Fractal branching pattern of the monopodial canine airway

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Wang, Ping M., and Steve S. Kraman. Fractal branching pattern of the monopodial canine airway. J Appl Physiol 96: 2194–2199, 2004; 10.1152/japplphysiol.00604.2003.—Unlike the human lung, monopodial canine airway branching follows an irregular dichotomized pattern with fractal features. We studied three canine airway molds and found a self-similarity feature from macro- to microscopic scales, which formed a fractal set up to seven scales in the airways. At each fractal scale, lateral branches evenly lined up along an approximately straight main trunk to form three to four two-dimensional structures, and each lateral branch was the monopodial main trunk of the next fractal scale. We defined this pattern as the fractal main lateral-branching pattern, which exhibited similar structures from macro- to microscopic scales, including lobes, sublobes, sub-sublobes, etc. We speculate that it, rather than a mother-daughter pattern, could better describe the actual asymmetrical architecture of the monopodial canine airway.

PULMONARY AIRWAYS ARE ORGANIZED in a complex branching arrangement to facilitate gas exchange in the lung. The branching airways in animals, such as the mouse, rat, dog, pig, donkey, and horse, are considered to exhibit a monopodial branching pattern (9, 14–17, 23), and the monopodial airway also has been used as the airway model for environmental research to compare with the human lung in aerosol deposition (2–5).

Existing theories for airway branching are based on a “mother-daughter” pattern and have been considered as either divergent or convergent (7, 19). However, this branching pattern involves a complicated airway tree structure with ~20 orders or generations. When branches divide with unequal diameters or there are trichotomic branching structures (6) in the monopodial branching pattern, it is difficult to accurately determine the branch generation or order number. For example, it is hard to understand how a branch could have a zero length in the canine airway tree (8).

A universal pattern frequently found in nature is the fractal form (1, 13). Fractal geometry, first described by Mandelbrot (11), exhibits a self-similarity feature at different scales. The structure of the airway tree has been previously described as following such fractal geometry (11, 20). The monopodial canine airway is asymmetric, with branches laterally arising from a central trunk (22, 23). Our hypothesis is that the monopodial canine airway follows a fractal branching pattern with a main lateral-branching structure. We examined canine airway casts to identify whether a fractal feature of self-similarity exists in the monopodial branching system, and we quantified the branch geometry in the main lateral-branching pattern at various fractal spatial scales.

METHODS

We made silicone molds of canine tracheobronchial trees, as previously described (21). In brief, the intact lungs from three normal adult mongrel dogs (weight 20–40 kg) were excised postmortem after the dogs were used for other research purposes. The lungs were inflated with compressed air at 25 cmH2O and dried for >48 h until the weight was constant. Then, we injected silicon sealer into the airways of the dried lungs via the trachea. After the silicone cured, the lung tissue was removed by immersion in sodium hydroxide solution (10 M). We measured lengths and diameters of the branches of the canine airway mold (Fig. 1) with a caliper and determined the relationship of branch geometry to the branching generation. All procedures were carried out in accordance with institutional guidelines at the University of Kentucky.

RESULTS

We found a self-similarity feature in the canine airways of each lobe at different magnifications ranging from macro- to microscopic scales, i.e., lobe to sublobe, sub-sublobe, etc. This pattern was evident at all scales of the airway. For example, in Fig. 2, we show five fractal generations in the intermediate lobe airways.

Main lateral-branching pattern. We define our terminology as follows. Main trunk is an approximately straight airway, from which arise lateral branches, and each lateral branch becomes the main trunk of the next smaller level or scale. Segment is the interval between two adjacent branching nodes along the main trunk. Fractal scales are each fractal level of the main lateral-branching structure, making up the entire canine airway. Generation refers to the branches in the main lateral-branching pattern.

The general structural features in the main-branching pattern of the monopodial canine airway, as seen in these three lungs, were as follows.

First, in the monopodial airway tree, branches laterally arise from a main (approximately) straight trunk to form a plane or wing structure. There were three to four similar two-dimensional (2D) lateral-branching wings surrounding a main trunk with an angle ranging from 90 to 150° degrees apart. This arrangement formed a three-dimensional (3D) structure to fill the relevant space (Fig. 3). We labeled the lateral-branch structures as A, B, C, and D wings based on their sizes, ranging from the largest to the smallest. The airway structure of the intermediate lobe shown in Fig. 2 is a specific sample of a lobe exhibiting three 2D lateral-branching (A-B-C) wings. The number of 2D lateral-branching wings surrounding a main

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trunk depends on the relevant space in the lung. For example, the cross section of a lobe cut perpendicular to the main trunk of the lobe will be triangular, because there will be three 2D lateral-branching wings with an angle of 105–150° apart. If the cross section is an approximate diamond shape, there will be four 2D lateral-branching wings with an angle of ~90° apart.

