



Anatomical and histological structure and morphometric parameters of the lungs of the red fox (*Vulpes vulpes*)

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The red fox (*Vulpes vulpes* Linnaeus, 1758) is a widely distributed representative of the family Canidae, characterized by high ecological plasticity and the ability to adapt to diverse natural and anthropogenic environments. Despite its considerable ecological and veterinary importance, the morphofunctional characteristics of its organs remain insufficiently investigated. Particular attention should be paid to the lungs, as they play a pivotal role in gas exchange, maintenance of homeostasis, and adaptation of the organism to environmental conditions. Comprehensive data on the gross and microscopic structure of the lungs are essential for comparative anatomy, veterinary morphology, clinical diagnostics, and experimental research. The aim of this study was to determine the morphofunctional characteristics of the lungs in sexually mature red foxes. Anatomical dissection, gross anatomical examination, histological analysis, morphometry, and statistical data analysis were employed. The lobar organization, topography, shape, linear dimensions, absolute and relative lung weights were assessed. Morphological examination demonstrated that the interlobar fissures were deep and extended to the principal bronchus. All lobes of both lungs were completely separated by fissures and were not connected by pulmonary parenchyma, except for the cranial and middle lobes of the left lung, which were fused dorsally. Organometric analysis revealed that the lungs measured 14.9 ± 0.35 cm in total length, 13.1 ± 0.30 cm in width, and 6.8 ± 0.28 cm in thickness. The lung development index reached $114 \pm 0.35\%$, corresponding to an elongated-expanded morphological type. The bronchial tree originated from the bifurcation of the trachea. Histologically, the bronchial wall consisted of three layers: the mucosa, the fibrous-cartilaginous layer, and the adventitia. Morphometric parameters of the large bronchi were as follows: external diameter, 3478 ± 29 μ m; internal diameter, 1750 ± 12 μ m; total wall thickness, 864 ± 9 μ m, including the mucosa (367.8 ± 7.8 μ m), fibrous-cartilaginous layer (404.6 ± 4.8 μ m), and adventitia (91.7 ± 1.6 μ m). Morphometric analysis also demonstrated statistically significant reductions in all linear parameters of the medium-sized bronchi and terminal bronchioles compared with the large bronchi, reflecting the structural organization of the bronchial tree along successive branching generations. The respiratory portion of the lung parenchyma accounted for $52.74 \pm 0.62\%$, whereas the connective tissue stroma comprised $47.26 \pm 0.75\%$. The mean alveolar volume was $90.4 \pm 1.6 \times 10^3$ μ m³. The findings of this study expand current knowledge of the gross and microscopic anatomy of the lungs in the red fox and contribute to the comparative anatomy of the respiratory system in carnivorous mammals. These data are of practical value for functional morphology, histology, and veterinary pathology and may be applied in veterinary education, forensic veterinary medicine, and future experimental and clinicopathological investigations. Furthermore, the obtained morphometric data provide a valuable basis for interspecies comparative analyses and for modeling respiratory pathological conditions in veterinary research.

Keywords: respiratory system; lung morphotopography; clinical anatomy; morphofunctional characteristics; anatomical dissection; cytoarchitecture; morphometric parameters.

Introduction

Biological processes are fundamental to the existence and functioning of living organisms (Bruggeman & Westerhoff, 2007), as they ensure the maintenance of homeostasis, metabolism, energy balance, growth, development, reproduction, and adaptation to environmental conditions (Cooke et al., 2023; Nanglu et al., 2023).

The contemporary scientific understanding of living organisms is based on the structural-functional concept (Kohl et al., 2010; Franco, 2013), according to which biological entities are regarded as integrated biological systems in which structure and function represent two inseparable and interdependent aspects of organization (Forestiero, 2022). In this context, both the human and animal body, like any biological system, is considered an open system because it continuously interacts with the external environment through the exchange of matter, energy, and information (Sterelny, 2017). A biological system is characterized by self-regulation, self-renewal, and self-reproduction and consists of a complex of physiological organ systems and tissues that function as a unified whole. Within this integrated organization,

organs and organ systems are structurally and functionally interconnected, forming a single living organism. Each level of biological organization possesses a specific structural arrangement composed of interdependent components, including cells, tissues, and organs, each performing specialized biological functions. In this regard, investigations of the functional systems of both domestic and wild animals are of considerable importance for comparative morphology (Turcotte et al., 2017; Geiger & Sánchez-Villagra, 2018), as they provide insights into adaptive structural modifications associated with environmental conditions, lifestyle, and the evolutionary history of a species (Heck et al., 2018; Barash et al., 2023).

