Effects of Inhalation Anesthetics on Airway Dynamics
Determined by Phasor Analysis of Respiratory Impedance
Using the Forced Oscillation Method

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By expressing the respiratory system as a two-compartment model and assigning a phasor in the complex plane to each impedance element in the model, the phasor of the respiratory impedance could be constructed graphically, the frequency characteristics determined from the locus of the latter and the effects of variations in the model elements on the frequency characteristics could also be expressed as the locus of the latter. Conversely, it is possible to detect small changes in mechanical properties of the respiratory system by plotting its frequency characteristics on the complex plane. We studied the effects of typical inhalation anesthetics, halothane, enflurane and isoflurane, on the airway dynamics by this method. The inhalation concentration of 1 MAC of halothane and/or enflurane was found to produce bronchodilation associated with a significant reduction in airway resistance, but isoflurane had no such effects. As the magnitude of changes in the real part at 1 Hz, the estimated airway resistance was \(-2.1 \text{ cmH}_2\text{O}/1/\text{s} \ (\sim 25\% \ \text{of the mean value})\) for halothane, and \(-0.8 \text{ cmH}_2\text{O}/1/\text{s} \ (\sim 11\%\) for enflurane.

(Key Words: airway dynamics, frequency characteristics of respiratory impedance, forced oscillation, halothane, enflurane, isoflurane)

INTRODUCTION
Volatile anesthetic agents are often the anesthetic of choice in asthmatic patients undergoing operations because they relax and dilate the bronchi. Moreover, inhalation of one of these agents may be a desparate yet dependable form of treatment in severe status asthmaticus.

To delineate this unique bronchodilator effect of volatile agents more precisely and quantitatively, we investigated the frequency response of respiratory impedance using the forced oscillation method in a group of patients with no serious complications selected from the routine O.R. roster. For this purpose, the respiratory system was represented in a two-compartment model and the frequency response of impedance was depicted as a locus on the complex plane. Changes in the mechanical properties of the respiratory system brought about by inhalation of the anesthetic at graded concentrations for an appropriate period were visually presented.

MATERIALS AND METHODS
The respiratory impedance was measured by the forced oscillation method shown in Fig. 1. The complex-wave produced by summing up the outputs of 16 sinusoidal wave generators covering 1–20 Hz were fed into a loudspeaker for use as the source of forced oscillation. The oscillation pressure and the induced air flow were converted into electrical signals using a pressure transducer (model MP–40, Validyne), and read into a microcomputer (model Z80B, Sharp Corp.) through an AD converter and low-pass filters, to calculate the impedance and

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phase difference by Fast Fourier Transformation. The calculated data were plotted on the complex plane and analyzed by comparing with the characteristics of the mechanical model of the respiratory system shown in Fig. 2. In the figure, the impedance of the large airway is defined as $Z_c$, composed of resistance $R_1$ and inductance $L$. The compliance of the small airway is expressed as $C_1$. The impedance of the lung periphery is composed of resistance $R_2$ and compliance $C_2$. The combined impedance made up of $C_1$, $R_2$ and $C_2$ is defined as $Z_p$, and the respiratory system is described as a two-compartment model made up of $Z_c$ and $Z_p$. For details of this technique the reader is referred to our previous paper (10).

Typical inhalation anesthetics, halothane, enflurane and isoflurane, were investigated for their effects on airway dynamics. Eighteen surgical patients aged 24–62 who had preoperatively been confirmed free of any respiratory and/or circulatory abnormalities were selected as subjects and divided into three groups of six patients each. They were premedicated with 50–100 mg of pentobarbital, 35–50 mg of pethidine hydrochloride and 0.5 mg of atropine sulfate to induce anesthesia and intubated with 5 mg/kg of thiopental and 1 mg/kg of succinylcholine chloride. Anesthesia was maintained with 4 l/min of $N_2O$ and 2 l/min of $O_2$ and mechanical ventilation was facilitated by pancuronium bromide. Measurements of the respiratory impedance were repeated at 15 minute intervals with a 0.5 MAC step-up to 2 MAC of halothane, enflurane or isoflurane. During each measurement, the respiratory circuit was disconnected, the oscillation source was connected with the endotracheal tube, the impedance was measured 3 times for about 15 seconds each time in an apneic condition, and the oscillation pressure and induced flow were recorded on a data recorder (model A67, Sony Corp.) along
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**Fig. 2** Equivalent circuit model of the respiratory system. The impedance of the large airway is defined as $Z_c$, made up of resistance $R_1$ and inductance $L$. With the airway compliance assumed to be confined to the small airway, its impedance is expressed by compliance $C_1$. The impedance of the pulmonary periphery is defined as $Z_a$, made up resistance $R_2$ and compliance $C_2$. The combined impedance of the part made up of $C_1$, $R_2$ and $C_2$ is defined as $Z_p$. The input impedance of the model, $Z_r$, corresponds to the respiratory impedance.

