Technical Note

AUTOMATED SYSTEM FOR DETAILED MEASUREMENT OF RESPIRATORY MECHANICS

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ABSTRACT. Objective. The mechanical properties of the respiratory system (i.e., elastance and resistance) depend on the frequency, tidal volume, and shape of the flow waveform used for forcing. We developed a system to facilitate accurate measurements of elastance and resistance in laboratory and clinical settings at the frequencies and tidal volumes in the physiologic range of breathing. **Methods.** A personal computer (PC) is used to drive a common clinically used ventilator while simultaneously collecting measurements of airway flow, airway pressure, and esophageal pressure from the experimental subject or animal at different frequencies and tidal volumes. Analysis analogous to discrete Fourier transform at the fundamental frequency (i.e., ventilator setting) is used to calculate elastances and resistances of the total respiratory system and its components, the lungs and the chest wall. We have shown that this analysis is independent of the high-frequency harmonics that are present in the waveform from clinical ventilators. **Results.** The system has been used successfully to make measurements in anesthetized/paralyzed dogs and awake or anesthetized human volunteers in the laboratory, and in anesthetized humans in the operating room and intensive care unit. Elastances and resistances obtained with this approach are the same as those obtained during more controlled conditions, e.g., sinusoidal forcing. **Conclusions.** Accurate, standardized measurements of lung and chest wall properties can be obtained in many settings with relative ease with the system described. These properties, and their frequency and tidal volume dependences in the physiologic range, provide important information to aid in the understanding of changes in respiratory function caused by day-to-day conditions, clinical intervention and pathologies.

KEY WORDS. Lung, mechanics: resistance, compliance, elastance.

INTRODUCTION

This technical note describes the details of an automated computer-ventilator-transducer system and analysis techniques that have facilitated the accurate measurement of respiratory system properties in the laboratory, operating room, and intensive care unit at the University of Maryland.

Problems in measuring respiratory mechanics

Evaluation of respiratory mechanics has been made with many different techniques. We have recently shown that measurements of the mechanical properties of the respiratory system, resistance and elastance, in the normal range of respiratory frequency and tidal volume, are especially useful for understanding breathing in different

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conditions [1-7]. Besides being relevant to the mechanical behavior during actual breathing, frequency and tidal volume dependences in the normal range contain useful information that is not obtained with other techniques [2,4,5,7]. This information increases the understanding of fundamental respiratory tissue behavior in different conditions, and may be clinically useful in detecting and treating respiratory pathologies. However, frequency and tidal volume dependences in the normal range of breathing also confound interpretation of "resistances" and "elastances" calculated from pressure and flow waveforms collected from mechanically ventilated patients. Although accuracy of calculation would be enhanced if pure sinusoidal forcing (i.e., consisting of a single "fundamental" frequency and amplitude) could be used, patient care precludes this. Rather, the pattern of inspiratory flow varies among ventilators and their settings, while that of expiratory flow is determined by passive recoil of the lungs. The resulting nonsinusoidal waveforms consist of a fundamental frequency and various high-frequency, low amplitude harmonics. Most analysis techniques do not account for these higher harmonics, and the "resistance" and "elastance" calculated from them may be ambiguous [2,4]. In the Methods and Materials section, we describe an approach to overcome these problems.

Minimum requirements for measuring respiratory mechanics

To make easily interpretable measurements from mechanically ventilated patients, spontaneous breathing efforts must be absent, since we have shown that respiratory muscle contraction changes the mechanical impedance of the respiratory system [3]. Phasic contractions would be especially problematic, since measured pressure changes would not merely represent the passive properties of the system. Airway flow must be measured, usually with a pneumotachometer in conjunction with a differential pressure transducer; patients are usually intubated with an endotracheal tube (ETT); and the pneumotachometer should be placed in line between the ETT and the "Y" piece of the ventilator tubing. The ETT should have a port to measure airway pressure (P_{aw}) at its tip (for example, NCC Malincrodt Hi-Lo Jet, Glens Falls, N.Y., U.S.A. Accuracy of elastance and resistance from such measurements has been verified by ourselves [7] and others [8]. To separate lung from chest wall properties, a thin-walled latex balloon attached to polyethylene tubing is used to measure esophageal pressure (P_{es}). In anesthetized patients, the balloon can be placed by first inserting it into wider, stiffer tubing (for example, an "esophageal stethoscope"); the tubing is inserted until the tip is estimated to be slightly past nipple level and then it is removed, leaving the balloon in place. Final placement is checked and adjusted with a method modified from Baydur and colleagues [9]: If the ETT is occluded, changes in P_{aw} and P_{es} (we monitor these as an X-Y plot on an oscilloscope) should be equal when the abdomen is compressed.