Body organs and organ systems operate as a highly integrated functional network (Iliukha, 2022; Horalskyi et al., 2024), enabling adaptive responses to changes in environmental factors, including temperature, humidity, light conditions, and other physicochemical parameters (Buchko et al., 2019; Wishart, 2019). For example, the cardiovascular system exhibits remarkable functional plasticity in response to physical exercise by optimizing blood circulation and enhancing oxygen delivery to active skeletal muscles (Cooper & Loxham,

2019; Eckhardt & Wu, 2021). Likewise, the respiratory system rapidly responds to alterations in the partial pressure of oxygen by adjusting pulmonary ventilation to meet changing physiological demands (Horalskyi et al., 2024). The endocrine system also plays a pivotal role in maintaining internal homeostasis and supporting long-term adaptive responses through hormonal regulation of metabolism, stress reactions, water-electrolyte balance, and numerous other physiological processes. At the same time, the central and peripheral nervous systems coordinate these responses by ensuring rapid signal transmission between the external environment and internal body structures, thereby enabling the organism to respond efficiently to environmental challenges (Sokulskyi et al., 2021; González et al., 2023). Thus, the biological system of an organism represents an open and dynamic entity that continuously interacts with its environment, providing the foundation for survival, adaptation, and evolutionary development (Simões-Costa et al., 2005; Buijendijk et al., 2020).

The red fox (*Vulpes vulpes*) represents an important subject in comparative anatomical research, particularly in studies investigating the anatomy and morphometry of the lungs. Owing to its ecological adaptability and its position among carnivorous mammals, the red fox serves as a valuable model for comparative investigations of respiratory morphology in species adapted to diverse natural habitats. The lungs of this species, which play a central role in maintaining physiological function under variable environmental conditions, provide an appropriate model for studying respiratory adaptations associated with different ecological niches.

In both wild and domestic animals, including livestock species, the maintenance of vital physiological functions depends directly on the efficiency of the respiratory system (Davenport et al., 2010; Fröhlich, 2024). Respiration supplies the oxygen required for aerobic metabolism and energy production, thereby supporting growth, reproduction, productivity, and adaptation to environmental changes (Perry & Burggren, 2007; Hsia et al., 2013). A comprehensive understanding of the normal morphoarchitecture and functional organization of the lungs, as well as the structural alterations associated with pathological conditions, is essential for elucidating not only the anatomical organization of the respiratory system but also the physiological mechanisms that sustain the organism as a whole. Such knowledge contributes to a better understanding of pulmonary gas exchange, adaptive responses to internal and external stimuli, and the impact of structural pulmonary alterations on systemic physiological functions.

Accordingly, investigations of the respiratory apparatus in different animal species are of both fundamental and applied significance for biology, veterinary medicine, zoology, and animal science. Respiration represents one of the principal physiological processes underlying life, constituting a complex physiological and biochemical mechanism responsible for oxygen uptake and carbon dioxide elimination (Molpeceres-Diego et al., 2021). The lungs are the primary organs of external respiration, and their structural organization exhibits pronounced species-specific characteristics reflecting the ecological niche and adaptive strategies of each species. Moreover, the coordinated functioning of the organism depends on the integration of individual organ systems into functional (physiological) systems, each specialized for the performance of distinct biological functions.

Therefore, a detailed investigation of the morphological organization of the lungs in both wild and domestic animals is scientifically justified and highly relevant. Such studies contribute substantially to the advancement of comparative anatomy, veterinary morphology, and zoology while providing a scientific foundation for applied fields, including veterinary medicine, animal health, ecology, and biodiversity conservation. These considerations determined the relevance of the present study and defined its scientific objectives.

