Microfocal X-ray CT imaging and pulmonary arterial distensibility in excised rat lungs

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Karau, Kelly L., Roger H. Johnson, Robert C. Molthen, Anita H. Dhyani, Steven T. Haworth, Christopher C. Hanger, David L. Roerig, and Christopher A. Dawson. Microfocal X-ray CT imaging and pulmonary arterial distensibility in excised rat lungs. Am J Physiol Heart Circ Physiol 281: H1447–H1457, 2001.—The objective of this study was to develop an X-ray computed tomographic method for measuring pulmonary arterial dimensions and locations within the intact rat lung. Lungs were removed from rats and their pulmonary arterial trees were filled with perfluorooctyl bromide to enhance X-ray absorbance. The lungs were rotated within the cone of the X-ray beam projected from a microfocal X-ray source onto an image intensifier, and 360 images were obtained at 1° increments. The three-dimensional image volumes were reconstructed with isotropic resolution using a cone beam reconstruction algorithm. The vessel diameters were obtained by fitting a functional form to the image of the vessel circular cross section. The functional form was chosen to take into account the point spread function of the image acquisition and reconstruction system. The diameter measurements obtained over a range of vascular pressures were used to characterize the distensibility of the rat pulmonary arteries. The distensibility coefficient α [defined by \( D(P) = D(0)(1 + \alpha P) \), where \( D(P) \) is the diameter at intravascular pressure (P)] was \(~2.8\%\) mmHg and independent of vessel diameter in the diameter range (about 100 to 2,000 mm) studied.

METHODS

Animal Preparation

Lungs from four Sprague-Dawley rats (267 ± 57 g) were prepared for imaging as follows. Each rat was anesthetized with pentobarbital sodium (40 μg/g body wt ip), the trachea was clamped, and the chest was opened. Heparin (200 international units in 0.2 ml) was administered via injection into the right ventricle. The pulmonary artery was cannulated with a saline-filled catheter [polyethylene tubing 1.67 mm inner diameter (ID); 2.42 mm outer diameter] via the conus arteriosis and the heart was dissected away. The lungs were removed from the chest, and suspended from the trachea and pulmonary arterial cannula. The lungs were ventilated with a gas mixture containing 15% O₂ and 6% CO₂ in nitrogen at 40 breaths/min with end-inspiratory and end-expiratory tracheal pressures of 8 and 3 mmHg, respectively. This served to eliminate any atelectasis occurring during the dissection. The pulmonary artery cannula was connected to a perfusion system primed with a physiological salt solution containing 5% bovine serum albumin (3), and the lungs were perfused.

X-RAY MICROCOMPUTED TOMOGRAPHY (CT) promises to be a valuable source of vascular structure-function information and vascular phenotypes of small laboratory animals (7, 13, 25, 36). The rat has been widely used to study pulmonary vascular remodeling (12, 17, 29, 32, 38) and is being used increasingly for physiological genomics in general (14, 15, 23, 41, 46) and for physiological genomics of the pulmonary vasculature in particular (21, 26, 29, 42, 47). Thus the objective of this study was to develop an approach for X-ray micro-CT measurement of pulmonary arterial diameters and their three-dimensional locations within the intact rat lung. The method was applied to the measurement of rat pulmonary arterial distensibility, which is a potentially useful pulmonary vascular phenotype for identifying quantitative trait loci (15, 41) as well as an input to rat lung physiome models (4, 16, 18, 40) used to understand pulmonary vascular function.

