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A Method of Calculating Total Respiratory System Compliance from Resonant Frequency: Validity in a Rabbit Model[1]

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ABSTRACT. Ten anesthetized, tracheotomized, adult rabbits were used to test the validity of a method for calculation of total respiratory system compliance from resonant frequency (C_r). Reference values were obtained during constant flow inflation of the relaxed respiratory system by dividing the volume gain by the related difference in pressure at the airway opening (inflation method compliance, C_i). The animals were connected to a new type of servo-controlled infant ventilator. Besides volume-controlled mechanical ventilation at constant inspiratory flow rate and intermittent mandatory ventilation, there is a negative ventilator resistance mode integrated in this device for resistive unloading (Schulze A, Schaller P, Gehrhardt B, Mädler H-J, Gmyrek D: Pediatr Res 28:79–82, 1990). To measure resonant frequency (f_r), the respiratory system was totally unloaded for a short period by a negative ventilator resistance exceeding the combined resistances of the endotracheal tube and airways. This evoked a continuous oscillation at f_r. By analogy with electrical circuit theory, C_r was calculated according to $C = 1/(4\pi^2 \cdot I \cdot f_r^2)$ where C is compliance and I is inertance. The inertance of the endotracheal tube is given and that of the bronchial tree was ignored assuming a much greater total cross-sectional area and therefore much lower inertance when compared with the endotracheal tube. Three pairs of $C_i - C_r$ values were obtained from each animal: *1*) during intact respiratory muscle activity; *2*) after pancuronium relaxation, and *3*) after surfactant depletion by saline washout. There was a significant linear correlation between C_i and C_r values with the regression line lying close to the identity line ($C_r = 1.1\ C_i - 0.74$; $r = 0.97$; $p < 0.0001$). C_i increased from 45.3 ± 9.4 to 47 ± 7.1 mL/kPa after pancuronium relaxation and dropped to 25.5 ± 5.2 after surfactant depletion. The corresponding C_r values were 49.5 ± 11, 51 ± 8.2, and 27 ± 5.9 mL/kPa, respectively. The f_r value decreased from 274 ± 33.2 min^{-1} before to 267 ± 21.4 after relaxation, and was 371 ± 39.5 min^{-1} after injury. (*Pediatr Res* 28: 599–602, 1990)

Abbreviations

C_i, total respiratory system compliance according to the inflation method
C_r, total respiratory system compliance according to the resonant frequency method
CMV, volume-controlled mechanical ventilation
CPAP, continuous positive airway pressure
ETT, endotracheal tube
f_r, resonant frequency
I, inertance
NVR, negative ventilator resistance
P_{ao}, pressure at the airway opening
$\dot{V}$, flow

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The respiratory system can be modeled by an electrical circuit with resistor, capacitance, and inductor in series. In such a model, the resistor represents the resistance to gas flow, the capacitance is analogous to respiratory system compliance (C), and the inductor is the gas inertance (I). Such systems are characterized by an ability to swing at their f_r. According to electrical circuit theory,

$$f_r = \frac{1}{2\pi\sqrt{I \cdot C}} \tag{1}$$

and therefore

$$C = \frac{1}{4\pi^2 \cdot I \cdot f_r^2} \tag{2}$$

Knowing f_r and I, we can calculate C. The background for obtaining f_r and I is as follows.

Determination of f_r. Resistance dampens the tendency of the resistor-capacitance-inductor system to oscillate at resonance. Therefore, resistance must be compensated for or eliminated to induce a continuous oscillation. The total resistance of the combined patient-ETT-respirator system equals the sum of the resistances of all parts. The only way to decrease total resistance is therefore to use an NVR because the patient's and the ETT's resistances are given. We used a ventilator that has been specifically designed for infants with their narrow ETT (1–4). It is an all-purpose, valveless ventilator with an NVR mode for resistive unloading of the respiratory-ETT system. Thereby, resonant oscillation was induced and measured.

Calculation of I. I of a gas in a tube is defined by

$$I = \rho \cdot \frac{4 \cdot l}{\pi \cdot d^2} \tag{3}$$

where ρ is gas density and l and d are the length and diameter, respectively. Since the total cross-sectional area of the bronchial tree increases from central to peripheral parts of the lung (5) and the diameter's exponent in the denominator in equation 3 is 2, it was assumed that the ETT constitutes the major I of the whole system. I of the bronchial tree was neglected.

