unexpected lung sounds.

It is also known to fix one or more microphones onto a subject's chest or back and to record lung sounds. U.S. Patent No. 6,139,505 discloses a system in which a plurality of microphones are placed around a patient's chest. The recordings of the microphones during inhalation and expiration are displayed on a screen, or printed on paper. The recordings are then visually examined by a physician in order to detect a pulmonary disorder in the patient.

US Patent No. 5,887,208, assigned to the assignee of the present application, discloses a method and system for analyzing respiratory tract sounds in an individual. Transducers are fixed over the thorax. Each transducer generates a signal indicative of pressure waves at the location of the transducer. An acoustic energy signal at each location is then determined from the recorded pressure waves. The acoustic energy signals can be subjected to an interpolation procedure to obtain acoustic energy signals at locations over the thorax where a transducer was not located. The acoustic energy signals at various times over one or more respiratory cycles can be displayed on a screen for viewing and visual analysis.

Chronic obstructive pulmonary disease (COPD) is a lung disease which is manifested clinically by a mid-life onset of slowly progressing symptoms that include chronic cough and sputum production, progressive and persistent dyspnea and wheezing, and is exacerbated by obesity and a long history of smoking. Diagnosis of COPD is typically done by administering a bronchodilator and then determining by spirometry the forced expiratory volume in 1 second (FEV1) and the forced vital capacity (FVC). A post-bronchodilator ratio of FEV1/FVC< 0.7 is usually taken as confirmation of an airflow limitation that is not fully reversible, and is thus indicative of COPD. Complete reversibility of airflow is useful in excluding COPD (a rise in FEV1 >400mL).

Asthma is a lung disease in which the airway walls are inflamed and tend to constrict in response to allergens and irritants. Symptoms of asthma include difficulty in breathing, wheezing, coughing, and chest tightness. Sputum production may also be increased.

In contrast to COPD, asthma is an early onset disease of intermittent, reactive symptoms such as episodic wheezing and dyspnea to such triggers as allergies and exercise. Asthma is associated with a family history of the disease. Asthma usually responds to bronchodilators, as determined by post-bronchodilator spirometery. A rise of 12% with an absolute rise in FEV1 of at least 200 mL is considered to be suggestive of bronchoreversibility. Thus, differential diagnosis between COPD and asthma is primarily based on a spirometric test, together with patient history. However, due to significant physiologic overlap in the spirometric data of COPD and asthma patients, bronchoreversibility, as determined by spiromtery, does not provide an unambiguous criterion of differential diagnosis of the two diseases. Additional tests, such as a chest X-ray, exhaled nitric oxide levels, and sputum analysis, may be performed to corroborate a diagnosis. However, there is also significant overlap in the patient responses to these tests as well.

SUMMARY OF THE INVENTION

In the following description and set of claims, two explicitly described, calculable, or measurable variables are considered equivalent to each other when the two variables are proportional to one another.

In its first aspect, the present invention provides a system for analyzing respiratory tract sounds. The system of the invention comprises one or more sound transducers that are configured to be applied to a substantially planar region of the chest or back skin of an individual. Each transducer produces an analog voltage signal indicative of pressure waves arriving to the transducer that is processed by a processor in accordance with the method of the invention.

In one embodiment of the method of the invention, the processor performs an event search of any one of the signals. In another embodiment, the processor is configured to calculate a representative signal by time averaging two or more of the signals and to perform an event search in the representative signal. The processor then determines one or more parameters of the events detected by the event search, such as the time that the events occurred, an intensity of the event, the height of a peak associated with the event, the width of the peak at half the height, half time to rise, half time to fall, or the area under the peak.

In one preferred embodiment, the transducers are divided into two or more sets of transducers. Each set is preferably a contiguous set of transducers in the transducer array and thus overlies a distinct region of the body surface. For example, the transducers may be divided into two sets, one of which consists of one or more transducers overlying the left lung, while the other consists of one or more transducers overlying the right lung. As another example, the transducers may be divided into six sets where the transducers overlying each lung are divided into three subsets (overlying the top, middle and bottom of the lung). For each of the two or more sets of transducers, the processor calculates a representative signal, as explained above and performs an event search on each of the representative signals. The processor then determines one or more parameters of the events detected by the search. The processor may also compare the value of any one or more of the parameters determined for one of the transducer sets with the value of the parameter determined for any one or more of the other transducer sets. For example, the processor may calculate a time delay between the occurrences of corresponding peaks in two sets. The processor may also determine a time delay between repeated occurrences of a particular type of event. The processor may further be configured to calculate a comparison of the values of various event parameters before and after administration of a treatment to the individual. The processor may further be configured to make a diagnosis based upon any one or more of the comparisons. For example, the processor may be configured to diagnose asthma or COPD.

Thus, in its first aspect, the invention provides a system for analyzing sounds in at least a portion of an individual's respiratory tract comprising:

(a) an integer N of transducers, each transducer configured to be fixed on a surface of the individual over the thorax, the ith transducer being fixed at a location x_i and generating a signal $Z(x_i,t)$ indicative of pressure waves at the location x_i; for i=1 to N at times t during a predetermined time interval; and

(b) a processor configured to:
receive the signals $Z(x_i,t)$ and to process the signals, wherein the processing comprises performing at least one event search; and
determining one or more event parameters for one or more events detected in an event search.

An event search may be performed on one or more of the signals $Z(x_i,t)$ or on one or more signals $P(x_i,t)$ wherein the signals $P(x_i,t)$ are obtained after performing one or more procedures on one or more of the signals $Z(x_i,t)$ selected from filtering, denoising, smoothing, envelope extraction, and applying a mathematical transformation. Alternatively or additionally, the transducers may be divided into one or more subsets and the processing comprises, for each of one or more of the subsets, calculating a representative signal from one or more of the signals $Z(x_i,t)$ or $P(x_i,t)$ obtained from transducers in the subset and performing one or more event searches on one or more of the representative signals. The representative signal of a transducer subset may be, for example, a summation or an average signal of the signals obtained by the transducers in the subset.

An event may be, for example, an entire breathing cycle, an inspiratory phase of a breathing cycle, or an expiratory phase of a breathing cycle. The event search may comprise performing any one or more of a peak search, an autocorrelation, a cross correlation with a predetermined function, and a Fourier transform.

One or more of the event parameters may be, for example, a time at which an event occurred, a duration of an event, a magnitude of an event, a height of a peak associated with the event, the width of a peak associated with the event in a signal at half peak height, a half time to rise of a peak associated with the event in a signal, a half time to fall of a peak, an area under a peak; a maximum of the signal during the event, a ratio of a maximum during an inspiratory phase to a maximum during an expiratory phase, a ratio of a duration of an inspiratory phase to a duration of an expiratory phase, and a morphology of a signal during the event.

The processor in the system may be further configured to calculate one or more comparisons between an event parameter value and a predetermined threshold or range of values. The processor may also be configured, for each of one or more pairs of a first representative signal and a second representative signal, to calculate one or more comparisons between an event parameter value calculated for the first representative function and an event parameter value calculated for the second representative function. The processor may be configured to make a diagnosis based upon one or more of the comparisons.

In a preferred embodiment of the invention, the processor is configured to:

(a) determine values of one or more initial event parameters;

(b) determine values of the one or more final event parameters and

(c) compare the values of the initial event parameters to the final event parameters.

In this embodiment, the processor may be configured to make a diagnosis based upon the comparison. The transducers may be divided into one or more sets, and an event parameter is a time at which an event occurred in a representative signal of each set. In this case, the comparison involves determining an extent of synchrony between two signals. Alternatively, or additionally, an event parameter is an average magnitude of a signal over a time period. In this case, the comparison may involve determining a difference in magnitude of two signals obtained during two distinct time periods. The processor may be configured to make a differential diagnosis. Specifically, the processor may be configured to diagnose asthma and/or COPD on the basis of the comparison.

In a most preferred embodiment, the processor is configured to make a differential diagnosis of COPD and asthma wherein :

the one or more initial event parameters are:

(i) an initial mean value of the signal over the predetermined time interval, $\mathbf{h}_0$, calculated for a representative signal obtained on a first subset of transducers prior to administration of a bronchodilator; and

(ii) an initial time delay, $\overline{\Delta\tau}_0$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

the one or more final event parameters are:

(i) a final mean value of the signal over a predetermined final time interval, $\mathbf{h}_1$, calculated for a representative signal obtained on the first subset of transducers after administration of the bronchodilator; and

(ii) an final time delay, $\overline{\Delta\tau}_1$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

and wherein the processing comprises:

(a) calculating a change in the mean value of the signal, Δh, where $\Delta h = h_1 - h_0$;

(b) calculating a change in $\overline{\Delta\tau}$, $\Delta(\overline{\Delta\tau})$, where $\Delta(\overline{\Delta\tau}) = \overline{\Delta\tau}_1 - \overline{\Delta\tau}_0$;

(c) making a differential diagnosis of COPD if $\Delta(\overline{\Delta\tau}) > d_1$, where d_1 is a predetermined first threshold;

(d) making a differential diagnosis of asthma if (i) $\Delta(\overline{\Delta\tau}) \leq d_1$; and if (ii) $\Delta(\overline{\Delta\tau}) < -d_1$;

(e) making a differential diagnosis of COPD if (i) $|\Delta(\overline{\Delta\tau})| < d_1$, and if (ii) $\Delta h \leq 0$;

(f) making a differential diagnosis of COPD if (i) $\Delta h \geq 0$, and if (ii) $\overline{\Delta\tau}_0 > d_2$, where d_2 is a predetermined second threshold; and

(g) making a differential diagnosis of asthma if (i) $\Delta h \geq 0$, and if (ii) $\overline{\Delta\tau}_0 \leq d_2$.

In another of its aspects, the invention provides a method for analyzing sounds in at least a portion of an individual's respiratory tract comprising:

(a) obtaining an integer N of signals $Z(x_i,t)$ indicative of pressure waves at locations x_i; for i=1 to N over the thorax at times t during a predetermined time interval; and

(b) processing the signals $Z(x_i,t)$, wherein the processing comprises performing at least one event search; and

(c) determining one or more event parameters for one or more events detected in an event search.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be carried out in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which:

Fig. 1 shows a system for obtaining an analyzing body sound in accordance with one embodiment of the invention;

Fig. 2 shows a flow chart for carrying out a method of analyzing body sounds in accordance with one embodiment of the invention;

Fig. 3 shows a flow chart of a method for making a differential diagnosis of asthma and COPD in accordance with one embodiment of the invention;

Fig. 4 shows placement of sound transducers over an individual's lungs;

Figs. 5a, **5b** and **5c** show signals obtained from a first individual;

Figs. 6a, **6b** and **6c** show signals obtained from a second individual;

Figs. 7a, **7b** and **7c** show signals obtained from a third individual;

Figs. 8a, **8b** and **8c** show signals obtained from a fourth individual;

Figs. 9a, **9b** and **9c** show signals obtained from a fifth individual; and

Figs. 10a, **10b** and **10c** show signals obtained from a sixth individual.