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for about 5 min at a flow rate ranging from 5 to 40 ml/min to remove residual blood from the lung vessels. The maximum pulmonary artery pressure at 40 ml/min was ~10 mmHg, which was maintained for ~20 s of the 5 min. The perfusate exited via the severed pulmonary vein. Once cleared of blood, the lung, still suspended from the cannulas, was placed in a 41 mm ID plastic cylinder, or the right lung and cardiac lobar arteries and bronchi were ligated and the respective lobes removed so that the remaining left lung could be placed in a 24 mm ID cylinder. The cylinder axis was located at the center of a horizontal turntable so that the lungs could be rotated 360° around a vertical axis between the X-ray source and detector with no other significant X-ray absorbing objects passing through the beam. The airway pressure was set at 6 mmHg, and the salt solution in the reservoir that was connected to the arterial catheter was replaced by perfluorooctyl bromide (PFOB), which was allowed to fill the arterial tree at a pressure of ~20 mmHg. The PFOB provided high X-ray contrast for the vessel lumen, and the surface tension at the PFOB-aqueous interface prevented its entry into the capillary bed. Thus only the arterial vessels were filled. Then the arterial pressure was set at 30 mmHg relative to the horizontal plane through the center of the X-ray image of the lungs. The lungs were rotated continuously at one degree per second. The image acquisition sequence was 5 to 10 frames at 30 frames per second beginning at each 1° increment to acquire 360 X-ray image sets in ~6 min. The same procedure was repeated with the arterial pressure set at 21 mmHg, 12 mmHg, and 5.4 mmHg and, again, with the pressure returned to 30 mmHg. The actual intravascular pressure within each vessel, relative to atmospheric pressure at the level of the vessel, was obtained from the vessel’s vertical distance from the pressure reference level at the central horizontal plane of the image and the PFOB density (1.94 g/ml).

**Imaging**

The X-ray system included a Fein-Focus FXE-100.50 X-ray tube with 3-μm focal spot, a North American Imaging AL5830-HP image intensifier set at either the 17.8 or 23 cm aperture, and a SMD 1M15 charge-coupled device (CCD) camera (Silicon Mountain Design, Colorado Springs, CO). The cylinder containing the rat lung was placed in the scanner so that its central axis was from 13 to 28 cm from the image-intensifier input surface and the acquired image was magnified on the image-intensifier face. Stage permits measured movements of the object perpendicular (in x and z directions) and parallel to the X-ray beam axis (y), and it can be rotated (θ).

**Image Preprocessing**

Each 8-bit planar image consisted of a 512 × 512 array of pixels ranging from 0 to 255 (minimum to maximum) X-ray intensity scale. Although the CCD camera had the capability of collecting 1,024 × 1,024 pixel images, we operated in the 512 × 512 mode for this study, because, with our present facilities, the larger image volume required impractical reconstruction time. The 512 × 512 reconstruction time on a Pentium-based 550 MHz personal computer was ~10 h. Before reconstructing the image volume from the 360 planar images, preprocessing of the individual images was performed in the following steps: 1) two-dimensional polynomial dewarping to correct the image-intensifier spatial distortion, 2) locating the axis of rotation and cropping the projection images to center on that axis, 3) flood-field division to correct for nonuniform illumination intensity, and 4) normalization of the intensity between projections to correct for any temporal drift.

**Dewarping.** The spatial distortion correction algorithm consisted of two steps. First, the uncorrected individual bb center of mass coordinates (x, y) were determined from the BB phantom image. These coordinates for each set of four neighboring BBs were represented by a set of eight equations (Eq. 1 and 2 for each BB, where i is bb number, 1, 2, 3 or 4). These equations were solved simultaneously for the coefficients a-h which map x’y’ via bilinear interpolation onto the known x,y coordinates of the grid vertices.

\[
x' = a x + b y + c x y + d
\]

\[
y' = e x + f y + g x y + h
\]

The process, illustrated in Figs. 2 and 3, shows the result of this dewarping on the bb phantom image. The comparison between Fig. 3, A and B, can be made by observing that the top row of BBs follows a curved line before, and a straight line after, dewarping. Because the image intensifier and X-ray source were fixed in space, the dewarping coefficients were independent of projection angle. The coefficients were applied to interpolate the correct location of each pixel of the 360 projection images in every lung or phantom data set.

**Central axis location.** The rotation axis was determined as the midpoint between the left- and right-most excursions of a high-contrast feature in a two-dimensional radon transform.
The uniform background on the BB phantom image was cropped so that the axis of rotation occupied the central column of pixels. This resulted in a final preprocessed image size of 497 x 497 pixels.

Spatial normalization. The flood-field image acquired with the same X-ray voltage, current, and geometry as the lung in a particular image volume. The maximum intensity for each pixel. Thirty frames were averaged to suppress temporal noise (primarily quantum mottle). The spatially corrected, cropped projections were then divided by the dewarping process described by Eqs. 1 and 2.