$$Z_c = R_1 + j \omega L$$

$$Z_p = \left( \frac{R_2 + 1/j \omega C_2}{1/j \omega C_1} \right)$$

with the ECG. The recorded data were analyzed after the operation.

**RESULTS**

Fig. 3 show changes in respiratory impedance with the inhalation of 1 MAC of halothane, enflurane or isoflurane. The vertical and horizontal ranges of the changes at each frequency point denote the standard deviations of the real and imaginary parts of the impedance. The frequency points of $Z_r (\omega)$ for halothane and those for enflurane shift to the left and upward on the complex plane in the low frequency band not higher than 8 Hz; the magnitude of change decreased with the rise in frequency, and no obvious changes were noted in the high frequency band not less than 9 Hz. No significant changes occurred with isoflurane in any of the frequency bands. The mean magnitude of change in the real part and that in the imaginary part at the lowest frequency of 1 Hz was $-2.1$ and $+1.5 \text{cmH}_2\text{O}/\text{s}$ ($-25$ and $+9.9\%$ of the mean values respectively) for halothane, and $-0.8$ and $+0.9 \text{cmH}_2\text{O}/\text{s}$ ($-11$ and $+7.4\%$) for enflurane. Fig. 4 illustrates typical changes in respiratory impedance with the inhalation of up to 2 MACs of halothane and enflurane. Because no prominent changes occurred even with 2 MACs of isoflurane, and also because they are similar to those illustrated in Fig. 3 (5), the figures for isoflurane are omitted. Significant changes occurred with halothane in relation to the inhalation concentration of up to 2 MACs, while the magnitude of change with 2 MACs of enflurane was smaller than with 1 MAC: in other words, no significant changes were observed.

**DISCUSSION**

The changes in the impedance loci with the inhalation of halothane and that of enflurane may be explained as follows. Fig. 5 shows the relationship between changes in the loci and changes in the model elements calculated with the values given in Table 1 as median values available from the literature (2, 18). The broken lines connecting the same frequency points of the loci indicate the directions of changes in the loci. The mathematical properties of the broken lines are omitted here, but they express the effects of changes in each model element on the respiratory impedance as a perfect continuous solution. Conversely, it is also possible to estimate changes in the model...
Fig. 3 Changes in the frequency characteristics with the inhalation of up to 1 MAC of halothane, enflurane and isoflurane. The widths of vertical and horizontal changes at each frequency point denotes the standard deviations of the real and imaginary parts. With halothane and enflurane, the frequency points of $Z_r(\omega)$ shift to the left and upward in the low frequency band, while with isoflurane, no significant changes occur.
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Fig. 3-b
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![Graph](image-url)

**Fig. 3-c**

**Title**: Isoflurane Concentration 0–1.2%

**Axes**:
- **X-axis**: Reactance ($cm H_2 O/1/s$)
- **Y-axis**: Resistance ($cm H_2 O/1/s$)
- **Z-axis**: Frequency (Hz)

**Legend**:
- Control
- Inhalation
Fig. 4 Changes in the frequency characteristics with the inhalation of up to 2 MACs of halothane and enflurane. Changes for halothane are in relation to its inhalation concentration, but the magnitude of change with 2 MACs of enflurane is smaller than that with 1 MAC; i.e., no significant changes occurred. Isoflurane is omitted because even 2 MACs of isoflurane failed to cause any significant changes.
Table 1 Typical values of model elements.

