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# Size-independent distribution of bronchial cartilage in four species of myomorph rodents

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## Abstract

The size-independent distribution of bronchial cartilage in the conductive bronchial tree of four species of myomorph rodents different in body weight was determined by the inspection of translucent cartilage-stained whole-lung-specimens in comparison to bronchial casts. The lungs of the harvest mouse, *Micromys minutus*, body weight 5–7 g, the laboratory house mouse, *Mus musculus*, body weight 35–45 g, the laboratory brown rat, *Rattus norvegicus*, body weight 200–400 g, and the African giant pouched rat, *Cricetomys gambianus*, body weight 1 200–1 800 g, show the same lobulation and ramification of the conductive bronchial tree. All four rodents possess dorsally open cartilaginous braces in the trachea and in both main bronchi up to the first ventral branch of the left lung or to the emerging bronchus of the right middle lobe. The distribution of cartilage tissue in the bronchial tree of the four species investigated is identical and shows no relation to the size of the lung or the bronchi. The definition of the term "bronchus" by the presence of cartilage is criticized and the function of intrapulmonary bronchial elements is discussed.

Key words: Rodentia, lung, airways, bronchi, cartilage

## Introduction

The generally assumed function of cartilage in any airway system is to keep the airways open and to prevent their collapse. In the literature the subject of the function of airway cartilage has been completely ignored. The present investigation determines the distribution of bronchial cartilage in the conductive bronchial tree of mammals of close phylogenetical relation, similar body proportions, comparable locomotory habits, and identical lung anatomy, differing mainly in their adult body size (Gehr et al. 1981). Previous studies of the author proved the four considered species to yield a good basis for this comparison. The lungs of *Micromys*, *Mus*, *Rattus*, and *Cricetomys* share all basic morphological parameters. The lung volumes of all four species are isometrical to their body weight. *Micromys*, *Mus*, *Rattus*, and *Cricetomys* all show an identical pattern of bronchial ramification and of lung lobulation (Valerius 1996). The influence of body size on the cartilaginous stiffening of the bronchi was expected to enlighten the functional relations under which these chondroid elements have evolved.

In compensation for the term "ring" the term "brace" or "C-shaped brace" is used in the present study for the larger extrapulmonary cartilaginous elements. According to the generally used nomenclature, smaller, irregular chondroid elements are called "plates" (Vanpeperstraete 1973).

## Material and methods

From previous studies (Valerius 1996; Dieterlen 1988), the biological data for the harvest mouse, *Micromys minutus* Pallas, 1771, the house mouse, *Mus musculus* Linnaeus, 1758, the brown rat, *Rattus norvegicus* Berkenhout, 1769, and the giant pouched rat, *Cricetomys gambianus* Waterhouse, 1840, are listed in table 1. The given mean values were taken from adult animals of both sexes. For a description of the method for preparing the silicon rubber casts, see Valerius (1996).

**Table 1.** Mean body weights, total body lengths and nose-rump lengths of *Micromys*, *Mus*, *Rattus*, and *Cricetomys*.

| Species (n) | body weight | total body length | nose-rump-length |
|---|---|---|---|
| *Micromys* (15) | 6.6 g | 111 mm | 56 mm |
| *Mus* (15) | 35.9 g | 198 mm | 102 mm |
| *Rattus* (14) | 255.9 g | 394 mm | 211 mm |
| *Cricetomys* (13) | 1447.5 g | 693 mm | 357 mm |

*Micromys* is one of the smallest mammals, whereas *Cricetomys* is a giant myomorph rodent and a medium-sized mammal. The lung sizes of all four species are compared in figure 1, the ramification of the bronchi in the left lung as represented by bronchial casts is shown in figure 2. *Micromys*, *Mus*, and *Rattus* are genera of the family Muridae, while the taxonomy of *Cricetomys* is subject to discussion. This animal may be placed either in the family of Cricetidae or in a separate family, the Cricetomyidae (Dieterlen 1988). Its lung anatomy is in all regards similar to that of the other three species.