Temporal normalization. Finally, three 20 x 20 pixel regions of interest (ROI) unobscured by the object in any projection were located within the volume. The mean intensity for the three ROI divided by the respective mean flood-field intensity was used as a scaling factor for each image. This scaling factor corrected for any temporal drift in the overall illumination intensity during planar image acquisition (24). This scaling step turned out to be unnecessary because there was no systematic temporal drift in the mean ROI intensities between projection images and the coefficient of variation (CV) in the mean ROI intensity for the 360 projection images comprising an image volume was only about 0.1% for these data sets.

Image Reconstruction

After preprocessing of the projection images, cone-beam reconstruction was performed on the projection data to yield an isotropic reconstruction matrix of 497 x 497 x 497 voxels representing volumes of 2.5 x 2.5 x 2.5 cm³ to 4.0 x 4.0 x 4.0 cm³. The Feldkamp (22, 24) cone-beam algorithm was utilized to weight the projection data to account for the variation in the angle of the incident X-ray beam at each pixel. The reconstruction was obtained by first convolving the weighted projection data, perpendicular to the rotation axis, with the Shepp-Logan (43) filter kernel. The filtered data were then back-projected from every angle. The advantage of the cone beam reconstruction was that it allowed for reconstruction of the entire volume from a single 360° scan. This minimized the scan time, which was important for maintaining tissue mechanical properties during the image acquisition period.

The postreconstruction voxel gray scale values (I) were equalized so that the range from air to PFOB was the same for all reconstructed volumes. First, a region of the volume known to contain only air was selected and its I values were averaged. \( \mu \) represents the average I value for air in a particular image volume. The maximum intensity for each pixel. Thirty frames were averaged to suppress temporal noise (primarily quantum mottle). The spatially corrected, cropped projections were then divided by the dewarping process described by Eqs. 1 and 2.

The right side of Fig. 4 is a three-dimensional rendering of the reconstructed image volume to provide a sense of the data set obtained as a result of these procedures. It was obtained after thresholding the CT volume to allow appreciation of the gross structure. In what follows, the full, unthresholded data set, exemplified by the two transaxial slices depicted in Fig. 4, was used to make quantitative measurements.

\[
I' = \frac{(I - \mu)(W - M)}{\xi - \mu} + M \tag{3}
\]
MEASUREMENTS

Mapping

The first step required for determining vessel dimensions was to locate the vessel segment (the portion of a vessel between consecutive bifurcations) in three-dimensional space. This served two purposes. One was to obtain an orthogonal slice through the segment for subsequent diameter measurement. The other was to identify the vessel segment so that the same vessel segment could be found in a different reconstructed volume. The vessel segment was located by observing a vessel cross section while progressing through the sequence of transaxial slices, as depicted in Fig. 5. Figure 5, left, is a three-dimensional rendering of a portion of a rat pulmonary artery. Figure 5, right, is the corresponding set of transaxial slices demonstrating identification of two bifurcations along the artery. The single ellipsoid becomes bilobular and then splits into two. The location where there is visible separation between the two new ellipsoids represents the crotch of the bifurcation. A series of steps was performed to identify the vessel segment between subsequent bifurcations within the image volume. First, the central voxel coordinates \((x_1, y_1, z_1)\) of each of the new ellipsoids in the slice at which the single ellipsoid completely separates into two were recorded. Second, taking each new ellipsoid individually and proceeding transaxially through the image volume, the coordinates of the central voxel of the ellipsoid were recorded in the slice preceding the slice where lobulation reoccurred \((x_2, y_2, z_2)\). The central axis of a vessel segment was approximated as the line segment connecting \((x_1, y_1, z_1)\) and \((x_2, y_2, z_2)\). The mapping procedure and coordinate locations are illustrated in Fig. 6. A particular vessel segment could be identified by counting the number of upstream bifurcations along the pathway leading to that segment.