Second, the branch conception here is not the same as the mother-daughter branching pattern described in other models (7, 8, 19) in which a segment arises between two adjacent branch nodes. In the main lateral pattern of the monopodial canine airway, we considered the branch to be a segment as long as the whole, straight trunk and tapered in diameter regardless of how many lateral branches developed from it.

Third, based on this branch concept, we conceived a new branch-generation system for the monopodial airway following a pattern of irregularly dichotomized branching. In Fig. 4, we show the designation of the branches in a 2D lateral-branching wing with six generations.

Fourth, for each wing, a quantitative relationship existed in the 2D lateral-branching structure. For example, there was a strong relationship between the log branch generation number and log branch length or diameter at the branch root in the intermediate lobe (Fig. 5, B and C) (P < 0.01). All correlation coefficients for the log-generation number vs. log-length or log-diameter regression exceeded 0.95. The relationship of...
length vs. diameter (at the root of the branch) in the A lateral-branching wing was also highly significant ($P < 0.002$) (plot not shown).

The lateral branches in a single 2D lateral-branching wing also evenly branch off from the main trunk. For example, the intervals between two adjacent lateral branches in the A lateral-branch wing are approximately the same at any fractal scale in the intermediate lobe airways (Fig. 6B) ($P < 0.03$), and the interval is proportional to the main trunk length. We may obtain an equation from Fig. 6B as

\[
\text{Main trunk length} = (\text{interval} \times \text{total lateral branch no.}) + \text{tail length} \tag{1}
\]

See Fig. 7 for the tail length, interval, and lateral-branch number. We also found, in the case shown in Fig. 6B, that the relationships between the scale number and average interval or total lateral-branch number (Fig. 6C) were

\[
\text{Interval} = 27.56 e^{-0.504 \text{ scale no.}} \tag{2}
\]

and

\[
\text{Total lateral branch no.} = 10.57 e^{-0.328 \text{ scale no.}} \tag{3}
\]

All parameters were significant ($P < 0.007$).

Combining Eqs. 1-3, we got

\[
\text{Main trunk length} = 291.4 e^{-0.832 \text{ scale no.}} + \text{tail length} \tag{4}
\]

We measured the other two airway trees and found the formula to be similar. Combining all data from the three canine airways together, we obtained

\[
\text{Main trunk length} = 257.7 e^{-0.793 \text{ scale no.}} + \text{tail length} \tag{5}
\]

Thus the set of five equations with 10 parameters shown in Fig. 6B can be reduced to one equation with only two parameters (scale number and tail length). With those quantitative relationships, it is possible to predict the main trunk length of the main lateral-branch structure if we know the scale number and the tail length in this 2D wing of the intermediate lobe of the canine monopodial airway.

Fractal main lateral-branching pattern in the canine airway tree. The fractal main lateral-branching pattern is a pattern that exhibits similar structures at different spatial scales from macro- to microscopic scales, including lobes, sublobes, sub-sublobes, etc. For example, the fractal scale number shown in the intermediate and other lobes was as many as seven because a similar main lateral-branching pattern was shown at different spatial scales of at least seven levels. (Figure 2 only shows the 5 largest scales because the smaller branches are too small to display in detail.) Thus, if the total irregularly dichromatic branching scales in each lobe are seven, and at each scale there are at least three 2D lateral-branching wings, then, for the canine lung with six lobes, the total number of the smallest branches shown in the airway casts (which is all that we could measure) will be at least: $2^7 \times 3^7 \times 6 \approx 1-2$ million.

In summary, we propose a new main lateral-branching pattern for the monopodial canine airway. The basic structure of this pattern includes one main trunk and three or four similar 2D lateral-branching structures (wings) surrounding it with an angle ranging from 90 to 150° apart, forming a 3D structure to fill the relevant space from the macro- to microscopic scales in the lobe 2. This main lateral-branching pattern exhibits a self-similarity fractal feature at different spatial scales from lobe, sublobe, etc. to form a self-similar fractal set, which includes up to seven levels of main lateral-branching structures.
DISCUSSION

We believe that this proposed fractal main lateral-branching pattern better describes the actual asymmetrical heterogeneous architecture of the monopodial canine airway than other patterns. The reasons are as follows.