DETAILED DESCRIPTION OF PREFERRED EMBDOIMENTS

Fig. 1 shows a system generally indicated by **100** for analyzing respiratory tract sounds in accordance with one embodiment of the invention. An integer N of sound transducers **105**, of which four are shown, are applied to a planar region of the chest or back skin of individual **110**. The transducers **105** may be applied to the subject by any means known in the art, for example using an adhesive, suction, or fastening straps. Each transducer **105** produces an analog signal **115** indicative of pressure waves arriving to the transducer. The analog signals **115** are digitized by a multichannel analog to digital converter **120**. The digital data signals $Z(x_i,t)$ **125**, represent the pressure wave at the location x_i of the ith transducer (i= 1 to N) at time t. The data signals **125** are input to a memory **130**. Data input to the memory **130** are accessed by a processor **135** configured to process the data signals **125**. The signals $Z(x_i,t)$ **125** may be processed, for example, by filtering, denoising, smoothing, and envelope extraction. The processed signals $P(x_i,t)$ may be subjected to a mathematical transformation F to yield transformed signals $\tilde{P}(x_i,t) = F(P(x_i,t))$. The signals $\tilde{P}(x_i,t)$ may be displayed on a display device **150**.

An input device such as a computer keyboard **140** or mouse **145** is used to input relevant information relating to the examination such as personal details of the individual **110**. The input device **140** may also be used to input values of the times t_1 and t_2 during which the signals are to be recorded or analyzed. Alternatively, the times t_1 and t_2 may be determined automatically in a respiratory phase analysis of the signals $P(x_i,t)$ performed by the processor **135**.

In one embodiment of the invention the processor **135** is configured to calculate at least one representative signal $R_S = R(\tilde{P}(x_i,t))$ of a subset S of the signals $\tilde{P}(x_i,t)$ where For example, R_S can be equal to a single signal $\tilde{P}(x_i,t)$ or R_S can be calculated by time averaging the signals $\tilde{P}(x_i,t)$ in the set S. R_S may be displayed on the display device **150.** The processor is further configured to perform an event search on R_S. The event may be, for example, any one or more of a predetermined segment of a respiratory cycle, such as the inspiratory phase, expiratory phase, or a subsegment thereof. An event may be identified by a characteristic morphology in a representative signal R_S . For example, an event may be defined by the presence of a peak in a representative signal R_S having one or more predetermined characteristics. As additional examples, an event may be identified by a local maximum, local minimum, inflection point, or a derivative of any order or radius of curvature above or below a predetermined value. An event can also be the entire recording. The processor **135** then determines one or more parameters of events detected by the event search, such as the time that the events occurred, the value of a parameter of a peak associated with the event, half time to rise, half time to fall, or the area under the signal during the event, the mean value, maximum or minimum of the signal during the event. The processor **135** may display any one of the representative signals R_S or the determined parameters on a display device **150.**

In one embodiment, the transducers **105** are divided into two or more sets of transducers. Each set is preferably a contiguous set of transducers in the transducer array and thus overlies a distinct region of the body surface. For example, the transducers may be divided into two sets, one of which consists of one or more transducers overlying the left lung, while the other consists of one or more transducers overlying the right lung. As another example, the transducers may be divided into six sets where the transducers overlying each lung are divided into three subsets (overlying the top, middle and bottom of the lung). For each of the two or more sets of transducers, the processor **135** calculates a representative signal, as explained above and performs an event search on each of the representative signals. The processor then determines one or more parameters of the events detected by the search. The processor **135** may display any one of the parameters on the display device **150.** The processor **135** may also compare the value of any one or more of the parameters determined for one of the transducer sets with the value of the parameter determined for any one or more of the other transducer sets for at least one representative signal. For example, the processor may calculate a time delay between the occurrences of corresponding events in two sets between two digital data signals $Z(x_i,t)$. Another example, the processor may calculate a time delay between the occurrences of repeat occurrences of an event type within $Z_k(x_i,t)$

Fig. 2 shows a flow chart for carrying out the method of the invention in accordance with one embodiment. In step **200** the signals $Z(x_i,t)$ are obtained from N transducers placed at predetermined locations x_i for i from 1 to N on the body surface, where the N transducers may be divided into two or more sets S_i. In step **205** values of t_1 and t_2 are either input to the processor **135** using one or both of the input devices **140** or **145,** or are determined by the processor. In step **210,** for each transducer set, a representative signal of the transducer set is calculated. In step **215,** one or more of the representative signals are displayed on the display device **150.** In step **220**, for each representative signal, an event search is performed on the representative signal. In step **225,** for each representative signal, values of one or more parameters of the events detected in the event search of the signal are determined, such as the times at which the events occurred or the mean value of the representative signal during the event. In step **230,** the determined parameter values are displayed on the display device. Finally, in step **235,** for each of one or more of the parameters, the values of the one or more parameters determined for each of the representative signals are processed, and in step **240**, the results of the processing is displayed on the display device **150.**

In one embodiment of the invention, three event types are used, the inspiratory phase, the expiratory phase, and the entire signal over a predetermined time interval. For the events inspiratory phase and expiratory phase, the parameter of the event is the time τ of the peak associated with each occurrence of the event. For the event consisting of the entire signal over the predetermined time interval, the parameter is the mean value **h** of the signal over the predetermined time interval. For the parameter τ, the processing consists of calculating the time delay $\Delta\tau=|\tau_1-\tau_2|$, where τ_1 is the time of a peak in a first representative signal and τ_2 is the time of the corresponding peak in a second representative signal. $\Delta\tau$ is a measure of the extent to which the two representative signals are in synchrony with each other. An average of the $\Delta\tau$, $\overline{\Delta\tau}$, may be calculated if the representative signals cover one or more respiratory cycles.

In another of its aspects, the invention provides a method for the differential diagnosis of COPD and asthma. In this aspect of the invention, prior to administration of a bronchodilator, **h** is calculated for a single representative signal and $\overline{\Delta\tau}$ is calculated for two representative signals, as explained above. Fig. 3 shows a flow chart for a method of differential diagnosis of COPD and asthma in accordance with this aspect of the invention. In step **300**, an initial **h**, h_0, is calculated as explained above in reference to Fig. 2. In step **305,** an initial $\overline{\Delta\tau}$, $\overline{\Delta\tau}_0$

is calculated as explained above. In step **310**, a bronchodilator is administered to the individual. In step **315**, a final **h**, $\mathbf{h}_1$, is calculated as explained above. In step **320**, a final $\overline{\Delta}\tau$, $\overline{\Delta}\tau_1$, is calculated as explained above. In step **325**, a change in **h**, Δh, following administration of the bronchodilator is calculated where $\Delta h = h_1 - h_0$. In step **330**, a change in $\overline{\Delta}\tau$, $\Delta(\overline{\Delta}\tau)$, following administration of the bronchodilator is calculated where $\Delta(\overline{\Delta}\tau) = \overline{\Delta}\tau_1 - \overline{\Delta}\tau_0$.

In step **335**, $\Delta(\overline{\Delta}\tau)$ is compared to a predetermined first threshold d_1. If $\Delta(\overline{\Delta}\tau) > d_1$, then the extent of synchrony of the two representative signals decreased as a result of the administration of the bronchodilator, and in step **340** a differential diagnosis of COPD is made, and the process terminates. If at step **335** it is determined that $\Delta(\overline{\Delta}\tau)$ does not exceed d_1, then in step **345** it is determined whether $|\Delta(\overline{\Delta}\tau)| < d_1$. If no (i.e. $\Delta(\overline{\Delta}\tau) < -d_1$), then the extent of synchrony between the two representative signals increased as a result of the administration of the bronchodilator, and in step **350** a differential diagnosis of asthma is made. If at step **345**, it is determined that $|\Delta(\overline{\Delta}\tau)| < d_1$, then the synchrony of the representative signals did not change significantly as a result of the administration of the bronchodilator, and the process continues with step **355** where the sign of Δh is determined. If $\Delta h \leq 0$, then h decreased following the administration of the bronchodilator and in step **360**, a differential diagnosis of COPD is made. If at step **355** it is determined that $\Delta h \geq 0$, then h increased following administration of the bronchodilator, and the process continues with step **365** where $\overline{\Delta}\tau_0$ is compared to a predetermined second threshold d_2. If in step **365** it is determined that $\overline{\Delta}\tau_0 > d_2$, then in step **370** a differential diagnosis of COPD is made. If in step **365** it is determined that $\overline{\Delta}\tau_0 \leq d_2$, then in step **375** a differential diagnosis of asthma is made, and the process terminates.

Examples

The system and method of the invention were used for differential diagnosis of COPD and asthma.

In the cases described below, 40 transducers were placed on a subject's back over the lungs at the locations indicated by the circles **400** in Fig. 4. The curves **405a** and **405b** show the presumed contours of the subject's left and right lung, respectively. As can be seen, the transducers were arranged in a regular orthogonal lattice with a spacing between the transducers in the horizontal and vertical directions of 5 cm. The signals $Z(x_i,t)$ were then recorded over several respiratory cycles. The processing of the signals $Z(x_i,t)$ to produce the signal $\tilde{P}(x_i,t)$ included band pass filtering between 150 to 250 Hz, envelope extraction and conversion to decibels relative to the saturation level of the transducer. For the parameter τ, the transducers were divided into two sets of 20 transducers. One set, referred to herein as *"the left set of transducers"* consisted of the transducers overlying the left lung which are shown in Fig. 4 within the contour **405a**. The other set, referred to herein as *"the right set of transducers"* consisted of the transducers overlying the right lung which are shown in Fig. 4 within the contour **405b**. A representative signal was calculated for each of the two sets of transducers as the mean of the signals $\tilde{P}(x_i,t)$ obtained by the transducers in the set. For the parameter h, the entire set of 40 transducers was used as a single set of transducers, and a representative signal was calculated as the mean of the signals $\tilde{P}(x_i,t)$ obtained by the transducers in this set.