Materials and methods

The study was conducted on the lungs of sexually mature red foxes (*Vulpes vulpes* Linnaeus, 1758). The specimens (n = 5) were collected following routine predator population management within the hunting grounds of a forestry district in the Zakarpattia region of Ukraine. Tissue collection was performed in accordance with the

current environmental protection legislation of Ukraine. All experimental procedures complied with the principles of Good Laboratory Practice (GLP, 1981), the General Ethical Principles for Animal Experiments adopted by the First National Congress on Bioethics (Kyiv, Ukraine, 2001), the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986) (European Convention, 1986), the Rules for Conducting Work Using Experimental Animals (Order of the Ministry of Health of Ukraine No. 281, November 1, 2000), and the Law of Ukraine On the Protection of Animals from Cruelty (No. 3447-IV, February 21, 2006) (Nichiporuk et al., 2022).

The lungs were subjected to anatomical dissection. Gross morphometric evaluation included determination of absolute and relative lung weights. Absolute lung weight (ALW) was measured using a RADWAG PS 6000/C/2 laboratory balance (Poland, 2022). Relative lung weight (RLW) was calculated according to the following equation: Relative lung weight (%) = (absolute lung weight / body weight) × 100.

Lung length, width, and thickness were determined by direct measurement. The lung development index (LDI) was calculated using the following formula: Lung development index (%) = (lung length / lung width) × 100.

For histological examination, tissue samples were fixed in a cooled 10–12% aqueous formalin solution for at least 24 h. Following fixation, the specimens were dehydrated, embedded in paraffin according to the protocol described by Horalskyi et al. (2019), and sectioned at a thickness not exceeding 10–12 µm using an MC-2 sliding microtome.

To evaluate the cytoarchitecture and histological organization of the lungs, paraffin sections (8–10 µm thick) were deparaffinized and stained with hematoxylin (Diapath, Italy, 2020) and eosin (Leica Geosystems, Germany, 2020).

Histomorphometric analysis of pulmonary tissue components was performed by light microscopy. On frontal histological sections from each tissue block (n = 14), the proportions of the respiratory parenchyma and connective tissue stroma were determined within a standardized area of 5.0 mm² using an MBS-10 light microscope (Micromed, 1998). The mean alveolar volume was measured by light microscopy using a Micros microscope (Austria, 2014) equipped with an ×8 eyepiece and ×20 objective at a constant tube length, following the methodology described by Horalskyi et al. (2019).

Histological specimens were photographed using a CAM V–200 digital microscope camera (Inter Med, China, 2017).

The anatomical and histological terminology used throughout this study follows the Nomina Histologica Veterinaria and the Nomina Anatomica Veterinaria.

Statistical analysis was performed using variation statistics with the licensed software package Statistica 7.0 (StatSoft Inc., USA). Numerical data are presented as the mean ± standard error of the mean (SE).

Results

The lungs of the red fox are paired, pink-colored parenchymatous organs. As in other mammalian species, they consist of the conducting airways, the respiratory portion of the lung, and blood vessels embedded within connective tissue, which collectively form two compact organs – the right and left lungs.

Topographically, the right and left lungs, together with the heart and other thoracic organs, are located within the thoracic cavity, where they closely appose the thoracic walls and occupy nearly the entire cavity. Consequently, the lungs conform to the shape of the thoracic cavity and exhibit the appearance of a laterally compressed truncated cone.

The pulmonary base is concave and obliquely oriented caudally, where it closely contacts the convex diaphragmatic surface. The apex of each lung extends cranially to the level of the first rib.

The left lung is slightly smaller than the right, reflecting the topographical position of the heart, which is displaced toward the left side and lies between the two lungs (Fig. 1).

Each lung is divided into cranial, middle, and caudal lobes by deep cranial and caudal interlobar fissures. In addition, the right lung possesses an accessory lobe located on its mediastinal surface, resulting in asymmetry between the right and left lungs with respect to their lobar organization (Fig. 1).