First, this branching pattern describes the 3D structure characteristics of the monopodial airway, such as the canine airway, in which a series of lateral branches monopodally diverge dichotomously from the main trunk (22). Thus, when two lateral branches in different lateral-branching wings monopodally arise at the same site of the main trunk to form trichotomic branching structures, it will be a simple matter to determine their branching generation numbers as the model of Horsfield et al. did (8). This main lateral-branching pattern points out the fractal 3D asymmetrically branching structure, which other models have been unable to because they only focused on each individual branching node or branch segment between adjacent nodes based on the mother-daughter pattern. We believe that this main lateral-branching pattern in the monopodial branching airways must play an important functional role in preferential distribution of ventilation to peripheral regions of the lung, especially during higher inspiratory flow rates, because the approximately straight monopodial main trunk in this airway arrangement may support an optimal internal flow for faster convective gas transport with less energy dissipation during high-airflow ventilation (3, 12). Thus homogeneous and synchronous gas exchange can be achieved in the whole lung in the narrow, cone-shaped, canine chest, especially during the heavy breathing demands associated with either chase or escape activities. A recent study (18) on the guinea pig lung using functional magnetic resonance microscopy showed that hyperpolarized helium was rapidly distributed within the straight main trunk in the monopodial airway during inspiration, indicating the main lateral-branching structure facilitates gas transport within a straight trunk, leading to fast and simultaneous gas exchange in the whole lung.

Second, compared with other models involving 17–20 generations/orders (6, 8, 19) based on the mother-daughter branching pattern, the monopodial canine airway tree only has up to seven fractal scales based on the main lateral-branching pattern, which simplifies the geometrical structural description of the monopodial canine airway. Also, this scheme emphasizes the overall fractal arrangement of the monopodial airway from macro- to microscopic spatial scales, which is not found in other models because they only focus on single branching nodes or segments in the mother-daughter branching pattern.

Third, the main lateral-branching pattern presents a more robust quantitative picture of the arrangement of the canine monopodial airway than other methods or models. Thus this fractal main lateral-branching pattern appears to give a better description of the 3D architecture in canine airway tree.

Kitaoka and Suki (10) suggested a formula to describe a method for predicting the diameter of the branches determined by the rate flow through them

\[ d_0^n = d_1^n + d_2^n \]  

(6)

where \( d_0 \) is a diameter of the parent branch and \( d_1 \) and \( d_2 \) are the diameters of daughters 1 and 2, respectively. We applied their formula to our data considering a lateral branch monopodally dichotomizing from the main trunk as the daughter 1 branch and the main trunk before and after this branching node are the mother branch and daughter 2 branch, respectively (Fig. 8, left). We can then calculate the value of \( n \) based on the
diameter ratios of two daughters to the mother branches as \( d_1/d_0 \) and \( d_2/d_0 \) based on Eq. 7 derived from Eq. 6
\[
1 = (d_1/d_0)^n + (d_2/d_0)^n
\]  
(7)

We found there to be a linear relationship between the daughter diameter (at the branch root) and the mother diameter (Fig. 8, left) of a lateral-branching wing in the intermediate lobe of the canine airway, indicating that the diameter ratio of the lateral branch (daughter 1) to main trunk at each node along the main trunk within this 2D wing was the same. This result was repeatable in all other lobes. The diameter ratio of \( d_1/d_0 \) or \( d_2/d_0 \) in this lateral-branching wing could be obtained from the slope of the linear regression. Then, we could calculate the \( n \) value with Eq. 6 for each lateral-branching wing based on the slope shown in the linear regression plot (Fig. 8). For example, the \( n \) value of the intermediate lobe of one canine airway cast shown in Fig. 8 is 2.4. We found that \( n \) values could be different in different 2D lateral-branching wings surrounding a same main trunk. Such \( n \) values ranged from 1.6 to 2.4 in four lateral-branching wings in the left-top lobe of the canine airway tree at the first fractal scale. A smaller \( n \) value indicates a smaller lateral-branched diameter compared with the main trunk diameter, and a smaller lateral-branch diameter indicates a shorter length of a lateral branch in this wing. Thus the lateral wing size is dependent on its \( n \) value to fill its relevant space. This result quantitatively describes the 3D branching structure in the main lateral-branching pattern. Thus, based on these specific features of the main lateral-branching pattern, it may be possible to predict the lateral-branching node locations and branching geometry in the monopodial canine airway. The same features shown in the branching structure of the intermediate lobe also appeared in other lobes in the monopodial canine airway (data not shown), and the results were repeatable in all three canine airway casts (Tables 1 and 2).

Several possible errors might exist in our analysis. First, the morphology of the silicon airway cast may not accurately duplicate the original because of lung drying and silicon shrinkage during the process of making the cast. Second, some peripheral bronchioles were not captured in the cast if the silicon sealer did not reach all terminal airways. Also, we analyzed the structural geometry in the main lateral-branching system with simple regression analysis. This may be too simple to describe the geometric features of the monopodial airway. The fluid dynamic implications of this main lateral-branching pattern, it may be possible to predict the lateral-branching node locations and branching geometry in the monopodial canine airway.

