Effects of age on elastic moduli of human lungs

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Lai-Fook, Stephen J., and Robert E. Hyatt. Effects of age on elastic moduli of human lungs. J Appl Physiol 89: 163–168, 2000.—The model of the lung as an elastic continuum undergoing small distortions from a uniformly inflated state has been used to describe many lung deformation problems. Lung stress-strain material properties needed for this model are described by two elastic moduli: the bulk modulus, which describes a uniform inflation, and the shear modulus, which describes an isovolume deformation. In this study we measured the bulk modulus and shear modulus of human lungs obtained at autopsy at several fixed transpulmonary pressures (Ptp). The bulk modulus was obtained from small pressure-volume perturbations on different points of the deflation pressure-volume curve. The shear modulus was obtained from indentation tests on the lung surface. The results indicated that, at a constant Ptp, both bulk and shear moduli increased with age, and the increase was greater at higher Ptp values. The micromechanical basis for these changes remains to be elucidated.

The effects of aging on the mechanical behavior of the human lung have been well described in relation to its P-V behavior (for review, see Refs. 5 and 13). Morphometric studies in human (12, 27) and dog (10) lungs showed that alveolar mean linear intercept (or alveolar diameter) increases, whereas alveolar surface area decreases with age. This behavior is associated with an increase in lung tissue elastin and little change in collagen content (21, 22). Studies relating K and μ to age have been carried out in pig lungs with ages from 5 to 95 days (18). K decreased whereas μ remained constant with age. This behavior is associated with pig lung development from neonatal to the early adult stage, in which alveolar size is reduced with age, a behavior opposite to that observed for the adult human.

Accordingly, in this study we measured the effects of age on K and μ at Ptp between 4 and 16 cmH2O in isolated adult human lungs obtained at autopsy. We showed that, in general, both bulk and shear moduli increased with age. These changes might be associated with surface forces induced by the increase in alveolar diameter with age and with tissue forces induced by the increase in elastin content with age.

METHODS

The left lungs from 20 human cadavers (7 female, 13 male) were obtained at autopsy from the pathology department of the Mayo Clinic. Lungs from subjects who had a known history of lung disease were excluded from the study. Also excluded were lungs that showed on post mortem examination any gross evidence of pathology, such as pulmonary edema, and any evidence of a smoking history.

Each lung was cannulated and inflated to check for air leaks from the pleural surface by immersion in saline. Any air leak was eliminated by deflating the lung and tying off the lung area surrounding the leak with string. After degassing in a vacuum jar, the leak-free lung was inflated with a syringe to total lung capacity (TLC), defined as the volume at 25 cmH2O Ptp (airway pressure relative to pleural pressure that was atmospheric). Static deflation P-V curves were measured by deflating the lung stepwise to deflation pressures of 16, 12, 8, 6, 4, 2, and 0 cmH2O Ptp. The collapsed lung at 0 Ptp was weighed and displaced in water to determine its residual volume. The total lung volume (air plus tissue volume) was calculated at each Ptp value.

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The following procedure was used to determine $K$ and $\mu$ (15). We measured $K$ from incremental changes in Ptp and lung volume. Small P-V loops were performed around deflation Ptp values of 16, 12, 8, and 4 cmH$_2$O. The increment in Ptp of these loops was $\sim$2–3 cmH$_2$O. To determine the $\mu$, indentation tests were performed at deflation Ptp values of 16, 12, 8, and 4 cmH$_2$O. In brief, the lung was held at a constant deflation Ptp. The middorsal surface of the lung was indented with the flat surface of a 3-cm-diameter cylindrical rod. The applied load ($L$) required to displace the rod incrementally into the lung surface was measured. The increment in displacement ($w$) was 2 mm and the maximum $w$ was limited to 1 cm to ensure a linear $w$-$L$ curve. Between each indentation test, the lung was inflated to TLC before deflating to the test Ptp to eliminate any distortion of the parenchyma caused by the indentation.

**RESULTS**

Pressure-volume behavior. Table 1 summarizes age, gender, TLC, and left lung weight of the subjects. Figure 1 shows lung volume as percent TLC (volume at 25 cmH$_2$O Ptp) vs. age at different Ptp values of 0, 2, 4, 6, 8, 12, and 16 cmH$_2$O. Linear regression analyses showed that volume increased significantly ($P < 0.05$) with age at all Ptp values except 0 cmH$_2$O (residual volume, $P > 0.05$). This indicated that the residual volume expressed as a fraction of TLC was invariant with age. The increased volume with age was a reflection of the changes in shape of the P-V curve with age as shown in Fig. 2. This figure shows the mean P-V curves at ages of 20, 40, and 60 yr obtained from the regression equations shown in Fig. 1. Note in Fig. 2 the shift of the P-V curve with increasing age toward a greater lung compliance ($\Delta V/\Delta P$) at the lower Ptp values, a characteristic of an emphysematic lung (17). The ratio of TLC (ml) to lung mass (M; g) was not significantly related to age by linear regression analysis: TLC/M = 10.7 – 0.066 age, $r^2 = 0.109$, $n = 18$, $P = 0.1$. This indicated that the change in shape of the P-V curve was not caused by an increase in TLC with age. Also, lung residual volume as a fraction of TLC was uncorrelated with age (Fig. 1, Ptp = 0 cmH$_2$O). This suggests that the material properties that were responsible for residual volume and TLC did not change with age, whereas those responsible for the intermediate lung volumes did.