The aim of our study was to test the validity of this "resonant method" for determination of total respiratory system compliance (6) in a rabbit model. The "constant flow inflation method" of compliance measurement (7–9) was used for comparison.

MATERIALS AND METHODS

Ventilator. Transducers for P_{ao} and $\dot{V}$ (10, 11) are mounted directly near the ETT adaptor. These sensors are components of two feedback loops for P_{ao} and $\dot{V}$, respectively. A microcomputer provides reference signals and switches one of the loops on-line while the other is off-line. To generate CMV, the $\dot{V}$ loop is on-line during the inspiratory part of the cycle. If a constant inspiratory $\dot{V}$ pattern is selected, the ventilator calculates C_i using the quotient of volume gain (ΔV) and ΔP_{ao} in a time frame starting after 10% of total inflation time until end inflation. Volume is calculated as the integral of $\dot{V}$. To allow for exhalation against a preset constant expiratory P_{ao}, the ventilator is switched over to the pressure feedback loop. In the CPAP mode for spontaneous breathing, the pressure feedback loop is only used to maintain a constant P_{ao}. To introduce an NVR, the $\dot{V}$ signal is additionally imposed on the error signal of the P_{ao} controller in such a manner that an inspiratory flow increases and an expiratory flow decreases P_{ao}. Henceforth, there is a difference between the preset baseline P_{ao} level and the instantaneous P_{ao}. The ratio ΔP_{ao} per $\dot{V}$ is constant at any moment. It has units of resistance (kPa·s/L). An adjustable amplifier of the $\dot{V}$ signal allows one to select the desired amount of NVR (0–15 kPa·s/L). NVR as used in this study was linear all over the $\dot{V}$ range. Against this, the positive resistance of the ETT and airways is nonlinear, *i.e.* it decreases with decreasing $\dot{V}$. Therefore, if the amount of NVR is increased, the total resistance of the combined lung-ETT-ventilator becomes negative over an increasing $\dot{V}$ range around zero flow level (Fig. 1). In this range, the respiratory system is totally unloaded. Therefore, a resonant oscillation occurs. Using the $\dot{V}$ signal, f_r is calculated by the ventilator's computer.

Animal model. Ten healthy adult rabbits weighing 4.4 ± 0.5 kg (range 3.8–5.1 kg) were studied. Anesthesia was induced with an i.v. bolus injection of 30 mg/kg sodium pentobarbital and maintained with intermittent doses of 2–5 mg/kg every 60 min. Infusion fluids were given at 3 mL/kg/h i.v. Tracheostomy was performed on each animal, and the trachea was cannulated with a 3.5-mm inner diameter uncuffed ETT (length 185 mm) that was secured in place by a peritracheal ligature. The animal was then connected to the ventilator in the supine position and ventilated conventionally with 100% oxygen, rate 60 cycles per min, inspiratory/expiratory ratio 1:1. Tidal volume was adjusted to maintain normocarbia. Rectal temperature was monitored and regulated between 38 and 39°C using a warming pad. An arterial line was inserted through the left carotid artery for intermittent determination of arterial blood gases by a pH/blood gas system (Radiometer, Copenhagen, Denmark). The animals were then allowed to breathe spontaneously via the ventilator