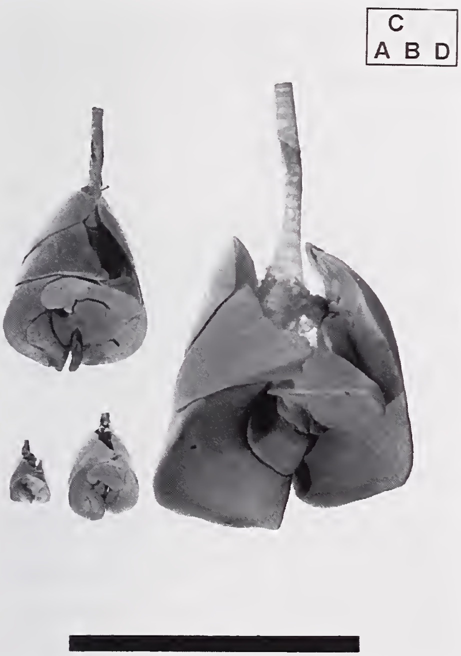


**Fig. 1.** Freeze-dried lungs of *Micromys* (A), *Mus* (B), *Rattus* (C), and *Cricetomys* (D), showing the identical lobulation and the size relations of the lungs in the ventral view. Scale bar represents 100 mm.


**Fig. 2.** Silicone rubber cast of the airways of the left lungs of *Micromys* (A), *Mus* (B), *Rattus* (C), and *Cricetomys* (D), view from ventral. Scale bar represents 10 mm.

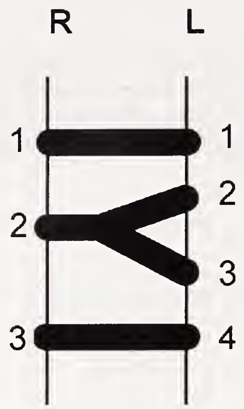


Fig. 3. Schematic drawing explaining the method of counting of the cartilage braces of the trachea. In this ventral view there are three free endings of braces on the right side and four free endings on the left side leading to an average of 3.5 braces in the illustrated part of the trachea.

For the purpose of this study three individuals each of *Micromys*, *Mus*, and *Cricetomys* and four *Rattus* were sacrificed, the lungs were stained and compared to lung casts of the same species.

All animals were killed by exposure to $CO_2$ and placed in a supine position. The trachea was opened and a cannula inserted. According to a method after Simson and van Horn (M. Güntert, Bern, Switzerland, pers. comm.) the whole embryos were rendered translucent.

The lungs were excised from the thorax and filled with a solution containing 80 volume% 96% alcohol, 20 volume% glacial acetic acid and 30 mg Alcian blue. The lungs were fixed and stained for two days, being filled with and submerged in this solution. Then, the specimens were dehydrated in 99% alcohol for three to five days and macerated in a 1% KOH solution for another few days (until the lung becomes soft and lucent). In the last step, the specimens were immersed in a solution of 79 vol.% bi-distilled water, 20 vol.% glycerine and 1% KOH until they were completely translucent. The specimens could be stored in a solution of 50 vol.% 96% alcohol and 50% glycerin for long periods.

The translucent specimens were then analysed with the help of a stereo microscope and the dorsal endings of the cartilaginous braces were counted on the right and the left side and the average was calculated (Fig. 3). Further, the cartilaginous elements in the right and in the left lung were counted.

The length of the trachea was measured from the lower margin of the cricoid to the bifurcation into the main bronchi. The outer diameter of the trachea was taken in the middle of the distance between the cricoid and the bifurcation.

## Results

In all species included in this study, only dorsally opened cartilaginous braces were found in the trachea and the main bronchi. Closed rings of cartilage encircling a bronchus could not be detected in any specimen. All four rodents showed the same distribution of chondroid braces over the identical parts of their conductive bronchial tree, regardless of the size of the lungs or the diameter of the bronchi. Figure 4 shows the stained translucent lungs of *Micromys*, *Mus*, *Rattus* and *Cricetomys*, all enlarged to the same size. For the original size relations of the lungs compare with figures 1 and 2.

### Cartilage in the tracheal wall

These four rodent species possess dorsally open cartilaginous C-shaped braces in the trachea. The number of these chondroid elements differed among the species. *Micromys* and *Mus* showed 14 and 13 braces, respectively, the larger species *Rattus* and *Cricetomys* both had an average of 24 elements (Tab. 2). The bifurcation of the trachea into the two main bronchi was not supported by cartilage in the carina.