Changes in pressure and flow are then measured during mechanical ventilation. To calculate mechanics, pressure and flow signals from several breaths are usually digitized through an analog/digital (A/D) converter, stored on a personal computer (PC), and ensemble averaged. We have described a way to get accurate measurements of elastance and resistance if inspiratory flow pattern is a step (as with most clinical ventilators), as long as inspiratory-to-expiratory (I:E) time ratio is 1:1 [2,4]. In this method, discrete Fourier analysis, considering only the fundamental frequency (i.e., the frequency setting of the ventilator) is performed on the averaged pressure and flow waveforms. The complex ratios of P_{aw} and P_{es} to flow can be used to calculate elastances and resistances of the total respiratory system (E_{rs} and R_{rs}) and chest wall (E_{cw} and R_{cw}), respectively. Lung elastance and resistance (E_L and R_L) equal the corresponding differences between the total and the chest wall. Alternately, if the difference between P_{aw} and P_{es} (P_L) is measured with a differential pressure transducer, E_L and R_L can be calculated from the complex ratio of P_L to flow. See Data Analysis in the Methods and Materials section for more details.

Limitations of most systems in measure respiratory mechanics

To facilitate ensemble averaging, it is important that the ventilator frequency is precisely set. Synchronization of ventilation and data collection is also helpful. Ability to change ventilatory parameters quickly, precisely, and conveniently from the keyboard is useful in many clinical settings, for example in the operating room, where time and space are limited.

Although, as mentioned above, measurements are possible if the inspiratory flow pattern is a step, as on most clinical ventilators, accuracy is enhanced if the inspiratory flow is sinusoidal [2,4]. Such a waveform is not usually available in clinical ventilators.

Since we have shown that elastance and resistance of the lungs and chest wall depend on frequency, even in subjects with healthy respiratory systems [1,6], it is important to repeat measurements at different frequencies. Moreover, we [5] and others [10,11] have shown that

the frequency dependence of elastance and resistance may be important in understanding respiratory behavior and in detecting pathology. If ventilator frequency is increased, the pressure at the end of a breath may not return to atmospheric, since the lungs may not have enough time to empty. Thus, pressure tends to increase as frequency increases, and the volume of the lungs at the end of a breath (i.e., functional residual capacity [FRC]) increases systematically. This type of positive end-expiratory pressure (PEEP) is called "intrinsic PEEP," and could be especially high in patients with lung pathology [12]. Even if "external" PEEP is purposely applied to increase FRC, as is often done clinically, FRC usually will increase if frequency is raised. We have shown that changes in FRC can have a large effect on elastance and resistance [13]. Unless FRC is prevented from increasing, measurements made as frequency is increased will be difficult to interpret, since changes in elastance and resistance will represent both frequency and FRC effects. As described below, we have devised a system to circumvent this problem.

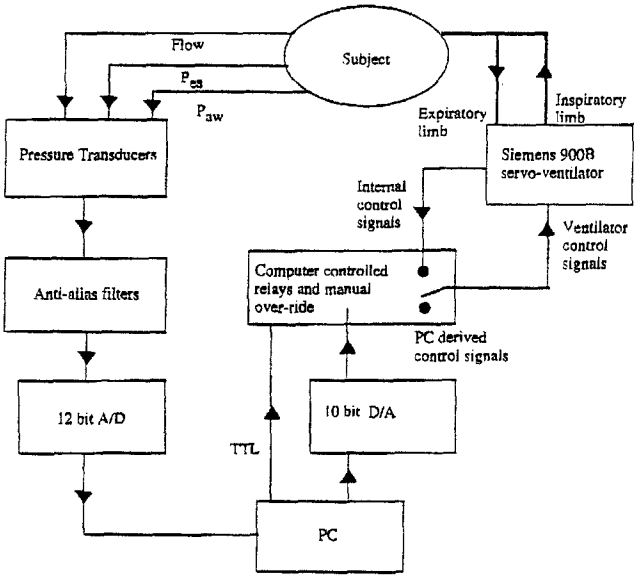

Fig. 1. Schematic diagram of the system used to control the ventilator and simultaneously record airway (P_{aw}) and esophageal (P_{es}) pressures and flow through the airways. See text for details.