Table 1: Data of the linear regression slope in the logarithmic relationship of the generation number vs. the branch length or diameter at the branch root in the A lateral-branch wing of the intermediate lobe of 3 canine airway casts

<table>
<thead>
<tr>
<th></th>
<th>Slope, mm (length)</th>
<th>Correlation Coefficient (r)</th>
<th>Slope, mm (diameter)</th>
<th>Correlation Coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cast 1</td>
<td>2.169</td>
<td>0.973</td>
<td>1.569</td>
<td>0.998</td>
</tr>
<tr>
<td>Cast 2</td>
<td>2.230</td>
<td>0.941</td>
<td>1.741</td>
<td>0.924</td>
</tr>
<tr>
<td>Cast 3</td>
<td>2.131</td>
<td>0.939</td>
<td>1.701</td>
<td>0.933</td>
</tr>
<tr>
<td>Mean</td>
<td>2.18</td>
<td>0.939</td>
<td>1.67</td>
<td>0.930</td>
</tr>
</tbody>
</table>

Table 2: Linear regression slope of the relationship between lateral branching node locations and lateral branch number at 5 monopodial fractal levels in the A lateral-branch wing of 3 canine airway casts

<table>
<thead>
<tr>
<th>Fractal scale</th>
<th>Slope</th>
<th>Correlation Coefficient (r)</th>
<th>Main Trunk Length, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cast 1</td>
<td>15.314</td>
<td>0.994</td>
<td>128.48</td>
</tr>
<tr>
<td>Cast 2</td>
<td>10.935</td>
<td>0.995</td>
<td>109.72</td>
</tr>
<tr>
<td>Cast 3</td>
<td>9.976</td>
<td>0.990</td>
<td>87.60</td>
</tr>
<tr>
<td>Fractal scale 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 1</td>
<td>10.494</td>
<td>0.990</td>
<td>71.00</td>
</tr>
<tr>
<td>Cast 2</td>
<td>13.596</td>
<td>0.996</td>
<td>92.24</td>
</tr>
<tr>
<td>Cast 3</td>
<td>10.002</td>
<td>0.998</td>
<td>72.73</td>
</tr>
<tr>
<td>Fractal scale 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 1</td>
<td>6.344</td>
<td>0.977</td>
<td>23.46</td>
</tr>
<tr>
<td>Cast 2</td>
<td>4.245</td>
<td>0.998</td>
<td>22.07</td>
</tr>
<tr>
<td>Cast 3</td>
<td>4.209</td>
<td>0.993</td>
<td>22.01</td>
</tr>
<tr>
<td>Fractal scale 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 1</td>
<td>4.131</td>
<td>0.976</td>
<td>12.28</td>
</tr>
<tr>
<td>Cast 2</td>
<td>3.323</td>
<td>0.977</td>
<td>12.81</td>
</tr>
<tr>
<td>Cast 3</td>
<td>3.752</td>
<td>0.987</td>
<td>16.16</td>
</tr>
<tr>
<td>Fractal scale 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 1</td>
<td>1.962</td>
<td>0.953</td>
<td>6.33</td>
</tr>
<tr>
<td>Cast 2</td>
<td>1.605</td>
<td>0.955</td>
<td>4.36</td>
</tr>
</tbody>
</table>

High correlations were shown at all fractal levels. Slope indicates that the lateral branching nodes are evenly distributed along the main trunk branch. Slope is proportional to the main trunk length (\( P < 0.0001 \)), indicating that the branching structure is regulated by the relevant space in the lobe.
pattern are also not well defined and need to be investigated further. In addition, we found that the monopodial, asymmetrical branching pattern mainly appears in the more proximal conducting airways rather than in the peripheral small airways of the canine lung. One possible reason for more symmetrical branching structures in the peripheral airways may be as follows. The canine cone-shaped rib cage limits the space for lung development. Thus the major conducting airways project into a gradually reduced space. However, there are some regions in the lobe where branches may develop into a gradually increased space, for which a symmetrical branching arrangement is more appropriate.

In the monopodial canine airway, we also found that, at the same fractal scale, 2D lateral-branching structures surrounding one main trunk may have different lateral-branch numbers or segments of different diameters or lengths. This may reflect the different space available for filling in the lobe. We speculate that the branching architecture of the airway is regulated by both flow dynamics for efficient gas exchange and the relevant space available within a fractal scale, the lobe, and the rib cage.

In conclusion, this fractal airway branching pattern could better describe the actual asymmetrical heterogeneous architecture of the monopodial canine airway without the problem of inappropriate ordering of the parent and daughter branches.

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