Locating Orthogonal Slices

The coordinates in three-dimensional space that defined the vessel central axis also provided an estimate of the vessel diameter. To identify the vessel segment, a series of steps was performed. First, the central voxel coordinates \((x_1, y_1, z_1)\) of each of the new ellipsoids in the slice at which the single ellipsoid completely separates into two were recorded. Second, taking each new ellipsoid individually and proceeding transaxially through the image volume, the coordinates of the central voxel of the ellipsoid were recorded in the slice preceding the slice where lobulation reoccurred \((x_2, y_2, z_2)\). The central axis of a vessel segment was approximated as the line segment connecting \((x_1, y_1, z_1)\) and \((x_2, y_2, z_2)\). The mapping procedure and coordinate locations are illustrated in Fig. 6. A particular vessel segment could be identified by counting the number of upstream bifurcations along the pathway leading to that segment.
segment midpoint. Two vectors that passed through this midpoint, orthogonal to the central axis and to one another, described an orthogonal plane with the vessel segment midpoint as the origin. Cubic interpolation was performed to obtain the GSN values of the orthogonal slice. This procedure is also illustrated in Fig. 6. Figure 7 is an actual vessel segment cross section that is elliptical in the transaxial slice but circular in the orthogonal slice. Although elliptical orthogonal cross sections may be observed in some vascular beds, normal pulmonary arteries are nearly circular (49), as confirmed by observation of the many orthogonal slices in the present study.

Measuring Diameters

Approaches for estimating vessel cross-sectional dimensions from CT data sets include the brightness/area product (5, 31), the full-width half-maximum (FWHM) (9, 39, 48) and others (37). Each method is based on assumptions regarding 1) the form of the blurring function resulting during image acquisition and processing [the point spread function (PSF)], 2) the size of the vessel relative to the PSF, 3) the thickness of the CT slice, and 4) the obliqueness of the vessel segment axis relative to the orientation of the CT slice. To take full advantage of the resolution obtainable with the high contrast images collected in this study, concepts underlying these methods were extended to derive a general diameter measuring technique applicable for the entire range of vessel diameters [both larger and smaller than the FWHM of the PSF (FWPSF)] as follows.

In a theoretical imaging system whose PSF is a delta function and the CT slice has no thickness, the intensity of the line of pixels (a line scan) across the minimum diameter of the elliptical cross section of an obliquely cut vessel would appear as a rectangular function. In reality, blurring is introduced in the image acquisition and reconstruction and by finite pixel size and slice thickness. The latter is eliminated by the use of only orthogonal slices, as indicated above. The actual blurred image of the vessel is then essentially the PSF, or blurring function, convolved with the theoretical vessel cross section. The FWHM approach applied to the line scans recovers the vessel diameter as long as the diameter is large enough compared with the FWPSF, but it overestimates the diameter when the diameter approaches the FWPSF. This can be appreciated by assuming a Gaussian distribution for the PSF as in Eq. 4

\[
PSF(x) = e^{-x^2/2\sigma^2} \tag{4}
\]

where \( x \) is the axis increment on which the PSF is defined and \( \sigma \) is the standard deviation. Half the maximum height of the PSF occurs at \( x = \pm 1.175 \sigma \). Thus the FWPSF is \( \approx 2.35 \sigma \). As the actual vessel diameter decreases below FWPSF, the FWHM of the blurred line scan approaches FWPSF. The smallest imaginable diameter may be thought of as almost a delta function that when convolved with the PSF would return the PSF, in which case the FWHM method would return the FWPSF rather than the diameter.

The behavior of a line scan across a vessel image is further demonstrated in Fig. 8, top, illustrating three sets of rectangular functions representing line scans of slices through the ideal (unblurred) image volumes containing cylinders of one X-ray-absorbing medium embedded in three different absorbing media (simulating different tissue densities). These functions were convolved with the PSF of Eq. 4 to simulate line scans of the reconstructed images (Fig. 8, bottom). The graph in Fig. 9A is the FWHM for the simulated line scans in Fig. 8, bottom. The FWHM versus the diameter relationship is independent of the GSN of the imbedding medium, and linearly proportional to diameter when the diameter is larger than FWPSF, but it approaches the constant FWPSF when the diameter is small. The GSN height (Gmax) of the simulated line scans above that of

![Fig. 7](image_url)