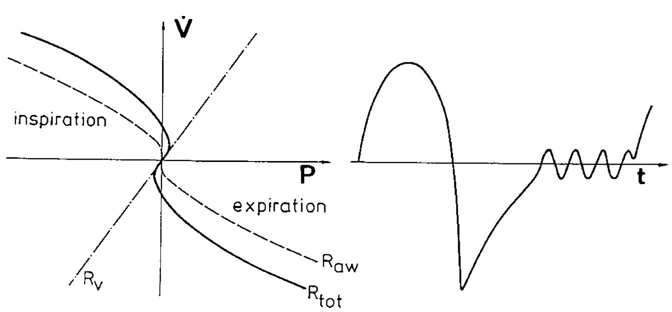

Fig. 1. Qualitative pressure (*P*)-flow ($\dot{V}$) characteristics (*left panel*) illustrating the effect of a negative ventilator resistance (R_v). The slope of a P–$\dot{V}$ characteristic, given by the quotient $\Delta P/\Delta\dot{V}$, represents resistance. Resistance of the airways (R_{aw}) is curvilinear. Against this, the ventilator's P–$\dot{V}$ relationship is linear with an inverse, *i.e.* negative slope. The total resistive load (R_{tot}) placed on the animal's spontaneous breathing effort equals the sum of R_{aw} and R_v. R_{tot} is smaller than R_{aw} and becomes negative around zero flow range. A scheme of a spontaneous breath over time (*t*) is projected on the *righthand side of the diagram.* When expiratory airflow slowly returns to zero flow level, the system starts to swing at f_r within a flow range characterized by negative R_{tot}.

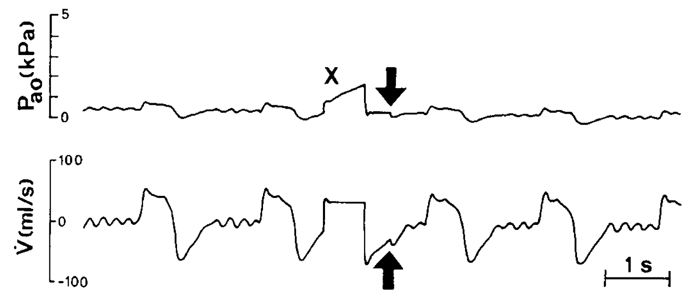

Fig. 2. Replica of original tracings. Intermittent mandatory ventilation with NVR mode. During spontaneous breathing, the P_{ao} varies around a baseline level of CPAP. Inspiratory air flow ($\dot{V}$) is above and expiratory $\dot{V}$ is below zero flow line. P_{ao} increases with inspiratory $\dot{V}$ and decreases with expiratory $\dot{V}$. There is no phase lag between $\dot{V}$ and P_{ao}. A resonant oscillation occurs at end expiration. The mandatory breath (*X*) is not synchronized with the spontaneous breathing activity. It starts at a substantial expiratory flow of a spontaneous cycle. After the initial resistive jump, P_{ao} rises linearly during constant flow inflation. This segment was used in our study for determination of inflation compliance. For passive deflation, the ventilator switches then to a constant expiratory positive pressure level. Before reaching zero flow level, the NVR mode is added (*arrows*), resulting in an accelerated expiration (time constant shortened) and shallow swinging.

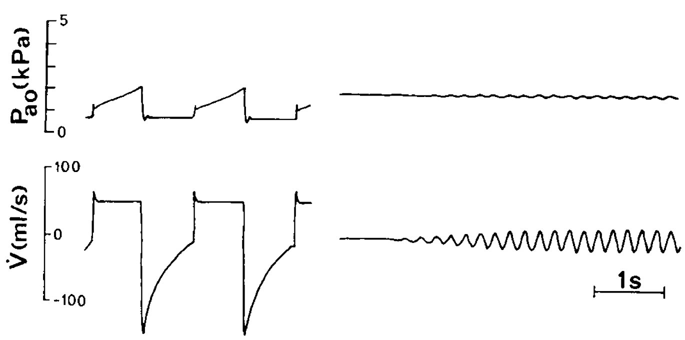

Fig. 3. Representative original tracings after pharmacologic relaxation. It is possible to calculate inflation method compliance during CMV at constant inspiratory flow (*left panel*). For determination of f_r, CPAP mode was commanded (*right panel*). A P_{ao} level previously characterized by linear increment during constant flow inflation was used. A permanent oscillation settled after introduction of negative ventilator resistance.