Representative signals were obtained before administration of a bronchodilator, and an initial average $\Delta\tau$ of the two representative signals, $\overline{\Delta}\tau_0$, was calculated, together with an initial h_0 as explained above. A 2.5mg dose of the bronchodilator albuterol was then administered to the subject via a nebulizer. 15 min after administration of the bronchodilator, a final $\overline{\Delta}\tau_1$ and h_1 were calculated. The change in the $\Delta\tau$ following administration of the bronchodilator, $\Delta(\overline{\Delta}\tau)$, was also calculated, as was the change in h, Δh.

Case 1

Fig. 5a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 5b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 5c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator.

The results are summarized in Table 1.

	$\overline{\Delta\tau}_0$ [# of frames]	$\overline{\Delta\tau}_1$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 58	***0.75***	***0***	***-50.88***	***-52.65***

Table 1

A significant increase occurred in the synchronization of the two lungs following administration of the bronchodilator as indicated by a very negative $\Delta(\overline{\Delta\tau})$ (-0.75). On the basis of this observation, the case was diagnosed as asthma, and this diagnosis was confirmed by spirometry and case history.

Case 2:

Fig. 6a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 6b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 6c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator. The results obtained for this case are summarized in Table 2.

	$\overline{\Delta\tau}_0$ [# of frames]	$\overline{\Delta\tau}_1$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 23	***0***	***1.43***	***-33.54***	***-39.37***

Table 2

A significant decrease occurred in the synchronization of the two lungs following administration of the bronchodilator as indicated by a very positive $\Delta(\overline{\Delta}\tau)$ (1.43). On basis of this observation, the case was diagnoses as COPD, and this diagnosis was confirmed by spirometry and case history.

Case 3:

Fig. 7a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 7b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 7c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator. The results obtained for this case are summarized in Table 3.

	$\overline{\Delta\tau}_0$ [# of frames]	$\overline{\Delta\tau}_1$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 30	***0***	***0***	***-48.35***	***-52.68***

Table 3

In this case, there no change was observed in $\Delta\tau$ ($\Delta(\overline{\Delta}\tau) = 0$). However, a decrease was observed in Δh. A diagnosis of COPD was therefore made which was confirmed by spirometry and case history.

Case 4:

Fig. 8a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 8b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 8c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator. The results obtained for this case are summarized in Table 4.

	$\overline{\Delta\tau_0}$ [# of frames]	$\overline{\Delta\tau_1}$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 7	***0***	***0***	***-49.51***	***-49.03***

Table 4

In this case the synchronization of the two lungs as well as the value of h were unchanged by the administration of the bronchodilator. A diagnosis of COPD was therefore made which was confirmed by spirometry and case history.

Case 5:

Fig. 9a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 9b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 9c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator. The results obtained for this case are summarized in Table 5.

	$\overline{\Delta\tau_0}$ [# of frames]	$\overline{\Delta\tau_1}$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 66	***0.67***	***0.67***	***-53.27***	***-51.76***

Table 5

In this case, the synchronization of the two lungs remained unchanged, and the value of h increased following administration of the bronchodilator. Before administration of the bronchodilator, the two lungs were unsynchronized. A diagnosis of COPD was therefore made which was confirmed by spirometry and case history.

Case 6:

Fig. 10a shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained prior to administration of the bronchodilator. Fig. 10b shows the representative signal obtained as above for the left lung (curve a) and the right lung (curve b) of a subject obtained after administration of the bronchodilator. Fig. 10c shows the average acoustic level in decibels of both lungs before (curve a) and after (curve b) administration of the bronchodilator. The results obtained for this case are summarized in Table 6.

	$\overline{\Delta\tau_0}$ [# of frames]	$\overline{\Delta\tau_1}$ [# of frames]	h_0 [db]	h_1 [db]
Patient # 9	***0***	***0***	***-52.00***	***-49.91***

Table 6

In this case the synchronization of the two lungs remained unchanged, and the value of h increased following administration of the bronchodilator. Before administration of the bronchodilator, the two lungs were synchronized. A diagnosis of asthma was therefore made which was confirmed by spirometry and case history.

CLAIMS:

1. A system for analyzing sounds in at least a portion of an individual's respiratory tract comprising:

(a) an integer N of transducers, each transducer configured to be fixed on a surface of the individual over the thorax, the ith transducer being fixed at a location x_i and generating a signal $Z(x_i,t)$ indicative of pressure waves at the location x_i; for i=1 to N at times t during a predetermined time interval; and

(b) a processor configured to:

receive the signals $Z(x_i,t)$ and to process the signals, wherein the processing comprises performing at least one event search; and

determining one or more event parameters for one or more events detected in an event search.

2. The system according to Claim 1 wherein an event search is performed on one or more of the signals $Z(x_i,t)$.

3. The system according to Claim 1 wherein an event search is performed on one or more signals $P(x_i,t)$ wherein the signals $P(x_i,t)$ are obtained after performing one or more procedures on one or more of the signals $Z(x_i,t)$ selected from filtering, denoising, smoothing, envelope extraction, applying a mathematical transformation.

4. The system according to Claim 1 wherein the transducers are divided into one or more subsets and the processing comprises, for each of one or more of the subsets, calculating a representative signal from one or more of the signals $Z(x_i,t)$ or $P(x_i,t)$ obtained from transducers in the subset and performing one or more event searches on one or more of the representative signals.

5. The system according to any one of the previous claims wherein one or more of the events are selected from an entire breathing cycle, an inspiratory phase of a breathing cycle, and an expiratory phase of a breathing cycle.

6. The system according to Claim 5 wherein the representative signal of a transducer subset is a summation or an average signal of the signals obtained by the transducers in the subset.

7. The system according to any one of the previous claims wherein the event search comprises performing any one or more of a peak search, an autocorrelation, a cross correlation with a predetermined function, and a Fourier transform.

8. The system according to any one of the previous claims wherein one or more of the event parameters are selected from the group comprising a time that an event occurred, a duration of an event, a magnitude of an event, a height of a peak associated with the event, the width of a peak associated with the event in a signal at half peak height, a half time to rise of a peak associated with the event in a signal, a half time to fall of a peak, an area under a peak; a maximum of the signal during the event, a ratio of a maximum during an inspiratory phase to a maximum during an expiratory phase, a ratio of a duration of an inspiratory phase to a duration of an expiratory phase, and a morphology of a signal during the event.

9. The system according to any one of the previous claims wherein the processor is further configured to calculate one or more comparisons between an event parameter value and a predetermined threshold or range of values.

10. The system according to Claim 4 wherein the processor is further configured, for each of one or more pairs of a first representative signal and a second representative signal, to calculate one or more comparisons between an event parameter value calculated for the first representative function and an event parameter value calculated for the second representative function.

11. The system according to Claim 9 or 10 wherein the processor is further comprised to make a diagnosis based upon one or more of the comparisons.

12. The system according to anyone of the previous claims wherein the processor is configured to:

(a) determine values of one or more initial event parameters;

(b) determine values of the one or more final event parameters and

(c) compare the values of the initial event parameters to the final event parameters.

13. The system according to Claim 12 wherein the processor is further configured to make a diagnosis based upon the comparison.

14. The system according to any one of Claims 12 or 13 wherein the transducers are divided into one or more sets, and an event parameter is a time at which an event occurred in a representative signal of each set and the comparison involves determining an extent of synchrony between two signals.

15. The system according to any one of Claims 12 to 14 wherein an event parameter is an average magnitude of a signal over a time period.

16. The system according to Claim 12 wherein the processor is configured to make a differential diagnosis.

17. The system according to any one of claims 13 to 16 wherein the processor is configured to diagnose asthma on the basis of the comparison.

18. The system according to any one of Claims 13 to 17 wherein the processor is configured to diagnose COPD on the basis of the comparison.

19. The system according to any one of the previous claims further comprising a display device.

20. The system according to Claim 19 wherein the processor if further configured to display on the display device a result of a calculation, diagnosis, or determination made by the processor.

21. The system according to Claim 9 wherein the processor is configured to make a differential diagnosis of COPD and asthma wherein :

(a) the one or more initial event parameters are:

(i) an initial mean value **h** of the signal over the predetermined time interval, $\mathbf{h}_0$, calculated for a representative signal obtained on a first subset of transducers prior to administration of a bronchodilator; and

(ii) an initial time delay, $\overline{\Delta}\tau_0$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

(b) the one or more final event parameters are:

(i) a final h, $\mathbf{h}_1$, calculated for a representative signal obtained on the first subset of transducers after administration of the bronchodilator; and

(ii) an final time delay, $\overline{\Delta}\tau_1$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

and wherein the processing comprises:

i) calculating a change in **h**, Δh, where $\Delta h = h_1 - h_0$;

ii) calculating a change in $\overline{\Delta}\tau$, $\Delta(\overline{\Delta}\tau)$, where $\Delta(\overline{\Delta}\tau) = \overline{\Delta}\tau_1 - \overline{\Delta}\tau_0$;

iii) making a differential diagnosis of COPD if $\Delta(\overline{\Delta}\tau) > d_1$, where d_1 is a predetermined first threshold;

iv) making a differential diagnosis of asthma if (i) $\Delta(\overline{\Delta}\tau) \leq d_1$; and if (ii) $\Delta(\overline{\Delta}\tau) < -d_1$;

v) making a differential diagnosis of COPD if (i) $|\Delta(\overline{\Delta}\tau)| < d_1$, and if (ii) Δh≤0;

vi) making a differential diagnosis of COPD if (i) Δh≥0, and if (ii) $\overline{\Delta}\tau_0 > d_2$, where d2 is a predetermined second threshold; and

vii) making a differential diagnosis of asthma if (i) Δh≥0, and if (ii) $\overline{\Delta}\tau_0 \leq d_2$.

22. A method for analyzing sounds in at least a portion of an individual's respiratory tract comprising:

(a) obtaining an integer N of signals $Z(x_i,t)$ indicative of pressure waves at locations x_i; for i=1 to N over the thorax at times t during a predetermined time interval; and

(b) processing the signals $Z(x_i,t)$, wherein the processing comprises performing at least one event search; and

(c) determining one or more event parameters for one or more events detected in an event search.