**Fig. 7.** Top: three-dimensional rendering of portion of a rat pulmonary artery. Bottom, left: transaxial slice with its elliptical cross section of the vessel due to the oblique angle between the vessel segment central axis and the imaging system axis of rotation. Bottom, right: orthogonal slice through the vessel showing the nearly circular cross section.
the imbedding medium (GSN_m) is constant for large cylinders and then becomes proportional to the diameter as the diameter decreases (Fig. 9B). Taken together, the quantity FWHM × (G_{max} − GSN_m), which approximates the area between the line scan and GSN_m is linearly proportional to the diameter over the entire diameter range (Fig. 9C) as is the actual area under the line scan (Fig. 9D). However, the slope of the area versus diameter line depends on GSN_m as summarized by Eq. 5

\[ D = \frac{A}{s_0 \cdot \left(1 - \frac{\text{GSN}_m}{\text{GSN}_{\max}}\right)} \]  

where A is the measured area, D is the measured diameter, s_0 is the slope of the area-diameter line when GSN_m = 0, and GSN_{max} is the maximum GSN for the entire image volume. To take advantage of the area for measuring diameter, s_0 can be determined by including, in the imaged volume, an object with known diameter and with similar X-ray absorbance as the vessel contrast medium. We obtain the area as follows.

Assuming a Gaussian PSF, the functional form of a line scan through the axis of a vessel can be approximated by Eq. 5, referred to subsequently as the modified Gaussian function (MGF) and illustrated in Fig. 10.

When the MGF is fit to the line scan, the integral of MGF − GSN_m produces an area proportional to diameter. Thus a method for measuring vessel diameters is achieved. However

\[
\text{MGF}(x) = \begin{cases} 
\text{GSN}_m + (G_{\max} - \text{GSN}_m) \cdot e^{-(k-a)^2/2\sigma^2} & x < (k-a) \\
\text{GSN}_m + (G_{\max} - \text{GSN}_m) & (k-a) \leq x \leq (k+a) \\
\text{GSN}_m + (G_{\max} - \text{GSN}_m) \cdot e^{-(k+a)^2/2\sigma^2} & x > (k+a) 
\end{cases}
\]  

there are additional practical problems involved in selecting a line scan that passes through the central voxel of the vessel cross section and in minimizing the effect of random variations in the estimated diameter resulting from using a single line scan. The solution for both was to obtain the orthogonal slices as indicated above and, then, to fit the MGF to the entire cylindrical cross section viewed as a surface of revolution using a least-square fit of Eq. 6. The result is an axially symmetric surface [the modified Gaussian surface (MGS)] such as illustrated in Fig. 10, which represents an average of all radial line scans through the center of the cylindrical vessel cross section. Thus the integral of Eq. 6 provides the value of A in Eq. 5.

RESULTS

The MGS fit method was tested on a phantom consisting of calibrated titanium alloy (90% titanium, 6% aluminum, and 4% vanadium) wire segments of 50, 100, 200, 460, 500, and 1,000 μm diameters. Two different surrounding absorbing media were obtained by immersing a portion of the wire lengths in a silicone gel medium, whereas the rest of the wire lengths were surrounded by only air. Figure 11 shows the image data in the same format as the simulations in Fig. 9.

To evaluate the effects of both the orientation and position of objects within the cone beam field of view, another phantom was constructed with 50 μm and 500 μm wires scattered in a medium of silicone gel so that they were oriented from 0 to 45° relative to the axis of rotation and 0 to 90° of the cone beam angle from the center to the edge of the field of view. The CV in the estimated diameter was 14.5% for the 50-μm wire and 9.4% for the 500-μm wire. Less than 4.1% of the variation in estimated diameter could be attributed to the angle relative to the axis of rotation and <7.4% to vertical distance above or below the central plane perpendicular to the axis of rotation. Although the wire phantom may not exactly reproduce the conditions of an actual vessel lumen imbedded in its unique tissue medium, the similarities of the average and CV of the standard deviations (s) of the PSF obtained with wire...
phantoms \[2.42 \pm 0.41 \text{ pixels (CV = 17\%)}\], and the 783 vessel diameters measured for the distensibility study indicated below \[2.03 \pm 0.36 \text{ pixels (CV = 18\%)}\] is one measure of consistency between the two.

Fig. 12 shows the results of the method applied to a large (1,150 \(\mu\)m) and a small (43 \(\mu\)m) artery in an image volume of a rat lung.