METHODS AND MATERIALS

The measuring system

The system used to measure respiratory mechanics by the Department of Anesthesiology at the University of Maryland system is outlined in Figure 1. The unique aspect of the system is that a PC is used to drive the ventilator and collect data simultaneously. The interface with the ventilator provides for automated control of frequency, tidal volume, and inspiratory flow waveform, and for synchronization between inspiration and expiration. The software allows for control of ventilatory parameters from the keyboard, and for data collection, storage, and analysis.

Three signals are diverted from the internals of a ventilator (900B Siemens, Solna, Sweden) to the PC to provide automated control of respiratory frequency and inspiratory flow waveform (there is no reason a 900C model cannot be used). Unless computer control is desired, these signals are returned unchanged to the ventilator, and the ventilator functions. Under computer control, these three signals are substituted with signals generated by the computer. The three signals are:

1. A transistor-transistor logic (TTL) timing clock that controls the opening and closing of the inspiratory and expiratory valves.
2. A TTL signal that indicates inspiratory flow. Automated control is assumed only at the transition between the end of expiratory flow and the start of inspiratory flow – i.e., the beginning of a breath.
3. An analog voltage that drives the stepping motor controlling the magnitude of the inspiratory flow. Expiration is passive and simply involves fully opening the expiratory valve.

In its normal working mode, a potentiometer on the front panel of the 900B adjusts tidal volume by changing the feedback resistance in an amplifier circuit. During automatic control, the 900B potentiometer is bypassed and replaced by a digital potentiometer. The digital potentiometer is adjusted by TTL outputs from the computer, and the value of the resistance required to produce a known tidal volume at each frequency is determined empirically. The controlling software also allows for minor incremental changes in the resistance to adjust for operating conditions by simple keyboard command ("up arrow" to increase volume; "down arrow" to decrease volume; about 1% change in tidal volume for each keystroke).

The three controlling signals and volume potentiometer are selected by computer-controlled relays. Thus, the computer could select whether the 900B runs as a stand-alone unit or is controlled externally. For safety concerns, the relays could be overidden by a manual switch on the front panel of the ventilator.

The flow waveform produced by our system is "quasi-sinusoidal": sinusoidal inspiration with expiration caused

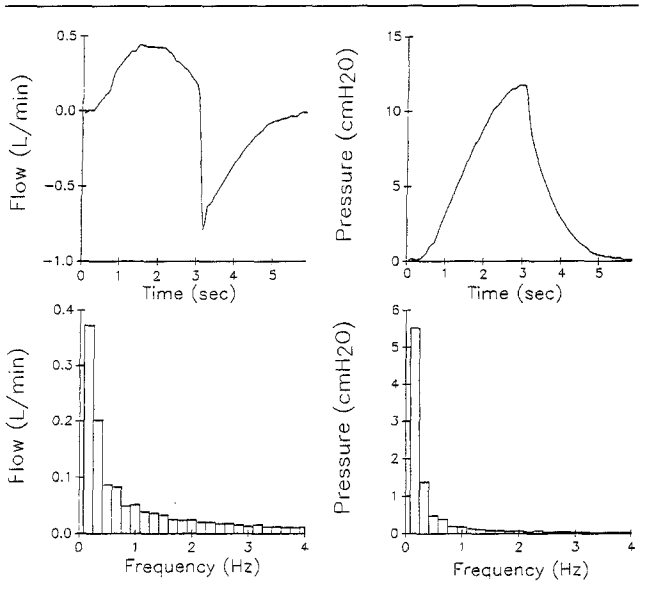

Fig. 2. (Top graphs) Examples of flow and airway pressure waveforms collected from an anesthetized subject during forcing at 800-ml tidal volume and frequency of 10 breaths/min (0.167 Hz). Each curve is the average of three breaths. (Bottom graphs) Magnitudes of flow and airway pressure at each harmonic frequency comprising the waveforms, calculated by discrete Fourier transform.

by passive deflation of the lungs and chest wall (Fig 2). Most of the magnitude of both flow and pressure are contained in the ventilator frequency (see Fig 2). The respiratory cycle is divided into 200 points, equally spaced in time, regardless of respiratory frequency. Analog data are output at each of the first 100 points to control the inspiratory valve and thus the flow waveform. A TTL clock signal is sent to the ventilator 100 times during a respiratory cycle. The internal Siemens logic opens the expiratory valve on the 50th clock signal (with the I : E ratio set at 1 : 1) and closes the valve on the 100th clock signal. Similarly, the Siemens inspiratory flag indicates true during the first 49 clock signals and indicates false otherwise. In addition, analog data are sampled at the same time that the clock signal is output, giving a sample rate of 100 times the fundamental frequency. The highest respiratory frequency we usually use is 30 breaths/min (0.5 Hz), giving a sample rate of 50 Hz. To remove spurious high-frequency components of the sampled data, 5-Hz anti-alias filters are used. After each breath, the computer pauses and checks that either the expiratory flow is less than a preset minimum or that P_{aw} was less than a preset minimum (i.e., PEEP). Input from the keyboard is monitored at the end of each breath. Keyboard input could relinquish automatic control, change or adjust the tidal volume, change the respiratory frequency, or initiate data collection.