The interlobar fissures are well developed and extend deeply to the level of the principal bronchus. With the exception of the cranial and middle lobes of the left lung, which remain connected dorsally by pulmonary parenchyma, all pulmonary lobes are completely separated from one another by deep fissures.

Four surfaces can be distinguished in each lung: the lateral (costal) surface, which is adjacent to the ribs; the medial (mediastinal) surface, facing the mediastinum; the caudal (diaphragmatic) surface,

which contacts the diaphragm; and the interlobar surfaces, located between adjacent pulmonary lobes (Fig. 1). The mediastinal surface exhibits distinct impressions produced by neighboring structures, including the aortic impression, cardiac impression, esophageal impression, and the groove for the caudal vena cava, reflecting the anatomical relationships of these organs situated between the right and left lungs.

Each lung also possesses two principal borders: a rounded dorsal border and a sharp ventral border (Fig. 1). The rounded dorsal border is closely associated with the thoracic vertebrae and the vertebral ends of the ribs. The sharp border is subdivided into the ventral border, which separates the costal and mediastinal surfaces toward the sternum, and the basal border, located at the pulmonary base.



Fig. 1. Gross anatomy of the lungs of the red fox (*Vulpes vulpes*): *a* – costal surface; *b* – mediastinal surface; 1 – trachea; 2 – tracheal bifurcation; 3 – right cranial lobe; 4 – right middle lobe; 5 – right caudal lobe; 6 – accessory lobe; 7 – left cranial lobe; 8 – left middle lobe; 9 – left caudal lobe; 10 – interlobar fissures; 11 – principal bronchi; gross specimen

The cranial lobe of the left lung is irregularly triangular in shape, with the greater portion situated cranial to the heart (Fig. 1). Its cranial region is elongated and tapered, extending to the midpoint of the dorsal border of the first rib. The costal surface is convex, whereas the mediastinal surface is smooth and slightly concave. The caudal portion of the cranial lobe partially overlaps the cranial region of the middle lobe.

The middle lobe of the left lung is irregularly triangular and exhibits a dorsoventrally concave configuration. Its craniocaudal border is thin and contains shallow indentations formed by its close apposition to the heart. The ventral border is sharp. Two weakly developed nipple-like projections are present at the craniocaudal angle. The caudal portion of the lobe is arcuate and overlies the atrium, while the caudocaudal angle is narrow and tapered. The costal surface is slightly convex.

The caudal lobe of the left lung is the largest lobe and has an irregular triangular shape with uneven margins (Fig. 1). Cranially, it borders the cranial and middle lobes, whereas dorsally it is adjacent to the cranial lobe. The rounded dorsal border extends from the level of the sixth to the twelfth–thirteenth ribs. The basal border is sharp and forms a slightly convex arch. The mediastinal surface is triangular and lies in close topographical relation to the thoracic aorta and esophagus, resulting in distinct aortic and esophageal impressions. The diaphragmatic surface merges smoothly with the mediastinal surface without a distinct boundary. Throughout its extent, this surface is concave and contains a centrally located oval depression corresponding to the dome of the diaphragm.

The cranial lobe of the right lung extends cranially to the caudal margin of the first rib. In the expanded state, its caudodorsal region reaches the caudal border of the seventh rib to approximately one-third of its height and is partially overlain by the cranial dorsal portion

of the caudal lobe. The mediastinal surface exhibits two distinct grooves corresponding to the cranial vena cava and the trachea dorsally, as well as a broad cardiac impression extending over most of its surface. The cranial border of the right cranial lobe bears two nipple-like projections. Both the ventral border and the caudodorsal region are thin and pointed.

The middle lobe of the right lung is completely separated from the remaining pulmonary lobes. Its dorsal border overlaps both the cranial and caudal lobes to approximately one-third of the height of the seventh rib. The surface facing the heart exhibits shallow cardiac impressions. When fully expanded, the right middle lobe is elongated and trapezoidal in shape.