23. The method according to Claim 22 wherein an event search is performed on one or more of the signals $Z(x_i,t)$.

24. The method according to Claim 22 wherein an event search is performed on one or more signals $P(x_i,t)$ wherein the signals $P(x_i,t)$ are obtained after performing one or more procedures on one or more of the signals $Z(x_i,t)$ selected from filtering, denoising, smoothing, envelope extraction, applying a mathematical transformation.

25. The method according to Claim 22 wherein the transducers are divided into one or more subsets and the processing comprises, for each of one or more of the subsets, calculating a representative signal from one or more of the signals $Z(x_i,t)$ or $P(x_i,t)$ obtained from transducers in the subset and performing one or more event searches on one or more of the representative signals.

26. The method according to any one of Claims 22 to 25 wherein one or more of the events are selected from an entire breathing cycle, an inspiratory phase of a breathing cycle, and an expiratory phase of a breathing cycle.

27. The method according to Claim 26 wherein the representative signal of a transducer subset is a summation or an average signal of the signals obtained by the transducers in the subset.

28. The method according to any one of Claims 22 to 24 wherein the event search comprises performing any one or more of a peak search, an autocorrelation, a cross correlation with a predetermined function, and a Fourier transform.

29. The method according to any one of Claims 22 to 28 wherein one or more of the event parameters are selected from the group comprising a time that an event occurred, a duration of an event, a magnitude of an event, a height of a peak associated with the event, the width of a peak associated with the event in a signal at half peak height, a half time to rise of a peak associated with the event in a signal, a half time to fall of a peak, an area under a peak; a maximum of the signal during the event, a ratio of a maximum during an inspiratory phase to a maximum during an expiratory phase, a ratio of a duration of an inspiratory phase to a duration of an expiratory phase, and a morphology of a signal during the event.

30. The method according to any one of Claims 22 to 29 further comprising calculating one or more comparisons between an event parameter value and a predetermined threshold or range of values.

31. The method according to Claim 25 further comprising, for each of one or more pairs of a first representative signal and a second representative signal, calculating one or more comparisons between an event parameter value calculated for the first representative function and an event parameter value calculated for the second representative function.

32. The method according to Claim 30 or 31 further comprising making a diagnosis based upon one or more of the comparisons.

33. The method according to anyone of Claims 22 to 32 further comprising:

(a) determining values of one or more initial event parameters;

(b) determining values of the one or more final event parameters; and

(c) comparing the values of the initial event parameters to the final event parameters.

34. The method according to Claim 33 further comprising performing a medical treatment of the individual after determining the initial event parameters.

35. The method according to Claim 34 wherein the medical treatment comprises administering a bronchodilator.

36. The method according to any one of Claims 33 to 35 comprising making a diagnosis based upon the comparison.

37. The method according to any one of Claims 33or 36 wherein the transducers are divided into one or more sets, and an event parameter is a time at which an event occurred in a representative signal of each set and the comparison involves determining an extent of synchrony between two signals.

38. The method according to any one of Claims 33to 36 wherein an event parameter is an average magnitude of a signal over a time period.

39. The method according to Claim 31 further comprising making a differential diagnosis.

40. The method according to any one of claims 34 to 39 further comprising diagnosing asthma on the basis of the comparison.

41. The method according to any one of Claims 34 to 40 further comprising diagnosing COPD on the basis of the comparison.

42. The method according to Claim 36 wherein the differential diagnosis is a differential diagnosis of COPD and asthma wherein :

(a) the one or more initial event parameters are:

(i) an initial the mean value **h** of the signal over the predetermined time interval, $\mathbf{h}_0$, calculated for a representative signal obtained on a first subset of transducers prior to administration of a bronchodilator; and

(ii) an initial time delay, $\overline{\Delta\tau}_0$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

(b) the one or more final event parameters are:

(i) a final h, $\mathbf{h}_1$, calculated for a representative signal obtained on the first subset of transducers after administration of the bronchodilator; and

(ii) an final time delay, $\overline{\Delta\tau}_1$, between a time of a peak in a signal calculated for a second transducer set and a time of a corresponding peak calculated for a third transducer set prior to administration of the bronchodilator;

and wherein the method comprises:

(a) calculating a change in **h**, Δh, where $\Delta h = h_1 - h_0$;

(b) calculating a change in $\overline{\Delta\tau}$, $\Delta(\overline{\Delta\tau})$, where $\Delta(\overline{\Delta\tau}) = \overline{\Delta\tau}_1 - \overline{\Delta\tau}_0$;

(c) making a differential diagnosis of COPD if $\Delta(\overline{\Delta\tau}) > d_1$, where d_1 is a predetermined first threshold;

(d) making a differential diagnosis of asthma if (i) $\Delta(\overline{\Delta\tau}) \leq d_1$; and if (ii) $\Delta(\overline{\Delta\tau}) < -d_1$;

(e) making a differential diagnosis of COPD if (i) $|\Delta(\overline{\Delta\tau})| < d_1$, and if (ii) $\Delta h \leq 0$;

(f) making a differential diagnosis of COPD if (i) $\Delta h \geq 0$, and if (ii) $\overline{\Delta}\tau_0 > d_2$, where d2 is a predetermined second threshold; and

(g) making a differential diagnosis of asthma if (i) $\Delta h \geq 0$, and if (ii) $\overline{\Delta}\tau_0 \leq d_2$.

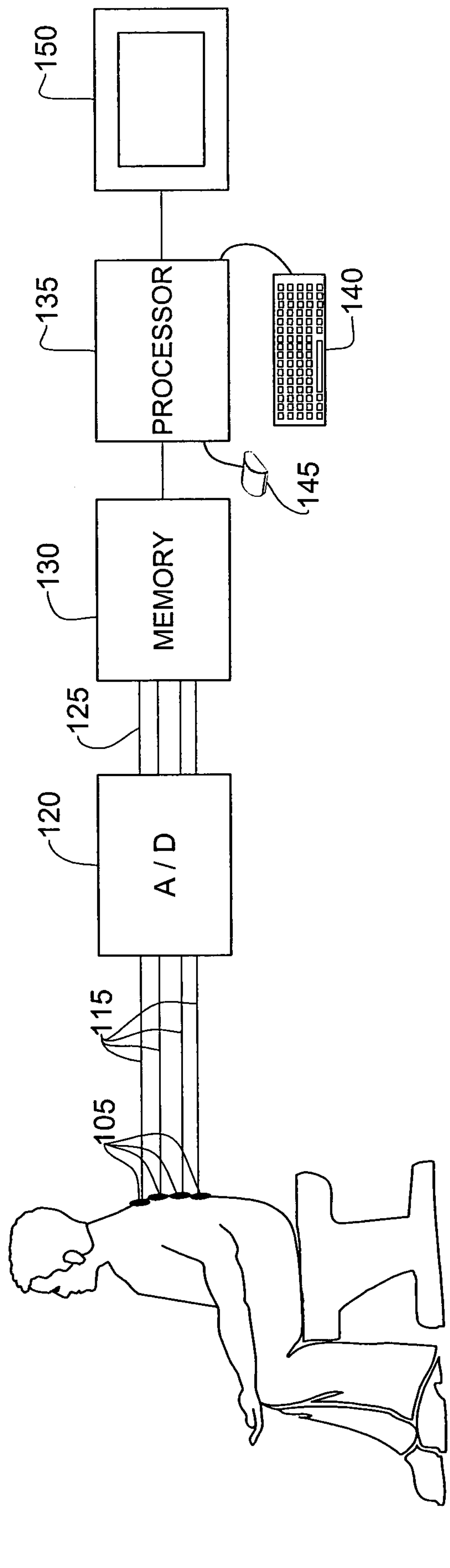

FIG. 1

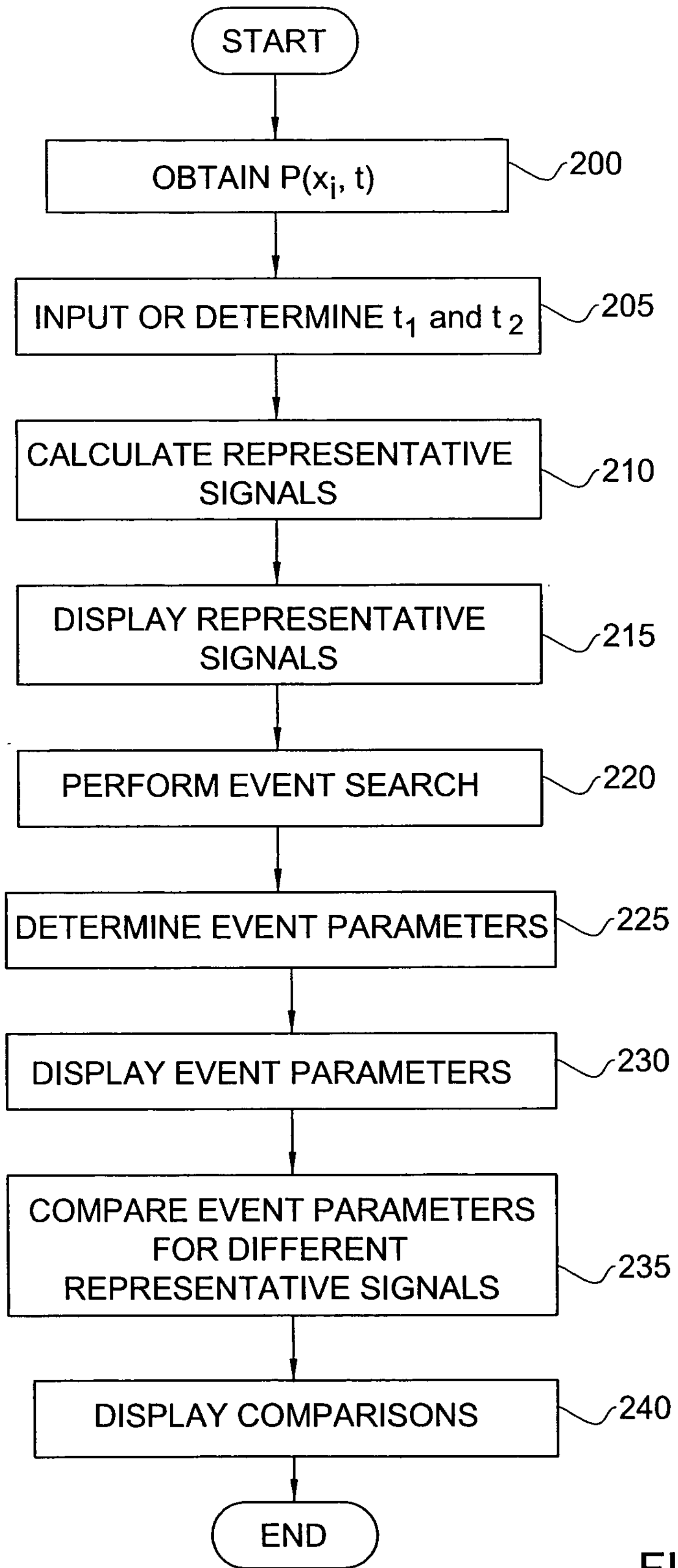
START
OBTAIN $P(x_i, t)$
200
INPUT OR DETERMINE t_1 and t_2
205
CALCULATE REPRESENTATIVE SIGNALS
210
DISPLAY REPRESENTATIVE SIGNALS
215
PERFORM EVENT SEARCH
220
DETERMINE EVENT PARAMETERS
225
DISPLAY EVENT PARAMETERS
230
COMPARE EVENT PARAMETERS FOR DIFFERENT REPRESENTATIVE SIGNALS
235
DISPLAY COMPARISONS
240
END