### Cartilage in the bronchial walls

Both main bronchi possess cartilage up to the site of the first bifurcation. In the left lung, the cartilaginous braces of the main bronchus extend down to the point where the first ventral branch leaves the main bronchus, and 4–5 small cartilaginous elements can

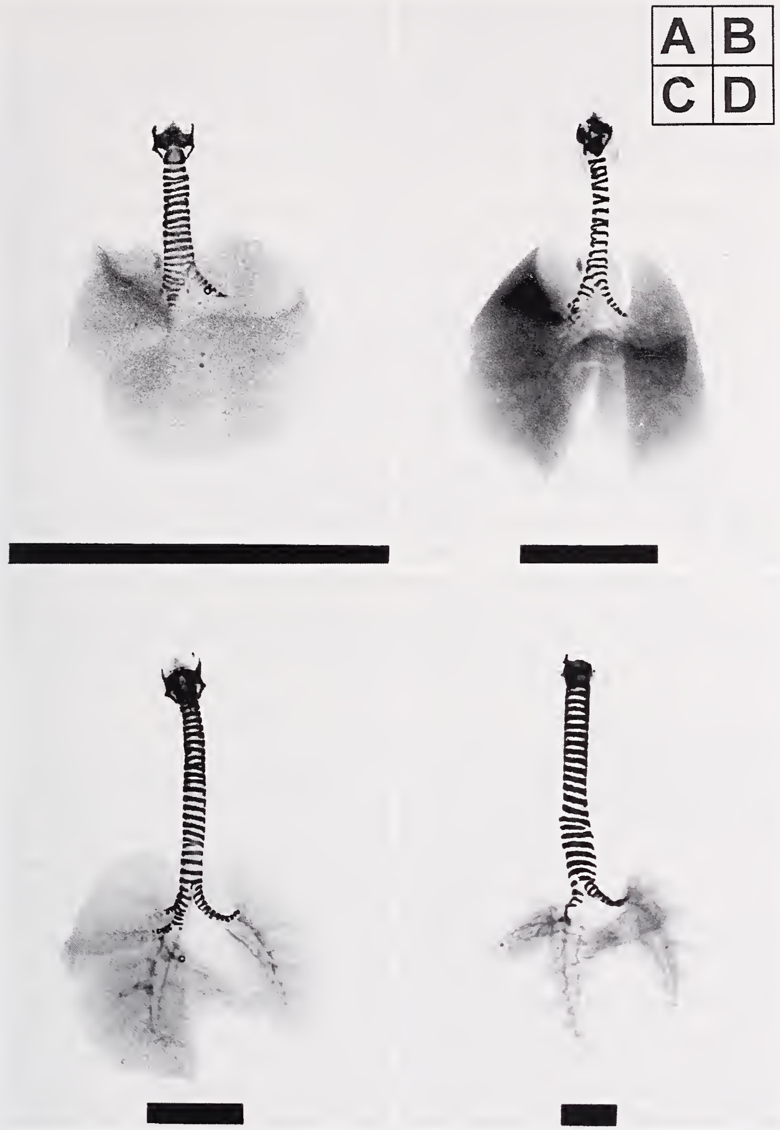


**Fig. 4.** Lungs of *Micromys* (A), *Mus* (B), *Rattus* (C), and *Cricetomys* (D). Translucent specimen showing the distribution and form of airway cartilage. All specimens are brought to identical size. Each scale bar represents 10 mm.

be found in this first ventral branch. In the right lung, the braces join the main bronchus down to the emerging bronchus of the middle lobe. Again, 3–4 cartilaginous elements can be found on this middle lobe bronchus (Tab. 3). In all specimens deserved, no cartilages could be detected in the carina. In the case of a bifurcation, the chondroid elements were placed in the wall opposite to the leaving branch, facing the carina (Fig. 5). Figure 4 shows the distribution of bronchial cartilage in the respiratory tracts of the four species.