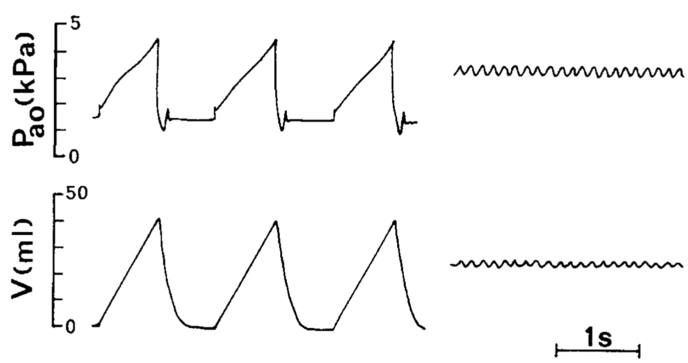

Fig. 4. Original tracings after surfactant depletion. Instead of the flow signal, its integral tidal volume (*V*) is recorded together with P_{ao}. In comparison with Figures 2 and 3, respiratory system compliance is severely decreased. This corresponds with an elevated f_r (*right panel*).

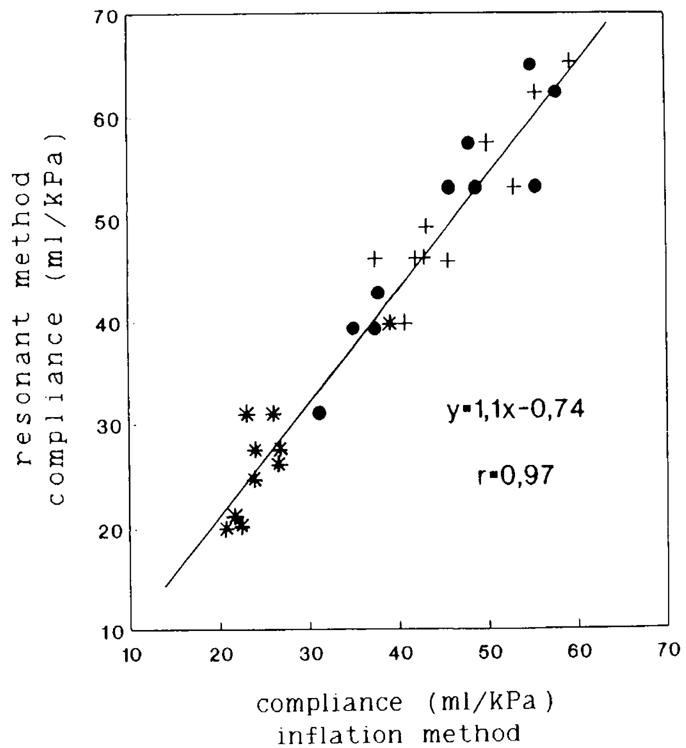

Fig. 5. Identity plot between total respiratory system compliance measured with the inflation method and corresponding values calculated from f_r. *Filled circles*, values measured during spontaneous breathing; *crosses*, after pancuronium relaxation; *asterisks*, after surfactant removal.

Table 1. C_i *and* C_r.*

	Before relaxation	After relaxation	Surfactant depleted
C_i (mL/kPa)	45.3 ± 9.4	47 ± 7.1	25.5 ± 5.2†
C_r (mL/kPa)	49.5 ± 11‡	51 ± 8.2‡	27 ± 5.9†
f_r (min^{-1})	274 ± 33.2	267 ± 21.4	371 ± 39.5†

* C_r was calculated from f_r of the respiratory system. Each of 10 rabbits was examined before and after pharmacologic relaxation and after washout of surfactant. Values are given as mean ± SD.

† Significantly different from values before and after relaxation ($p < 0.05$).

‡ Significantly different from C_i ($p < 0.05$).

while on intermittent mandatory ventilation mode. The volume-controlled cycles were used for measurement of C_i. Only relaxed inflations were accepted for evaluation. Additional spontaneous breathing activity during the mechanical inflations could be easily detected by on-line inspection of $\dot{V}$, volume, and P_{ao} records (8). Mean values of at least 10 measurements were used for evaluation. NVR mode was superimposed on backup CPAP during spontaneous breathing between mechanical breaths. Resonant oscillations occurred during the periods of near zero flow at end expiration. Calculation of C_r was based on the frequency of these oscillations (Fig. 2). Afterward, neuromuscular paralysis was initiated and maintained with i.v. pancuronium bromide (0.2 mg/kg/h). Compliance measurements were repeated during CMV. A CPAP period with NVR was temporarily set to determine f_r (Fig. 3). Pulmonary lavage was then performed to remove surfactant according to the standard method (12) six to 10 times over a 20- to 30-min period with normal saline at a pressure not exceeding 4 kPa (approximately 100 mL each wash). Adequate pulmonary lavage was considered to have been achieved if the arterial oxygen tension on CMV was 13 kPa or less after a 15- to 30-min postlavage control period. Mean airway pressure was elevated after the second or third lung wash. Compliance determinations were repeated in the same manner after the pulmonary lesion was established. C_i and f_r measurements were performed at the same airway pressure range (Fig. 4).