FIG. 2

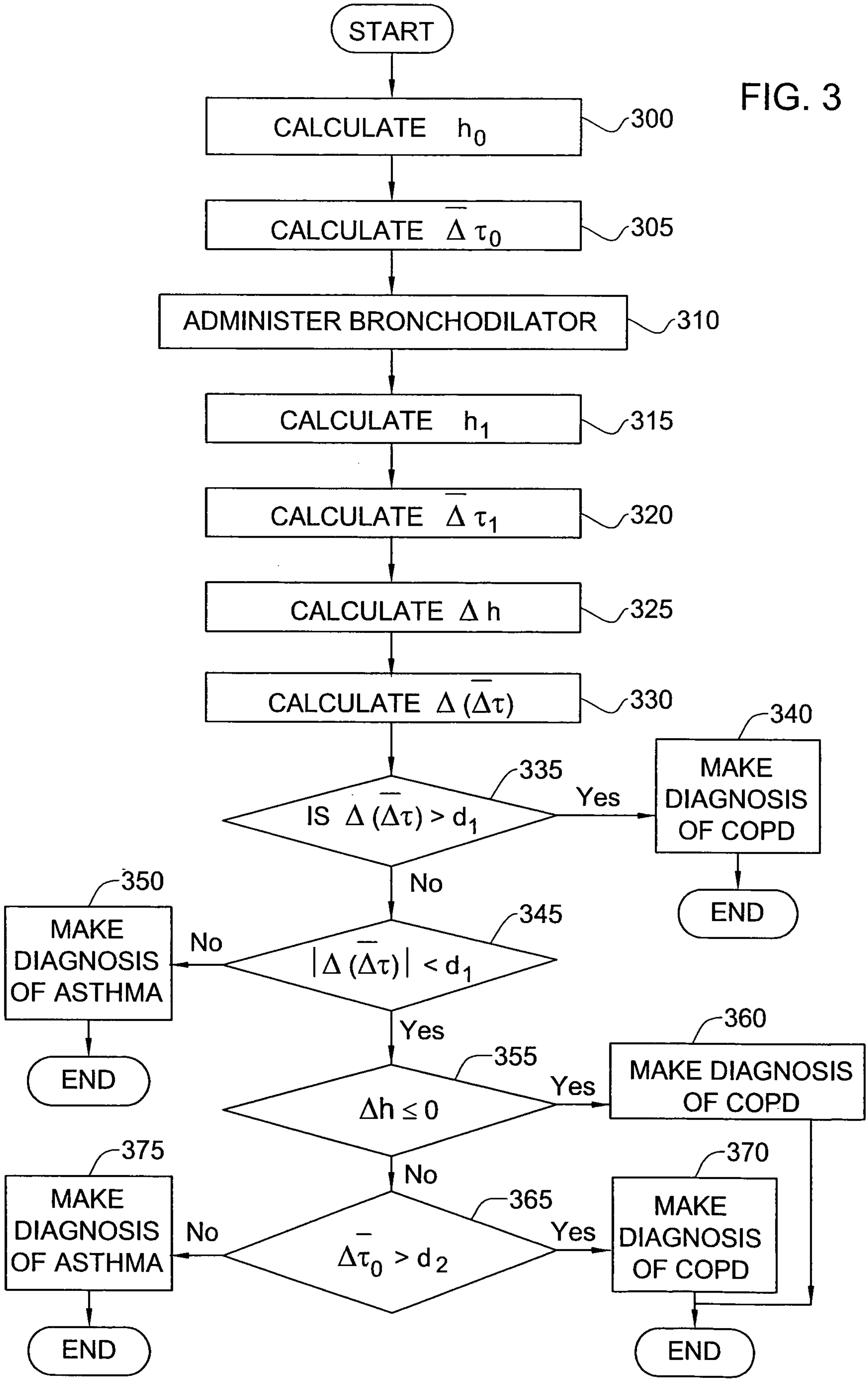
START
CALCULATE h_0
300
CALCULATE $\bar{\Delta}\tau_0$
305
ADMINISTER BRONCHODILATOR
310
CALCULATE h_1
315
CALCULATE $\bar{\Delta}\tau_1$
320
CALCULATE Δh
325
CALCULATE $\Delta(\bar{\Delta\tau})$
330
IS $\Delta(\bar{\Delta\tau}) > d_1$
335
Yes
MAKE DIAGNOSIS OF COPD
340
END
No
$|\Delta(\bar{\Delta\tau})| < d_1$
345
No
MAKE DIAGNOSIS OF ASTHMA
350
END
Yes
$\Delta h \leq 0$
355
Yes
MAKE DIAGNOSIS OF COPD
360
No
$\bar{\Delta}\tau_0 > d_2$
365
Yes
MAKE DIAGNOSIS OF COPD
370
No
MAKE DIAGNOSIS OF ASTHMA
375
END
END