**Table 2.** Diameter and length of trachea, in absolute terms and in % of nose-rump length, and number of cartilagineous braces in the trachea of *Micromys*, *Mus*, *Rattus*, and *Cricetomys*.

| Species (n) | outer diameter of trachea | % of nose-rump length | length of trachea | % of nose-rump-length |
|---|---|---|---|---|
| *Micromys* (3) | 2.0 mm | 3.6% | 6.8 mm | 12.2% |
| *Mus* (3) | 2.0 mm | 2.0% | 13.0 mm | 12.7% |
| *Rattus* (4) | 4.1 mm | 1.9% | 30.8 mm | 14.6% |
| *Cricetomys* (3) | 6.3 mm | 1.8% | 45.7 mm | 12.8% |

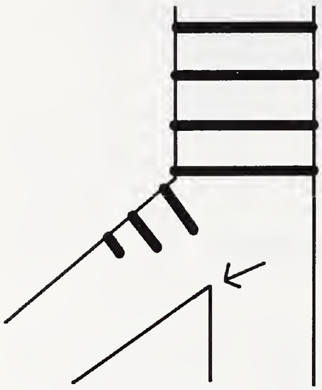

**Fig. 5.** Schematic drawing explaining the distribution of cartilage elements in a lobar bronchus exiting from the main bronchus. The arrow indicates the position of the carina. See also Fig. 4.

**Table 3.** Number of tracheal and bronchial cartilage braces in *Micromys*, *Mus*, *Rattus*, and *Cricetomys*.

| Species (n) | braces in the left main bronchus | braces in right main bronchus | braces of trachea* |
|---|---|---|---|
| *Micromys* (4) | 6.8 | 5.5 | 14.0 |
| *Mus* (3) | 8.0 | 5.0 | 13.7 |
| *Rattus* (4) | 8.5 | 9.5 | 24.0 |
| *Cricetomys* (3) | 8.4 | 6.0 | 24.0 |

* mean of left and right brace endings per trachea

## Discussion

### Functional aspects

The diameter of the airways and the stiffening of the airway walls by cartilaginous braces do not correspond, at least not when the trachea and the extrapulmonary bronchi are compared to the intrapulmonary bronchi, and when the intrapulmonary bronchi are compared to each other according to their positions and diameters.

All extrapulmonary airways in all four species are equiped with cartilage, regardless of their diameter. All intrapulmonary airways lack cartilage, at least, they possess no chondroid tissue soon after the bronchus enters the lung tissue.

Vanpeperstraete (1973) described principal differences in the form of intrapulmonary and extrapulmonary airway cartilage for several mammalian species (rat, dog, sheep, cow, pig, horse). He found regular braces in the trachea and main bronchi and described a sharp boundary to the irregular cartilage elements surrounding the intrapulmonary bronchi.

Extrapulmonary airways have regularly arranged, open C-shaped braces of cartilage. The dorsal part of the airways always remains free of cartilage, so that the airway is never completely surrounded by skeletal elements. The smooth airway musculature connects the open ends of the braces. For this reason, cartilage and muscles are arranged in the same layer of the airway wall.

Extrapulmonary airways in all mammals require cartilage stiffening in order to remain open under differing ambient pressures. The consequences of a pathological destabilisation of the tracheal cartilage elements in man reflects this function (Riede and Costabel 1993). A softening of the tracheal cartilage braces, tracheomalacia, results in a compression of the trachea known as "scabbard trachea" with a narrowing of its lumen.

Intrapulmonary airways in contrast show irregular elements, called plates. A single element is never closed around a bronchus in land-living mammals, but the plates cover the entire circumference of the bronchi. The musclature of these intrapulmonary bronchi in man lies between the epithelium and the cartilage as a closed layer, so that muscles and cartilage form two clearly separate layers of the bronchial wall (Duncker 1994). The cartilage elements in the intrapulmonary bronchial tree do not supply sites of fixation to the bronchial musculature.

These findings point to different functional parameters in extrapulmonary and intrapulmonary airway wall structure.

The intrapulmonary bronchial skeleton consisting of connective tissue and irregular cartilaginous plates is arranged external to the bronchial musculature, the latter determinig the diameter of the bronchi. These plates are not suitable for maintaining a patent bronchus because they do not regularly embrace more than half of the circumference of the bronchi.

The mechanism for maintaining intrapulmonary bronchi in an open condition in land-living mammals is the traction from the expanded lungs acting on these bronchi and the elastic retraction force of the respiratory lung tissue itself. The bronchial tree of mammals, apart from the function of distributing the oxygenated air as evenly as possible over the exchange surface, fulfills a second function, i. e., it is the main skeletal structure of the soft flexible lung tissue. It is hypothesized here, that when intrapulmonary airways in land-living mammals possess cartilage, as for example in man, it helps to prevent overexpansion of the bronchi and, additionally, acts as a fixation for the connective tissue, which stabilizes the inner structure of the lungs. As a consequence of this function, an instability of the intrapulmonary bronchial wall by distruction or aplasia of the cartilage plates leads to a widening of the bronchi, the condition known as bronchiectasis.