Calculation of C_r. The I of the ETT used in these experiments was calculated from the tube's dimensions according to equation 3. Gas density of pure oxygen at 33°C is 1.28 kg/m^3. Thus, I had the value 0.0245 $kPa \cdot s^2/L$. Based on equation 2, this yields C_r when f_r is known.

Statistics. The paired *t* test was used to test for significant differences in mean values. All *p* values of <0.05 were considered to represent significant differences. Data are presented as mean ± 1 SD. The least squares method was used to obtain the best fitting line for Figure 1.

RESULTS

Three pairs of compliance values were taken into consideration from each animal: before relaxation, after relaxation, and after surfactant depletion. There was a significant linear correlation between C_i and C_r values ($p < 0.0001$) with the regression line lying close to the identity line (Fig. 5).

C_r exceeded the values obtained by the inflation method significantly before and after pancuronium. The difference between C_r and C_i did not reach the level of significance after surfactant removal (Table 1).

Pharmacologic muscle relaxation resulted in a slight but nonsignificant increase in C_i, whereas the drop in C_i values after surfactant depletion was highly significant. The same holds true for C_r values, which reflect the variations in f_r.

DISCUSSION

It has been shown in our study that total respiratory system compliance, when calculated from f_r, is virtually identical to the C_i in tracheotomized rabbits.

This confirmed an important assumption underlying this approach for calculation of C_r—that the I of the ETT constitutes the overwhelming part of the combined ventilator-ETT-lung system. Moreover, it is possible to conclude that oscillations induced by resistive unloading with the NVR mode are indeed oscillations at f_r. Thereby, NVR has proved to be an elegant method for determination of the f_r of the combined ventilator-ETT-respiratory system in healthy and surfactant-depleted lungs as well.

That C_r values slightly exceeded C_i probably reflects the fact that the total I is a little bit higher than that of the ETT alone, which was only taken into account for calculation of C_r values. The ventilator itself has an inertial property in addition to the I of the bronchial tree. This has not yet been determined quantitatively and remains to be clarified.

The internal compressible volume of the infant ventilator used in our study amounts to 2 mL (4). Compliance of that volume is 2 mL/100 kPa (20 μL/kPa). Therefore, the impact of the ventilator's compliance on the f_r of the combined ventilator-ETT-lung system can be neglected.

The theoretical concept used is only valid for a homogeneous lung model. Such an oversimplified model neglects the nonuniform regional compliances that exist, especially in injured lungs. A multicompartmental lung is supposed to have regional differences in f_r. Therefore, the C_r method as described here should be used with caution until more detailed data are available from more complex models and a broad spectrum of clinical situations. However, we have shown that at least the rabbit plus ventilator system before and after lung lavage behaves like a simple, first order resistor-capacitance-inductor system. When measured with the NVR mode, we found defined f_r that fit the predictions based on the homogeneous model.

In comparison with conventional methods for determination of total respiratory system compliance in intubated infants, as the inflation or the occlusion method (13), our approach offers the following advantages: *1*) It works not only after putting respiratory muscles at rest, but also when there is spontaneous breathing activity; *2*) An "intrinsic positive end expiratory pressure" leads to an error in the occlusion method (14), but is irrelevant for the resonant method; and *3*) The occlusion method requires two single points for measurement of P_{ao} and is therefore unable to detect inconstancies of the compliance over this relatively large P_{ao} range (13). Against this, it is possible to evaluate the compliance course in a P_{ao} range by varying the preset baseline P_{ao} level in a ramp-like manner and recording the effect on f_r.

On the other hand, a ventilator system with the capability of resistive unloading is necessary to use this f_r method. This might be considered a drawback as such ventilators are not yet commercially available.

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