FIG. 3

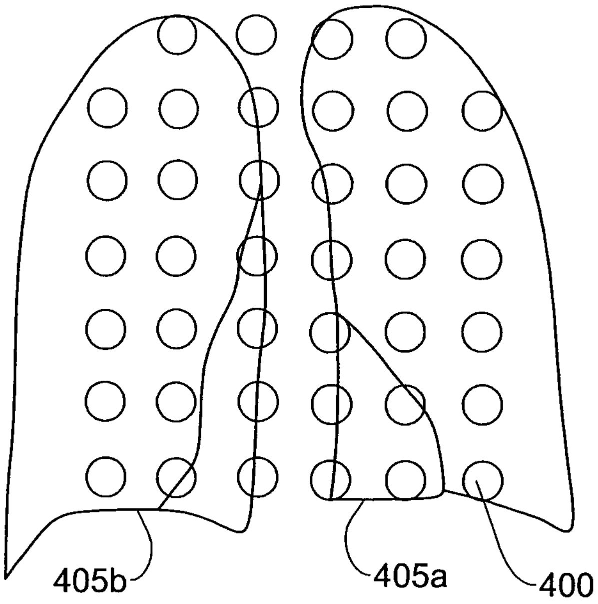

FIG. 4

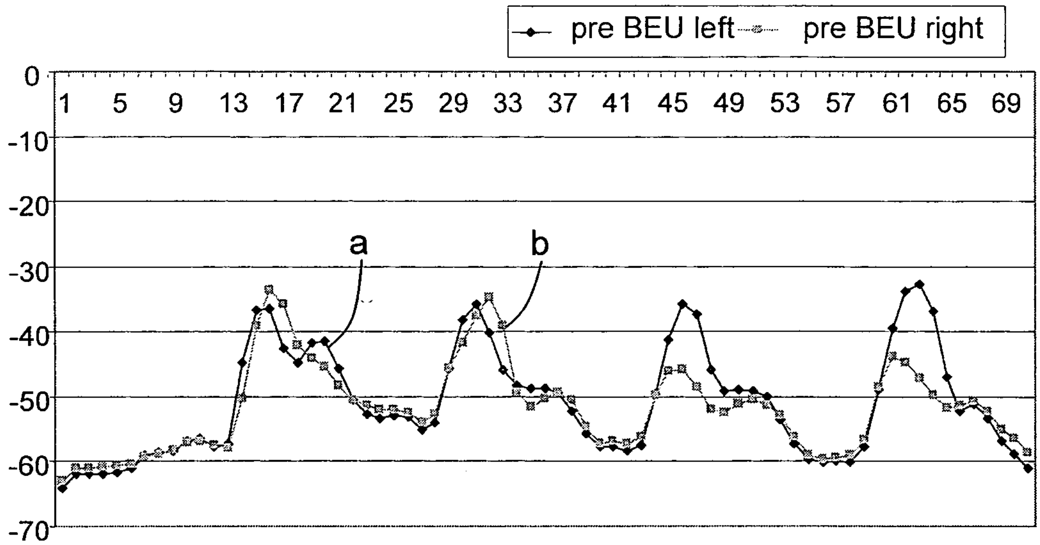

FIG. 5A

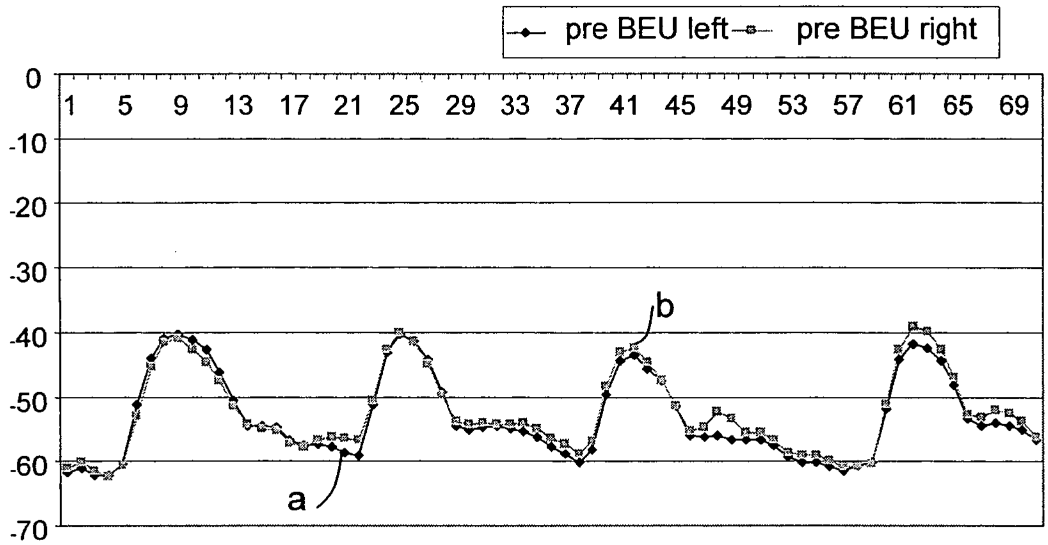

FIG. 5B

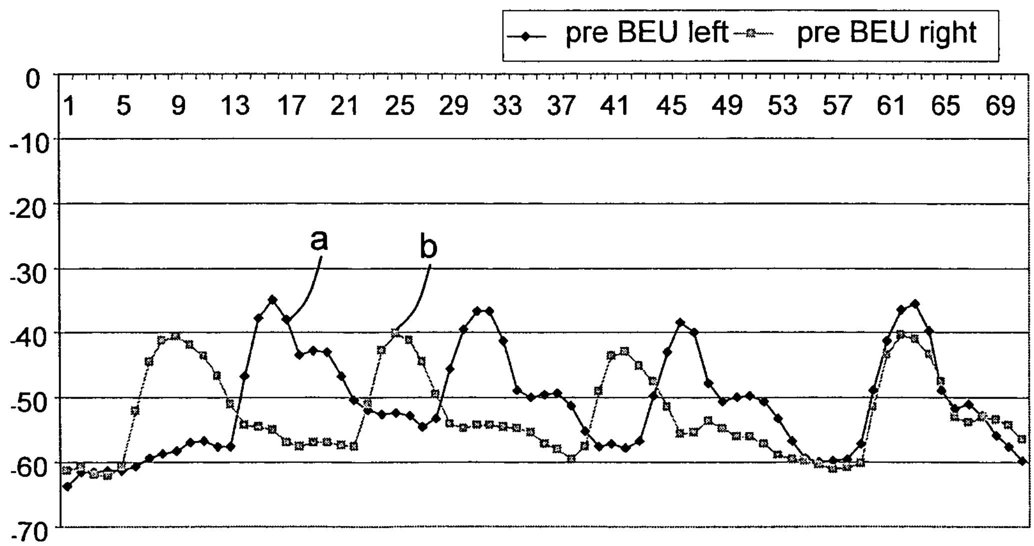

FIG. 5C

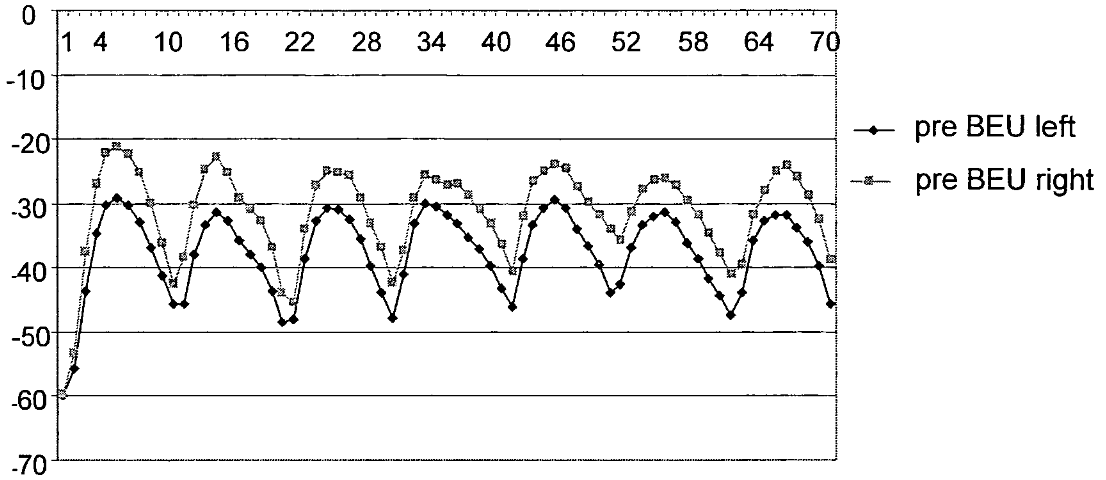

FIG. 6A

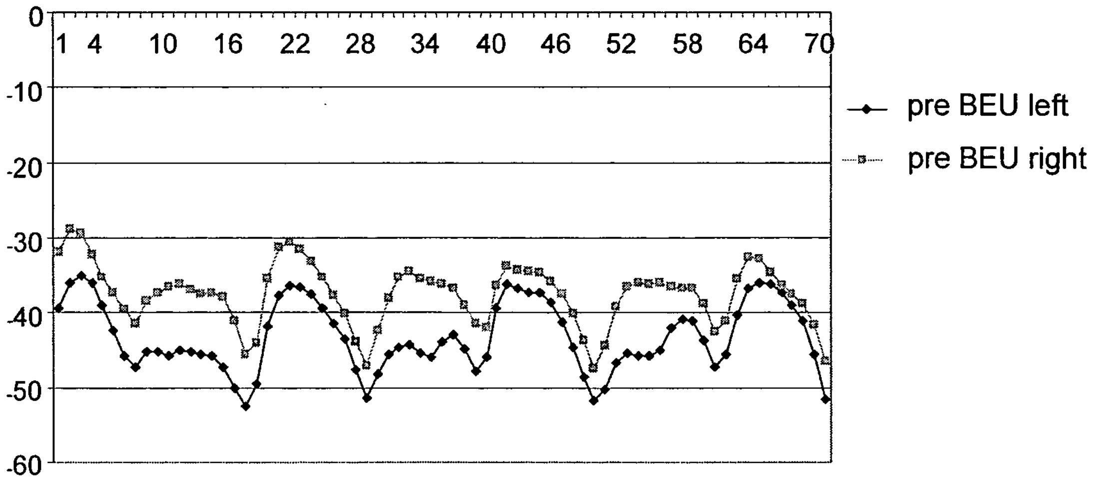

FIG. 6B

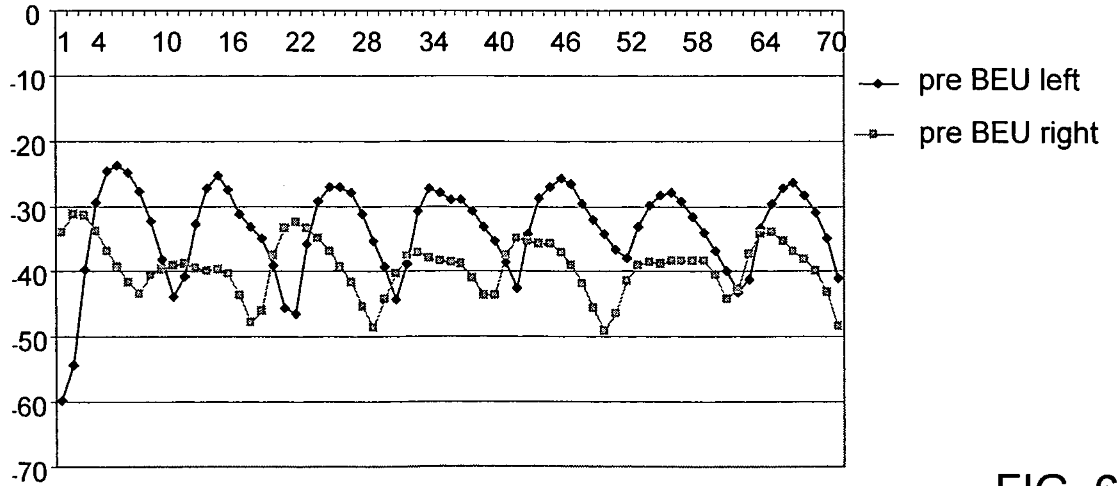

FIG. 6C

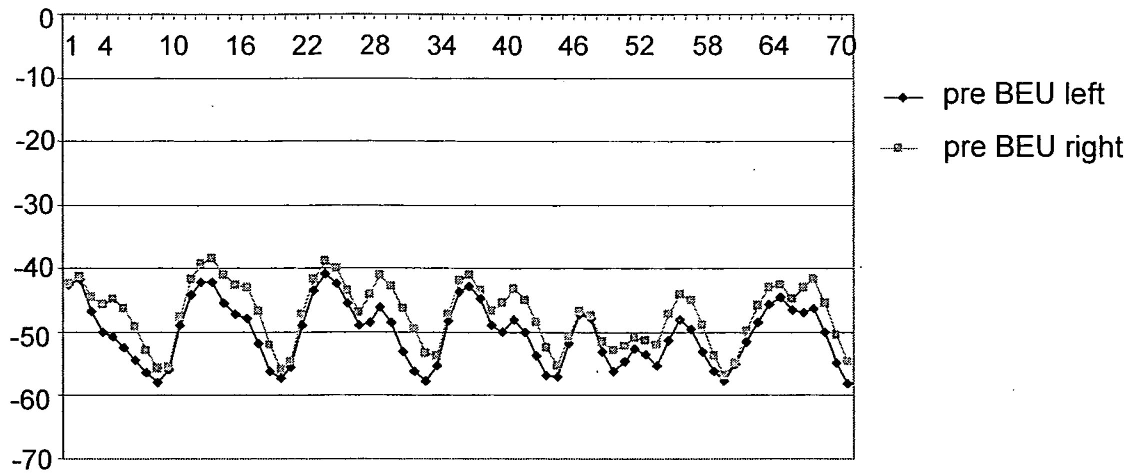

FIG. 7A

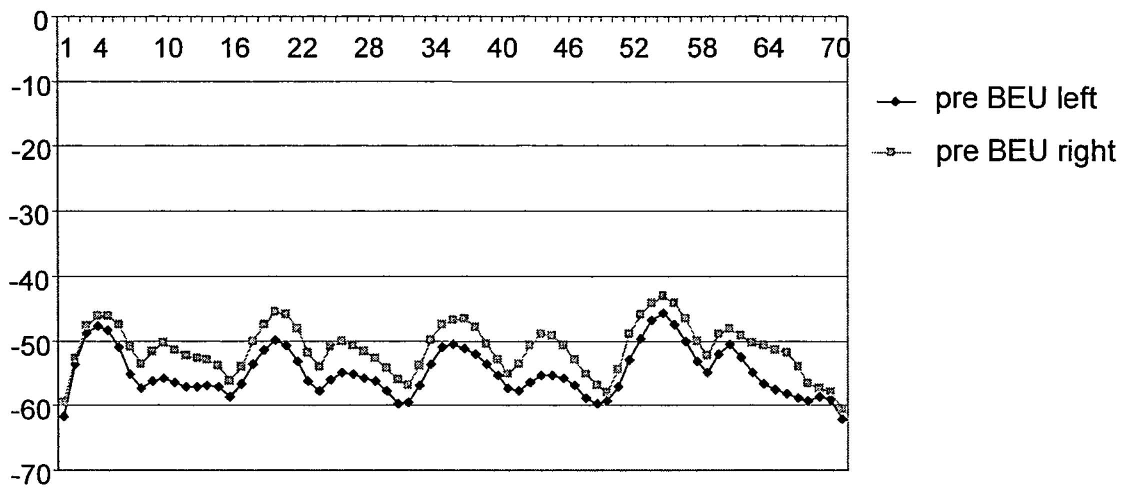

FIG. 7B

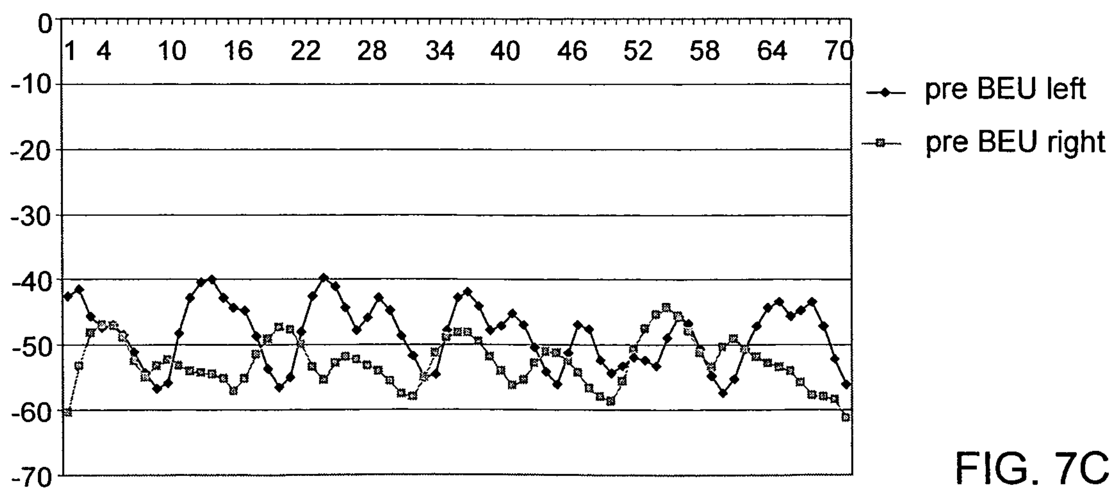

FIG. 7C

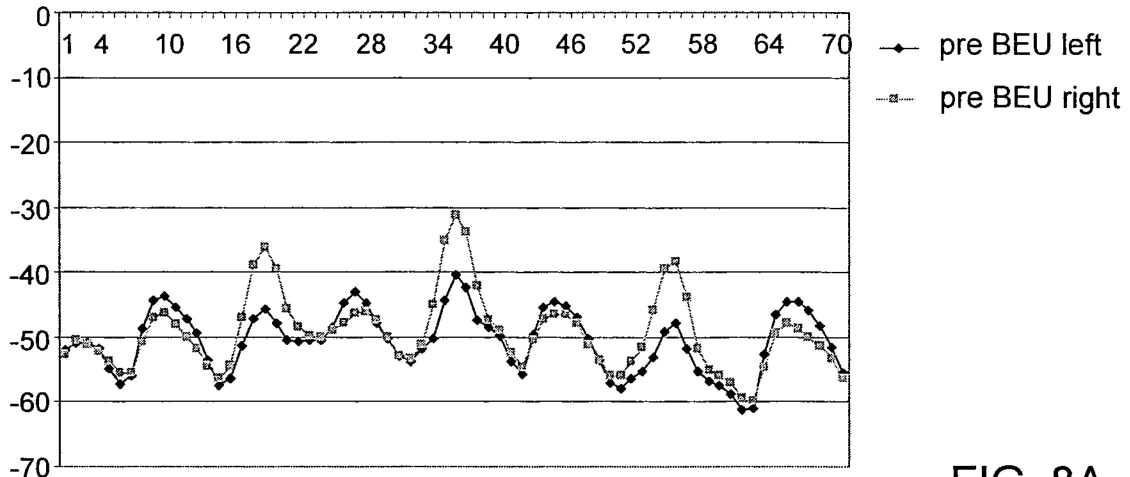

FIG. 8A

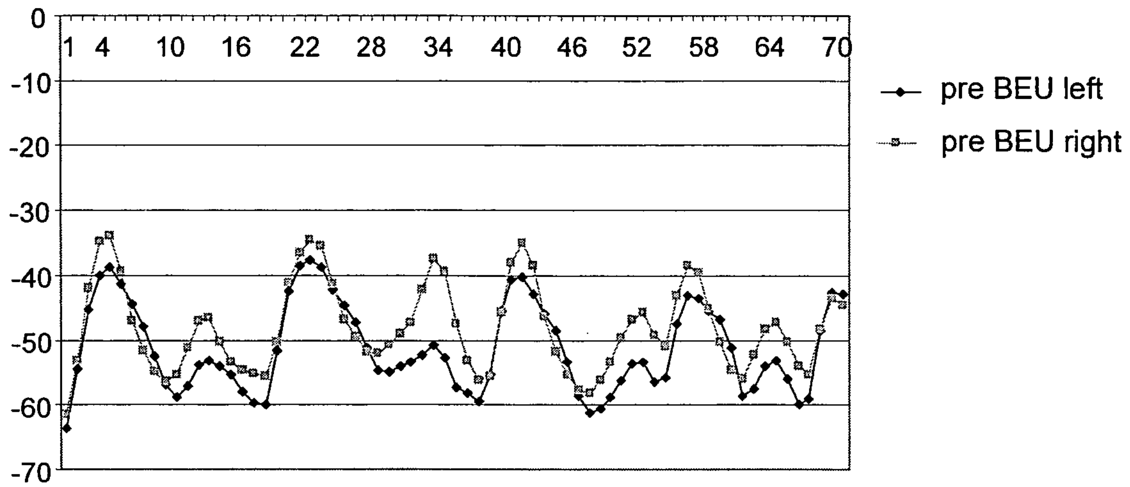

FIG. 8B

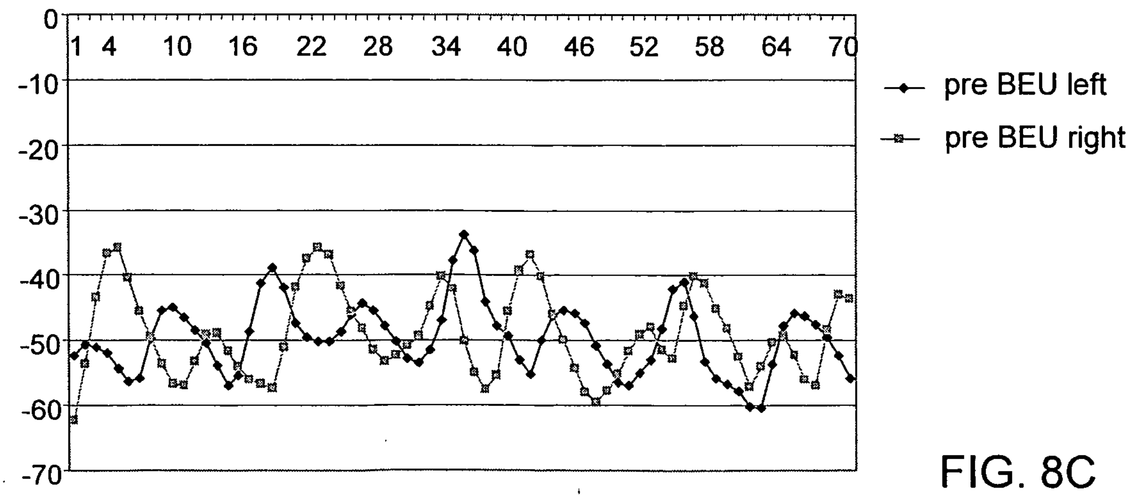

FIG. 8C

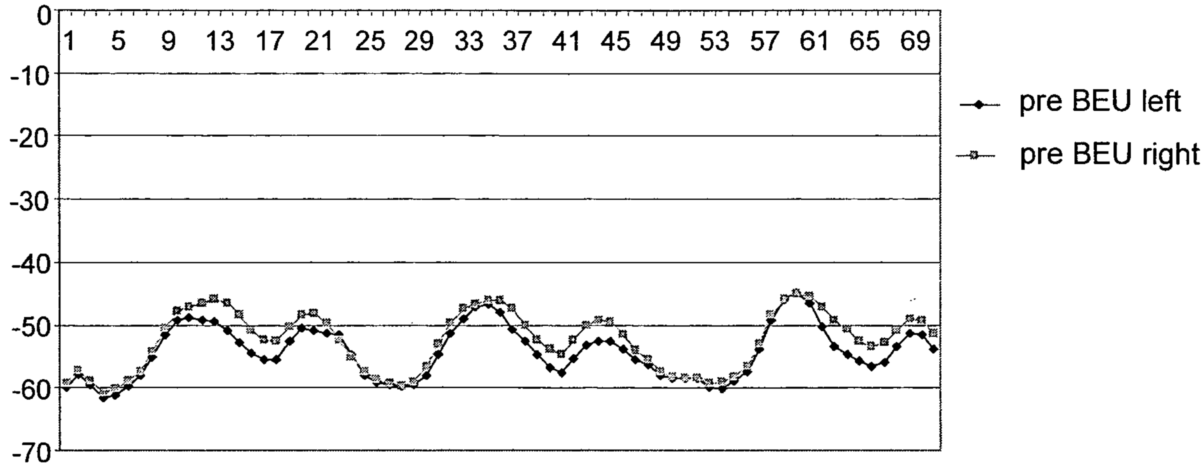

FIG. 9A

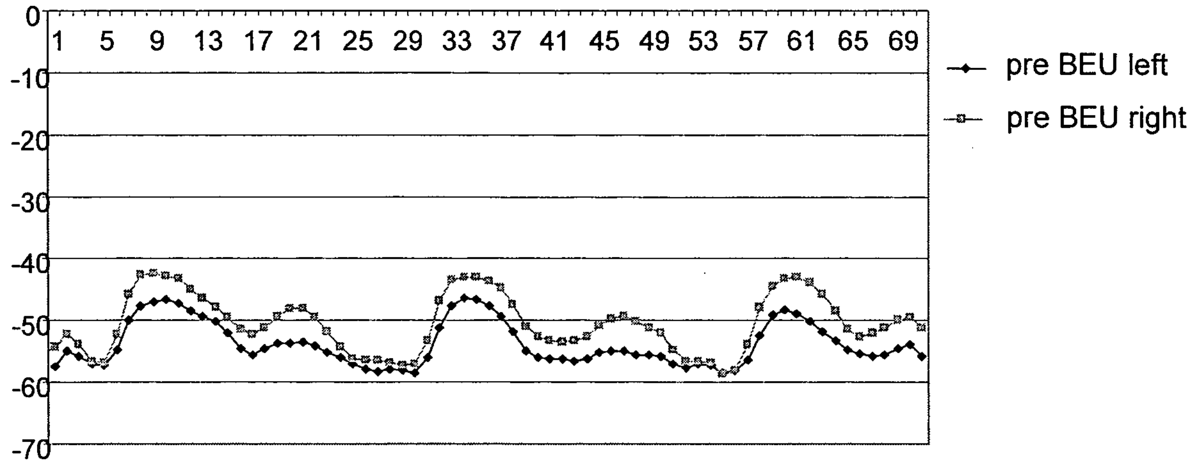

FIG. 9B

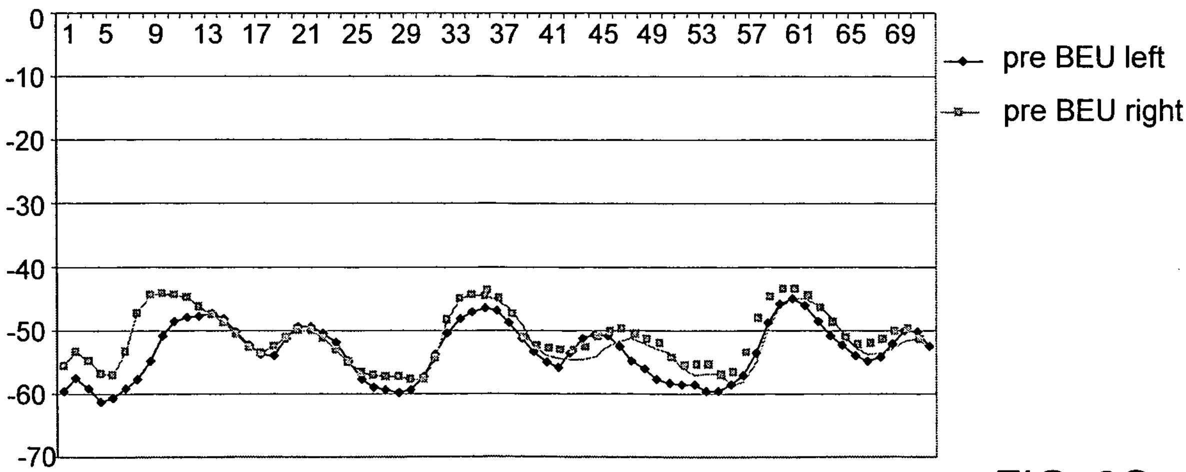

FIG. 9C

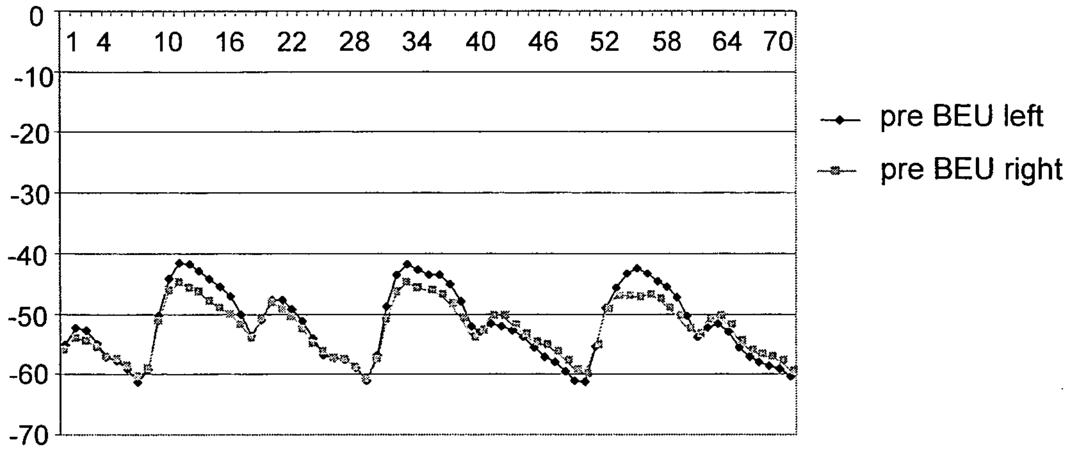

FIG. 10A

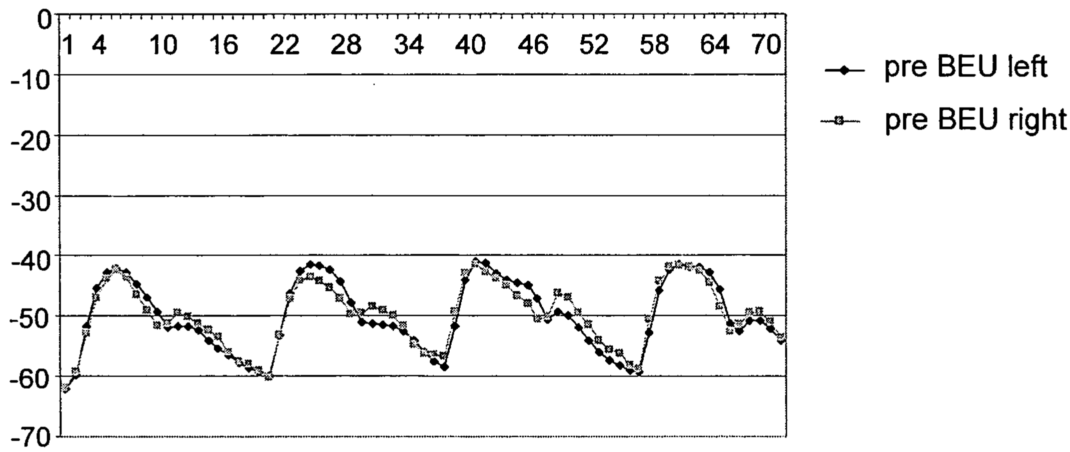

FIG. 10B

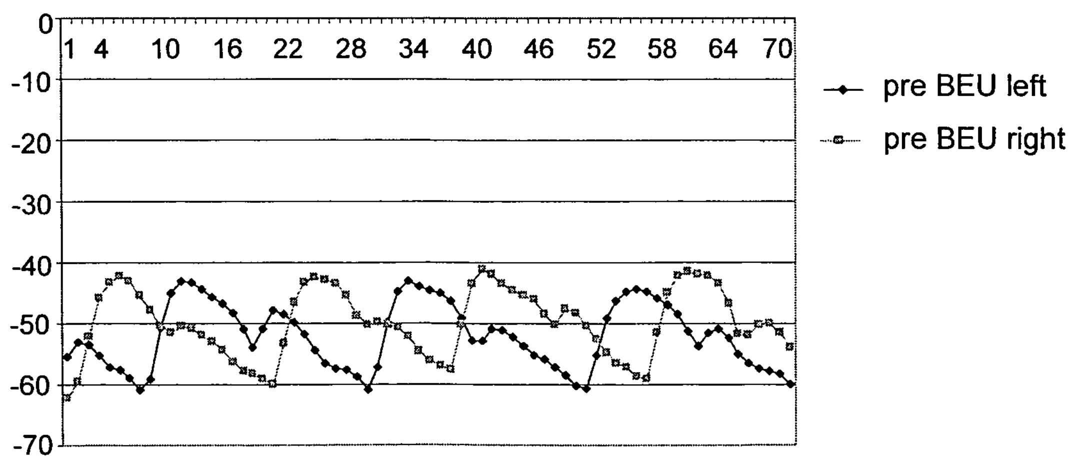

FIG. 10C

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2009/000400