To investigate the distensibility of rat pulmonary arteries, 162 arterial vessel segments ranging from \(\sim 106\) to 1,681 \(\mu\)m at the lowest pressure and from about 151 to 2,743 \(\mu\)m at the highest pressure were measured at the five intravascular pressure settings. Over this range of pressures and vessel sizes, the diameter versus pressure relationship was nearly linear, as exemplified in Fig. 13 by a representative group of vessel segments covering the range of diameters studied. Therefore, the diameter versus pressure data were parameterized by a slope \((\beta)\) and intercept \([D(0)]\) using Eq. 7 after Yen et al. (49) and others (2)

\[
D(P) = \beta P + D(0)
\]  

where \(P\) is the intravascular pressure (in mmHg), \(D\) is the vessel diameter (in \(\mu\)m) and \(D(0)\) is the diameter extrapolated to \(P = 0\).

The values of \(\beta\) for all the measured vessel segments are plotted versus \(D(0)\) in Fig. 14. Because the fractional differences in diameters over the pressure range studied are small, and because \(\beta\) and \(D(0)\) are highly correlated in the regression analysis for Eq. 7, errors in the diameter measurements can have a proportionately larger impact on the estimates of \(\beta\) and \(D(0)\) than on the estimates of the individual vessel diameters. This is reflected in the fact that the CV in the paired
measurements obtained at the high pressure was only 4.1%, whereas the average of the coefficients of variations in β and D(0) (standard error of the estimate divided by the estimated value) calculated for the individual vessels were 29 and 28%, respectively. Also the distributions of the coefficients of variation were highly skewed as reflected by the fact that respective medians were only 20 and 12%. To graphically represent the distribution of the standard errors of the estimates in Fig. 14, the gray level of the symbol representing \( D(0), β \) for each vessel is inversely proportional to the standard error. The key observation from this weighting of the data symbols is that the outlying points tend to have large standard errors. Thus the variability in the relationship between β and D(0) includes a component that is due to the amplification of errors in the diameter measurements resulting from the transformation resulting from fitting Eq. 7 to the data. To evaluate the relationship between β and D(0) for the data in Fig. 14, linear regression was carried out assuming proportionate errors in both y and x values, i.e., by minimizing the sum of the squared distances orthogonal to the regression line (10). The values were either weighted equally or they were weighted according to the standard error of the estimate as indicated by the symbol gray levels in Fig. 14. Also, the intercept was either a free parameter or fixed at zero. The F-test was used to determine whether the weighting significantly altered the fit and whether a nonzero intercept was supported by the data. The results were essentially the same whether the data were weighted or not, and there was no significant improvement in the fits when the intercept was free. The latter implies that the average vessel distensibility, \( α \), defined as β/D(0) for an individual vessel, was independent of vessel size with the average value approximated by the slope of the Fig. 14 graph. The slope was 2.85 ± 0.19 for the weighted and 2.82 ± 0.19%/mmHg (SE) for the unweighted fit. The average of the values of α calculated for each individual vessel was 3.23 ± 0.56%/mmHg (SD) (CV = 110%), but the distribution is quite skewed as expected for this transformation of the diameter data (34). This is reflected by the fact that the median of the individual values was 2.73%/mmHg, and thus closer to the regressed values from Fig. 14.

Discussion

The key aspects of the methodology were generally discussed above as motivation for the various steps in the process. In summary, the approach taken was to use the geometric magnification obtainable with a small focal spot to obtain high-resolution CT images of the rat lung with the pulmonary arterial tree contrast enhanced by the brominated perfluorocarbon. The three-dimensional image volume was reconstructed with isotropic resolution using a cone beam reconstruction algorithm. The vessel diameters were then obtained by fitting a functional form to the image of the circular vessel cross section. The functional form was chosen to take into account the PSF of the image acquisition and reconstruction system. The diameter measurements obtained over a range of vascular pressures were used to characterize the distensibility of the rat pulmonary arteries.