## Nomenclature aspects

In the human anatomical nomenclature (Warwick and Brookes 1989), the terms "bronchus" and "bronchiolus" are defined by the presence or absence of cartilage, respectively, in the airway walls (Duncker 1994). According to this terminology obviously homologous parts of the bronchial tree of different animals have to be called "bronchi" in man and other larger mammals, but "bronchioli" in smaller species, simply because of the presence or absence of cartilage. For interspecific comparative investigations and descriptions of the mammalian lungs, a distinction between bronchi and bronchioli cannot be based on the criterion of cartilage in the wall. For example, in the myomorph rodents studied here, the principal airway of each lung should be called the main bronchiolus. The use of the diminutive for the largest intrapulmonary airways of an animal does not appear appropriate. On the other hand, in marine mammals the chondroid rigidity of the airways even includes the terminal bronchioles. In these marine forms cartilaginous spirals or closed rings occur (Belanger 1940; Denison et al. 1971; Engel 1956; Fiebiger 1915/16; Kooyman and Sinnett 1979; Wislocki 1929, 1942). They obviously keep the airways open against external water pressure.

The distinction between bronchi and bronchioli should be limited to human anatomy, where the term "bronchioli" has a long tradition. Neither the distribution of cartilage, nor the diameter, the epithelial lining, or the types of glands present, or any other morphological structure yields a basis for the definition of the term "bronchioli" that would be applicable to mammals of different body size or adapted to different environments. In consequence, the last generations of airway branches before opening into the acini should be called terminal bronchi and respiratory bronchi.

The term "cartilaginous ring" should be avoided as long as the element does not form a closed ring. To my knowledge, no such closed rings have ever been described in any trachea or bronchial tree of land-living mammals.

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## Zusammenfassung

### *Größenunabhängige Verteilung von Bronchialknorpeln bei vier Arten myomorpher Nagetiere*

Die Verteilung und die Form knorpeliger Stützelemente in der Wand der Luftwege von vier verschieden großen mäuseartigen Nagetieren wurden an Hand von knorpelgefärbten Aufhellungspräparaten dargestellt. Die Trachea und die extrapulmonalen Bronchen der euroasiatischen Zwergmaus, *Micromys minutus*, der Hausmaus, *Mus musculus*, der Wanderratte, *Rattus norvegicus* und der Gambia-Riesenhamsterratte, *Cricetomys gambianus*, weisen ausschließlich dorsal offene, regelmäßig angeordnete Knorpelspangen auf. Innerhalb des rechten Lungenflügels dehnt sich die Knorpelaussteifung mit wenigen Elementen bis auf den Abgang des Mittellappenbronchus vom Hauptbronchus aus, auf der linken Seite bis auf den ersten großen ventralen Bronchus, der den linken Hauptbronchus verläßt. Bei allen vier Arten setzt sich die Knorpelauskleidung bis zu einem identischen Punkt im Verzweigungsgefüge des Bronchialbaums fort und nicht bis zu einem bestimmten Durchmesser eines Bronchus. Aufgrund der sehr uneinheitlichen Knorpelverteilung in den Lungen der Säugetiere verschiedener Familien, Körpergrößen und Lebensweisen sollte der Begriff „Bronchiolus" in der zoologischen und veterinärmedizinischen Terminologie nicht gebraucht werden. Es gibt keine Kriterien, die eine artübergreifend sinnvolle Definition des Terminus „Bronchiolus" ermöglichen könnten. Nach der Funktion der Knorpelelemente in der Bronchialwand landlebender Säuger sollte unterschieden werden zwischen extrapulmonalen Knorpelspangen, die das Lumen der Luftwege offenhalten, und intrapulmonalen Knorpelelementen, die zur Stabilisierung der Bronchen gegen den sie weitenden Zug und als Ansatz für das die innere Lungenstruktur stabilisierende Bindegewebe dienen. Bei tauchenden Säugetieren dienen auch die intrapulmonalen Knorpelelemente der Offenhaltung der Bronchen.

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