Each P-V curve was fitted to the relationship (20): 

$$\text{Ptp} = \alpha_1 e^{\alpha_2 V}$$

which in linear form is $\ln \text{Ptp} = \ln \alpha_1 + \alpha_2 V$. Figure 3 shows the values of $\alpha_1$ plotted vs. age. Note that $\ln \alpha_1$, a measure of the elasticity of the lung, decreased significantly ($P < 0.05$) with increasing age: $\ln \alpha_1 = -0.22 - 0.037$ age, $r^2 = 0.59$ (solid line, Fig. 3). This equation is comparable to that found previously

### Table 1. Data on human lungs

<table>
<thead>
<tr>
<th>Subject Number</th>
<th>Age, yr</th>
<th>Sex</th>
<th>Lung Mass, g</th>
<th>TLC, ml</th>
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<td>2</td>
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<td>F</td>
<td>302</td>
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M, male; F, female; TLC, total lung capacity.

![Fig. 1. Lung volume (V) measured as percent total lung capacity (%TLC) vs. age (yr) at constant transpulmonary pressure (Ptp) values of 0, 2, 4, 6, 8, 12, and 16 cmH$_2$O. Linear regression equations are shown.](http://jap.physiology.org/Downloadedfrom)
(20): ln $\alpha_1 = -0.35 - 0.044$ age (dotted line, Fig. 3). By contrast, $\alpha_2$, a measure of the maximal lung volume, was uncorrelated with age: $\alpha_2 = 2.23 \times 10^{-3} - 9.2 \times 10^{-6}$ age, $r^2 = 0.015$, $P = 0.6$. The latter result is consistent with that reported previously (20).

$K$, $\mu$, and Poisson ratio. We determined from the experiments the values of $K$ and $\mu$ that are required to describe the lung parenchyma as a linear elastic continuum. Each constant was evaluated at Ptp values of 4, 8, 12, and 16 cmH$_2$O. $K$, a measure of the resistance of the lung in response to a uniform expansion, was calculated from the formula $K = V(DP/\Delta V)$, where $\Delta P/\Delta V$ was the slope of the small P-V loop and $V$ was the lung volume at the test Ptp. Figure 4 shows the values of $K$ plotted vs. age at the constant test Ptp values of 4, 8, 12, and 16 cmH$_2$O. Linear regression analyses of the data showed that, at each test Ptp, $K$ increased significantly ($P < 0.05$) with age. The rate of the increase in $K$ with age increased with the increase in Ptp, with values of 0.25, 0.65, 1.28, and 1.71 cmH$_2$O/yr at the test Ptp values of 4, 8, 12, and 16 cmH$_2$O, respectively.

The slope of the $L$-$w$ curve of the indentation tests was used to calculate $\mu/(1-\sigma)$ from the elasticity solution for the indentation of an elastic half-space with a rigid cylindrical rod (15)

$$\frac{\mu}{1-\sigma} = \frac{(L/w)}{(2\pi d)}$$

(1)

Here $\mu$ is the shear modulus of the lung parenchyma, $\sigma$ is the Poisson ratio, and $d$ is the rod diameter. From elasticity theory, $\mu$ is related to $K$ and $\sigma$ as follows

$$\mu = 3K(1-2\sigma)/(2(1+\sigma))$$

(2)

Thus with the values of $K$ from the incremental P-V test (Fig. 4), values of $\mu$ and $\sigma$ were computed from Eqs. 1 and 2. Figure 5 shows values of $\mu$ vs. age at constant test Ptp values of 4, 8, 12, and 16 cmH$_2$O.
Linear regression analyses of the data showed that \( m \) increased significantly (\( P < 0.05 \)) with age at all test Ptp values except 4 cmH\(_2\)O. The corresponding values of \( s \) are shown in Fig. 6. Note that \( s \) increased significantly (\( P < 0.05 \)) with age at all Ptp values except 16 cmH\(_2\)O.

Figure 7 shows values of \( K \), \( m \), and \( s \) plotted vs. Ptp at ages of 20, 40, and 60 yr as determined from the linear regression equations shown in Figs. 4–6. Like the P-V behavior (Fig. 2), both \( K \) and \( m \) increased with age at each Ptp measured. However, the fractional increase in \( K \) was greater than that in \( m \) at each Ptp, resulting in an increase in \( s \) with age at each Ptp value. Thus there was a tendency of the lung parenchyma to become more like an incompressible material (\( s < 0.5 \)) with increasing age; that is, the lung became more resistant to uniform expansion in relation to its resistance to shear.

**DISCUSSION**

The major finding of this study is that both \( K \) and \( m \) of human lungs increase with age at constant Ptp. This indicates that the lung parenchyma becomes more resistant to both uniform expansion and shear deformation with increasing age.