Data collection

Typically, "baseline" measurements are first made at 10 breaths/min and a tidal volume determined by the attending physician (usually about 800 ml). PEEP may or may not be applied. Pressure and flow signals are continually monitored for lack of noise or indications of spontaneous breathing, and for reproducibility between each breath. If acceptable, collection and storage of three breaths of data (100 points/breath) to a disk file is initiated by a keyboard stroke. Frequency or tidal volume is then changed by another keystroke and, after one or two transient breaths, collection can be repeated. In patients, we usually collect data at eight combinations of frequency and tidal volume. This is accomplished in less than 5 min. If conditions remain constant, we can repeat the sequence. If conditions change – for example, during a surgical intervention or a change in PEEP – we repeat measurements when stability is achieved for the necessary 5 min. During periods where no keystroke is used to collect and store data, the software will automatically initiate collection and analysis of three breaths each time 12 breaths go by in succession. Lung, chest wall, and total elastances and resistances, as well as tidal volume and time, are displayed on screen and printed out. Thus, a continual, printed record of the course of the study is available.

Data analysis

The data collected over a period of three breaths is superimposed to produce one averaged breath. Because data collection is synchronized with the ventilator, it is trivial to determine the start and end of each breath:

$$X(n) = [X(n) + X(n+100) + X(n+200)]/3 \quad n = 1, \ldots, 100.$$

The average flow is subtracted from the flow signal to remove transducer or electronic drift. The flow signal is then integrated to give volume, and tidal volume is taken as the peak volume during the breath. For flow and each measured pressure waveform, we use an algorithm to perform a simplified version of discrete Fourier transform at the fundamental frequency only (where $k = 1$):

$$X(k) = 1/N \sum_{n=0}^{N-1} x(n) * \cos(2\pi kn/N) - jx(n) * \sin(2\pi kn/N).$$

Thus, the real and imaginary parts of the waveform can be written as:

$$\mathrm{Re} = 1/N \sum_{n=0}^{N-1} x(n) * \cos(2\pi kn/N).$$

$$\mathrm{Im} = 1/N \sum_{n=0}^{N-1} x(n) * \sin(2\pi kn/N).$$

The resistance is calculated as:

$$\text{Resistance} = \mathrm{Re}[X(\mathrm{p})/X(\mathrm{f})],$$

where p = pressure and f = flow. This equates in the frequency domain to:

$$\{[\mathrm{Re}(\mathrm{f}) * \mathrm{Re}(\mathrm{p})] + [\mathrm{Im}(\mathrm{f}) * \mathrm{Im}(\mathrm{p})]\}/[\mathrm{Re}(\mathrm{f})^2 + \mathrm{Im}(\mathrm{f})^2].$$

The elastance is calculated as:

$$\text{Elastance} = \mathrm{Im}[X(\mathrm{p})/X(\mathrm{f})] * \mathrm{w},$$

where w = the fundamental frequency times 2π. This equates, in the frequency domain, to:

$$(\{[\mathrm{Re}(\mathrm{f}) * \mathrm{Im}(\mathrm{p})] - [\mathrm{Im}(\mathrm{f}) * \mathrm{Re}(\mathrm{p})]\} * \mathrm{w})/[\mathrm{Re}(\mathrm{f})^2 + \mathrm{Im}(\mathrm{f})^2].$$

Respiratory system inertance is assumed to be negligible, and there is good evidence that this is so at the frequencies we are measuring [14,15].