The vessel distensibility results indicate that over the vessel diameter range studied the distensibility of the rat pulmonary arteries (2.8%/mmHg) is within the range of values for pulmonary arteries of larger species studied previously. In summarizing the data available at the time, Al-Tinawi et al. (2) found that an average value of about 2%/mmHg was consistent with measurements on dog, cat, and human pulmonary arteries over the full range of arterial diameters. However, the variability from study to study tends to confound the issue of possible species differences. The distensibility of rat pulmonary arteries has been studied previously either by mounting isolated vessel segments on wires so that the force and distance between the wires could be measured (12, 28) or by cannulating isolated vessel segments such that the transmural pressure could be manipulated while the diameters were monitored via video microscopy (32). The distensibility calculated for the cannulated arteries in the 500- to 700-μm diameter range was also about 2.8%/mmHg (32). For the wire-mounted vessels segments in the 120-μm to 1-mm diameter range studied, the average was about 3.7%/mmHg (12, 28). The somewhat larger latter values might have something to do with the different vessel preparation. The distensibility in the present study is defined by the intravascular pressure rather than transmural pressure. Transmural pressure is also affected by transpulmonary pressure and lung volume (1, 27, 45). Thus the distensibility values obtained in this study have to be considered to be specific for the transpulmonary pressure used. It is also possible that transmural pressure is a variable contributing to the range of previously reported values in other species. Such questions can be addressed in future studies using the methods described herein.

Although it has been suggested by some studies that pulmonary arterial distensibility may be vessel size...
dependent (33), the summary provided by Al-Tinawi et al. (2) suggested that the distensibility of the pulmonary arteries of the various species studied is nearly the same for vessels of any size, or that any systematic dependence on vessel size is small compared with the variability among vessels of a given diameter. In this regard, the present rat lung data are consistent with the results from the larger species. This diameter independence may be somewhat surprising given how vessel wall composition varies over this diameter range (17). However, there may be an adaptive advantage to the constancy of this mechanical property.

Figures 13 and 14 reflect two key relationships, namely, the nearly linear diameter versus pressure relationship for the individual vessels over the pressure range studied and the diameter independence of the vessel distensibility over the diameter range studied. One functional consequence of such relationships is that they tend to minimize the sensitivity of the distribution of flow among the branches of a heterogeneous, asymmetric, vascular tree to changes in total flow rate. If the distensibility were diameter dependent, for example decreasing or increasing in proportion to vessel diameter, increasing cardiac output would tend toward a redistribution of flow to, or away from, respectively, the smaller branch at an asymmetric bifurcation. Likewise, because of the arterial-to-venous pressure drop through the vascular network, a nonlinear diameter versus pressure relationship might have a similar effect when the pressure drop is affected by a change in total pulmonary flow. This can be appreciated by noting that the inflow pressure ($P_{\text{in}}$) versus flow ($Q$) relationship for a distensible vessel segment having a cylindrical configuration at $D(0)$, length $L$, outflow pressure $P_{\text{out}}$, viscosity $\mu$, distensibility $\alpha$, defined by $D(P) = D(0)(1 + \alpha P)$, and Poiseuille flow (19, 30, 50) is

$$P_{\text{in}} = \frac{([640QL\mu\alpha]/\pi D(0)^4] + (1 + \alpha P_{\text{out}})^{5/3} - 1}{\alpha}$$  \hspace{1cm} (8)$$

Changes in total pulmonary blood flow have been accompanied by changes in the spatial distribution of pulmonary blood flow to lesser and greater extents in different experimental settings (6, 8, 11, 35, 44), and various factors may be involved. However, it might be assumed that the observed distensibility pattern helps to maintain the robustness of the flow distributing network in the face of changing flow, thereby helping to keep the pulmonary flow distribution within bounds appropriate for efficient gas exchange, regardless of the cardiac output.

One of the anticipated uses of this pulmonary vascular imaging approach is for the collection of more extensive pulmonary vascular morphometric data. In the past, pulmonary vascular morphometry has been carried out mainly on a small number of plastic casts of

Figure 15 shows the effect of changing flow into a simulated vascular tree made up of the asymmetrical branches depicted in Fig. 16 when $\alpha$ is constant for all vessel segments, regardless of $D(0)$ and with $\alpha$ as a function of $D(0)$. With $\alpha$ constant, the relative distribution of flow among the branches and out the outlets is independent of the total flow entering the tree. However, with $\alpha$ either directly or inversely proportional to $D(0)$ the flow distribution is dependent on the total flow, as exemplified by the outlet flow distributions in Fig. 15.

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