**Method.** We used the local loops of the P-V curve rather than the slope of the deflation P-V curve to determine \( K \). This resulted in values of \( K \) (reciprocal of the specific compliance) that were larger than those based on the slope of the deflation P-V curve (Fig. 2). One reason for using the small P-V loops was the absence of any measurable hysteresis, a behavior expected of an ideal elastic material. Also, the small perturbation in P-V behavior satisfied the assumption of elasticity theory that stresses and strains imposed on an initial isotropic state were linearly related.

We used the indentation test on the lung surface to determine \( \mu/(1-\sigma) \), from which both \( \mu \) and \( \sigma \) can be calculated from Eqs. 1 and 2 if \( K \) is known. The elas-

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**Fig. 5.** Shear modulus (\( \mu \), cmH\(_2\)O) vs. age (yr) at constant Ptp values of 4, 8, 12, and 16 cmH\(_2\)O. Note the significant increase in \( \mu \) with age as shown by linear regression equations at all Ptp values except 4 cmH\(_2\)O.

**Fig. 6.** Poisson ratio (\( \sigma \)) vs. age (yr) at constant Ptp values of 4, 8, 12, and 16 cmH\(_2\)O. Note the significant increase in \( \sigma \) with age as shown by linear regression equations at all Ptp values except 16 cmH\(_2\)O.
ticity solution of the indentation test (Eq. 1) assumed that the lung surface was flat with boundaries that were an infinite distance from the site of indentation. This assumption was closely approached because the rod diameter was small compared with the distance between the rod and the lung boundary. We assumed that the lung was a homogeneous elastic material and neglected the effect of the pleural membrane in resisting the force of indentation into the lung. This effect was minimized by using a large enough rod diameter (9, 15, 18).

Comparison with previous results. Elastic moduli measured in a variety of mammals (dog, pig, horse, and rabbit) showed that K values equaled 4–6 Ptp and \( \mu \) values were 0.7–0.9 Ptp in the Ptp range between 4 and 25 cmH_2O (9, 15, 25). The values of K and \( \mu \) measured in human lungs in the present study were consistent with this behavior for an age of \( \sim 20 \) yr (Fig. 7). As age increased above 20 yr, there was a trend toward greater values for K. These changes with age were associated with a greater lung volume at each Ptp value as age increased (Fig. 2), in agreement with previous studies using isolated human lungs at autopsy (4, 7, 12) and with in vivo measurements in humans (28). The increased lung volume at each Ptp with age is consistent with an increase in lung tissue elastin and a constant collagen content with age (22). The latter result explains why TLC did not increase with age (1).

Except for one subject (subject 19, Table 1) of age 10 yr, all the lungs studied were in the adult age group (>17 yr). Thus the age-related increases in elastic moduli measured in this study were associated with the aging process that included both intrinsic and extrinsic factors rather than with changes due to lung development. Thus extrinsic factors such as smoking and unknown disease on the age-related change in the elastic moduli cannot be ruled out. The effect of lung development on elastic moduli measured in the pig lung between the ages of 12 h and 85 days showed higher K and \( \mu \) values in the newborn compared with the 3- to 5-day-old lung and a constant \( \mu \) and a decreasing K as age increased from 5 to 85 days (18). These changes with age due to lung development are opposite to those observed in the present study.

Models relating the microstructural properties of lung parenchyma to the macrostructural properties have shown that tension in the alveolar walls is the major determinant of K and \( \mu \) (11, 25, 26). Both tissue and surface forces contribute to tension in alveolar walls. Surface forces that arise from the alveolar air-liquid interface are modified by pulmonary surfactant (23, 24). The contribution of tissue forces to the elastic constants can be measured by studying the lung filled with saline (8). Studies in rabbit lungs showed that an increase in alveolar surface tension imposed by washing isolated lungs with liquids of constant surface tensions caused a decrease in K and an increase in \( \mu \) (26).

Morphometric studies have shown that, at a constant Ptp, alveolar mean linear intercept and mean alveolar diameter increase with age whereas alveolar surface area decreases (8, 27). Thus in the absence of any change in surface active properties of pulmonary surfactant with age, the increase in K and \( \mu \) with age might be related to changes in alveolar configuration that result in changes in surface forces. An increase in intrinsic tissue forces might also contribute to the increase in K and \( \mu \) with age. The increased tissue elastin content with age (22) might contribute to the intrinsic tissue force and the increase in K and \( \mu \) with age. These effects need to be evaluated in saline-filled lungs.

Summary. The greater stiffness of lung parenchyma with increasing age as measured by K and \( \mu \) is consistent with the behavior found in many body organs, such as systemic arteries (2). An increased K has also been found in lungs with chronic obstructive pulmonary disease and in emphysematous lungs with \( \alpha_1 \)-antitrypsin deficiency (17). The increased K and \( \mu \) of the lung with age implies that deformation characteristics of structures embedded within the lung parenchyma depend on age. Specific examples include the force interaction among lung parenchyma, blood vessels, and airways, and its effects on perivascular interstitial pressure (14), blood flow, and flow in airways.
The physiological effects of aging arising from these interactions need to be evaluated.

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