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<tr>
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<th>L</th>
<th>R1</th>
<th>R2</th>
<th>C1</th>
<th>C2</th>
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<td>cmH$_2$O/1/s</td>
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Fig. 5 Changes in the loci calculated by substituting the values in Table 1 as median values into the circuit model. The broken lines connecting the same frequency points of the loci are the directions of changes in the loci.
Elements from changes in the shape of phasor loci. Table 2 shows their qualitative relations. The frequency at which the locus crosses the real axis is given as the resonant frequency, and the gradient of the locus to the imaginary axis as the magnitude of the gradient. If changes in the low frequencies of about 0–8 Hz differed in direction from those in the high frequencies of about 8–15 Hz, they were classified as LF (low frequency band) and HF (high frequency band). From Fig. 5 and Table 2, analysis of the changes in the impedance loci caused by halothane and/or enflurane can be summarized as follows:

1. In Fig. 5 (3) illustrating the relationship between peripheral resistance $R_2$ with respiratory impedance $Z_r$, it is obvious that the frequency points of $Z_r$ in the low frequency band shift to the right and downward on the complex plane as $R_2$ increases. Inhalation of halothane and/or enflurane caused changes in the opposite directions, i.e., $R_2$ was reduced by these agents.

2. In Fig. 5 (2) illustrating the relationship between the small airway compliance $C_1$ and $Z_r$, the frequency points in the low frequency band shifted to the left and upward on the complex plane as $C_1$ increased. Halothane and/or enflurane caused changes in the same directions, i.e., $C_1$ was increased by these agents.

3. In Fig. 5 (4) illustrating the relationship between the peripheral compliance $C_2$ and $Z_r$, the frequency points shifted upward and slightly to the right on the complex plane as $C_2$ increased. Since the small shift to the right was presumably offset by the change in $R_2$, $C_2$ was also increased by these agents.

4. No obvious changes occurred in $Z_r$ in the frequency band not less than 8 Hz in any case. These findings indicate that the anesthetics exerted only slight effects on large airway resistance $R_1$, and they failed to reduce the resistance. It is for this reason that $R_1$, as illustrated in Fig. 5 (1), caused a left-to-right shift in all frequency bands.

To summarize our interpretation of these results, halothane and enflurane reduced the airway resistance, and also led to a more compliant state although the effects of changes in hemodynamics in the airways by inhalation of the anesthetics should not be ignored. The effect of halothane seemed more potent than that of enflurane, while isoflurane exerted practically no such effect.

A number of investigators have reported the effects of inhalation anesthetics on airway dy-

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Table 2 Changes in the phasor loci caused by an increase in model elements. The frequency characteristics of impedance vary qualitatively, mostly as shown in the table with an increase in model elements. The resonance frequency denotes the frequency of the point where the locus crosses the real axis, and the magnitude of the gradient denotes the gradient of the locus to the imaginary axis.

<table>
<thead>
<tr>
<th></th>
<th>MAGNITUDE</th>
<th>PHASE</th>
<th>REAL</th>
<th>IMAGINARY</th>
<th>GRADIENT</th>
<th>RESONANT FREQUENCY</th>
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<td>$R_1$</td>
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<td>–</td>
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<tr>
<td>$C_1$</td>
<td>↑</td>
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<td>✹</td>
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<td>$C_2$</td>
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Notes: ↑ increase, ↓ decrease, ✹ constant, ✹ irrelevant.
dynamics. It has been reported that halothane blocks bronchoconstriction induced by histamine injection or by vagal stimulation, and it is widely indicated for anesthetizing patients with asthma (8, 16). It has further been reported that halothane increases bronchial distensibility and also markedly increases bronchial compliance even in normal subjects (3). There are also quite a few reports indicating that halothane reduces airway resistance itself (5, 13). Except for reports that halothane reduces pulmonary compliance (6), they all reveal that the effects of halothane on the respiratory system. The results of our analysis are in good agreement with these reports. On the other hand, there are reports that enflurane causes relaxation of bronchial smooth muscle (4, 11, 16), and also reports that enflurane causes bronchoconstriction (12). It has also been reported that enflurane produces no marked effects on the respiratory system (14, 17). In other words, there are no unanimously supported conclusions on the effects of enflurane. In the present study, up to 1 MAC of enflurane reduced the airway resistance and increased the compliance, in the same way as halothane, but its effects seemed weak. These findings were also consistent with our clinical experience. It has been reported that isoflurane, like enflurane, inhibits bronchoconstriction (9), but it has also been found that isoflurane increases pulmonary resistance and decreases static compliance (15), and that isoflurane exerts no effects on airway dynamics (1, 7). There seems to be no definitive view about the effects of isoflurane. In Japan, isoflurane is about to be launched for clinical use, and no clinical data are available yet. The results of the present study have shown that isoflurane has weaker effects on the respiratory system than both enflurane and halothane.

REFERENCES