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/04 A61B5/08 A61B7/00 A61B7/02 G06F19/00
ADD. A61B7/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DELLINGER R P ET AL: "Dynamic visualization of lung sounds with a vibration response device: A case series" RESPIRATION, KARGER, BASEL, CH, vol. 75, no. 1, 1 January 2008 (2008-01-01), pages 60-72, XP008095653 ISSN: 0025-7931	1-10,12, 13,15, 19,20
Y	page 62, left-hand column, line 1 - page 64, right-hand column, line 32; figures 1,2a,2b,3,4 page 65, right-hand column, line 10 - page 67, right-hand column, line 30; figures 7a,7b page 69, right-hand column, lines 22-42 page 70, left-hand column, lines 20-25 page 71, right-hand column, line 35 - page 72, right-hand column, line 11 -----	11,14, 16-18,21

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 July 2009	03/08/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Daoukou, Eleni

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2009/000400

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/011132 A (UNIV BELFAST [GB]; MURRAY JIM [GB]; DONNELLY PETER [GB]; FEE JOHN PATR) 13 February 2003 (2003-02-13)	1,9,11
A	page 9, line 11 - page 10, line 22; figures 1,3 page 12, line 25 - page 14, line 11 page 14, line 29 - page 15, line 4 -----	16
X	WO 97/29687 A (GULL MEDICAL SOFTWARE SYSTEMS [IL]; TSIVION YORAM [IL]; SHACHAR MENASH) 21 August 1997 (1997-08-21)	1
A	page 6, lines 3-9; figures 1,3 page 7, lines 1-24 page 9, line 29 - page 10, line 7 page 10, lines 10-24; figures 10,11 page 11, lines 18-28; figure 15 -----	16-18
X	EP 0 956 820 A (KARMEL MEDICAL ACOUSTIC TECHNO [IL]) 17 November 1999 (1999-11-17)	1
A	paragraphs [0101] - [0106], [0117] - [0127], [0147] - [0179]; figures 1,2,4 -----	2-4,12, 14
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2009/000400

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2009/000400

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 22-42
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IL2009/000400

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