RESULTS

Examples of laboratory experiments

If values for elastance and resistance obtained during forcing with "quasi-sinusoidal" flow waveforms delivered by our system (see Fig 2) are the same as those during true sinusoidal forcing, then the effect of higher harmonics in the quasi-sinusoidal waveform can be ignored. Thus, elastances and resistances corresponding to unique frequency and tidal volume can be measured, and interpretation will be straightforward. We have used our system to measure E_{rs} and R_{rs} in awake human volunteers, relaxed with breathing voluntarily suspended to allow themselves to be ventilated, and to compare results to sinusoidal forcing from a piston pump driven by a linear motor [4]. Values for E_{rs} and for R_{rs} measured at eight combinations of frequency and tidal volume, did not differ between the two types of forcing ($p > 0.5$), if discrete Fourier analysis was used for calculations. Analogous results were obtained in anesthestized/paralyzed dogs for elastances and resistances of the lung, chest wall, and total respiratory system, even when the lungs were made severely edematous with an injection of oleic acid into the right atrium [2]. Other experiments in human volunteers demonstrated that our system could be used to measure the effects of posture [16], changes in FRC [13], and anesthesia, with or without complete muscle paralysis [17], on lung and chest wall mechanics.

Examples of clinical experiments

We have used our system to measure anesthetized/paralyzed patients before and after cardiac surgery with cardiopulmonary bypass [7]. Although chest wall properties were not affected by bypass, E_L and R_L were greatly increased after bypass. Moreover, after bypass, E_L and R_L displayed negative dependences on tidal volume and R_L displayed a large negative dependence on frequency, which was consistent with the effects of pulmonary edema we had previously measured in dogs [5]. Thus, our approach may not only identify the effect of a given condition or intervention, but also affords quantification of frequency and tidal volume dependences, which are potentially helpful to identify mechanisms behind those effects. We have also made measurements in the surgical intensive care unit at the University of Maryland Hospital in anesthetized or sedated patients with healthy lungs or severely pathological lungs [18].

DISCUSSION

We have demonstrated a system enabling quick, accurate, and easily interpretable measurements of lung and chest wall mechanical properties in mechanically ventilated patients. The system facilitates systematic measurements at different tidal volumes and respiratory frequencies in the normal ranges, which greatly adds to ability to understand mechanical behavior and to detect the presence or onset of pathology. The computer-ventilator interface overcomes the problem of FRC increasing as frequency is increased, and the analysis method is not affected by the inherent inability of clinical ventilators to control expiratory flow pattern. Nonlinearities (i.e., tidal volume dependences) are not only accounted for, but provide useful information. For example, tidal volume dependence is enhanced during pulmonary edema; this may be an important indicator of onset of pathology [5]. The entire system can be fit onto a relatively small cart that can be moved easily in and out of operating rooms and from bed to bed in the intensive care unit. Measurements at different frequency/tidal volume combinations can be made quickly (only 4 or 5 breaths are needed at each combination), without interfering with patient

care. The system will enable us to understand better how respiratory system mechanical behavior in the physiologic range is affected by lung and chest wall pathology, surgical procedures, and clinical interventions. In the laboratory, meaningful measurements of how the respiratory system changes in the range of daily postures and tasks can be made in subjects voluntarily suspending their breathing efforts.

Other widely used methods for measuring respiratory system mechanics have several limitations. For example, imposition of small amplitude, high-frequency flow oscillations for a brief period can enable calculation of elastance and resistance in a range of frequencies [19]. Frequencies are typically much higher than the normal range of breathing, and tidal volume effects are ignored. Inertial effects at high frequency also complicate interpretation. Thus, values for elastance and resistance may differ from those during mechanical or spontaneous breathing. In addition, we have shown that differences in lung resistance between healthy and edematous lungs become much less as frequency increases above the normal range [5]. It has also been pointed out that in most of the studies using high-freqeuncy oscillations, the volume amplitude varies with frequency, which may obscure the frequency dependence of elastance and resistance due to nonlinear harmonic distortions and cross-talk [20]. Another widely used technique uses flow interruption during the ventilatory cycle to calculate resistance, assuming a linear viscoelastic model containing at least four elements [21]. How the nonlinearities of respiratory system properties affect the validity of this model is unknown. Furthermore, it is intuitively difficult to grasp the frequency and amplitude to which the flow interruption value for resistance corresponds. How this resistance relates to a normal breathing pattern is not directly interpretable, and how its magnitude would be expected to change in pathology where, for example, frequency and/or amplitude dependence may change is difficult to predict.

In summary, measurements of resistances from flow interruption are constructs from the proposed flow interruption model, and are not easily applied to breathing. Dynamic elastance from the flow interruption technique is sometimes calculated from pressure measured at points of zero flow. We have shown that such values for elastance during nonsinusoidal forcing are not very different from those during sinusoidal forcing, if frequency and tidal volume are accounted for [2,4]. However, as the flow interruption method is usually applied, the frequency to which measurements of dynamic elastance corresponds is ambiguous.

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