The caudal lobe of the right lung is triangular in shape and, similarly to its counterpart in the left lung, is adjacent to the cranial and middle lobes. In addition, it is contiguous with the accessory lobe. The caudal lobe is separated from the cranial, middle, and accessory lobes by deep interlobar fissures extending to the lobar bronchi. Its cranial border is straight and topographically contacts the dorsal region of the cranial lobe. The caudal border is thin and lies against the diaphragmatic dome. The dorsal border is rounded and thickened cranially, gradually becoming thinner toward the caudal end. The ventral border is relatively thick and does not extend to the sternum. The costal surface of the caudal lobe is convex, whereas the diaphragmatic surface is concave. The mediastinal surface is flat and bears distinct impressions produced by the thoracic aorta and esophagus, as well as a dorsal impression corresponding to the vertebral column. A nipple-like projection is present at the craniocaudal region of the right caudal lobe.

The accessory lobe is present only in the right lung. It is relatively small and located on the caudal aspect of the mediastinal surface (Fig. 1). This lobe originates as a subdivision of the caudal lobe and

remains connected to it by a common bronchovascular pedicle. The accessory lobe is bilobed. Its slender cardiac process extends toward, but does not reach, the apex of the heart, occupying the space between the heart and the diaphragmatic dome. The second process, which is somewhat smaller, partially surrounds the esophagus and gradually tapers caudally toward the diaphragm. The accessory lobe remains completely separated from the caudal lobe by an interlobar fissure.

Organometric analysis demonstrated that the mean total lung length of the red fox was 14.9 ± 0.35 cm, with a width of 13.1 ± 0.30 cm and a thickness of 6.8 ± 0.28 cm. The right lung measured 14.9 ± 0.65 cm in length, 5.8 ± 0.20 cm in width, and 6.8 ± 0.23 cm in thickness, whereas the corresponding dimensions of the left lung were 13.2 ± 0.25 cm, 5.4 ± 0.28 cm, and 5.9 ± 0.43 cm, respectively. The calculated lung development index was $114 \pm 0.35\%$, indicating that the lungs of the red fox belong to the elongated-expanded morphological type (Table 1).

The mean absolute lung weight of the red fox was 83.2 ± 1.35 g, whereas the relative lung weight was $1.01 \pm 0.03\%$. The absolute weight of the left lung was 35.6 ± 1.13 g, while that of the right lung was 47.6 ± 2.13 g, which was 1.34-fold greater than the left lung ($P < 0.05$). The lung asymmetry coefficient was 1:1.33 (Table 2).

Lobe-specific organometric analysis demonstrated that the caudal lobes possessed the greatest absolute mass in both lungs, followed by the cranial lobes, middle lobes, and the accessory lobe. The absolute weight of the right caudal lobe was 18.2 ± 1.1 g, whereas that of the left caudal lobe reached 20.7 ± 1.1 g. The absolute weight of the right cranial lobe (14.9 ± 0.85 g) was significantly greater than that of the left cranial lobe (8.7 ± 0.85 g) by a factor of 1.7 ($P < 0.01$). The abso-

lute weights of the middle lobes were 7.8 ± 0.70 g for the right lung and 6.2 ± 0.73 g for the left lung. The accessory lobe of the right lung had an absolute weight of 6.7 ± 0.85 g (Table 2).

Table 1
Species-specific linear morphometric parameters of the lungs of the red fox (*Vulpes vulpes*) ($\bar{x} \pm SD$, $n = 5$)

Lung parameter	Value
Total lung length, cm	14.9 ± 0.4
Total lung width, cm	13.1 ± 0.3
Total lung thickness, cm	6.80 ± 0.3
Lung development index, %	114 ± 0.4
Left lung	
Length, cm	13.2 ± 0.3
Width, cm	5.4 ± 0.3
Thickness, cm	5.9 ± 0.4
Right lung	
Length, cm	14.9 ± 0.7
Width, cm	5.8 ± 0.2
Thickness, cm	6.8 ± 0.2

The relative contribution of the caudal lobes to the total lung weight was the greatest among all pulmonary lobes, accounting for $24.82 \pm 0.95\%$ in the left lung and $21.83 \pm 0.52\%$ in the right lung. The cranial lobes contributed $10.36 \pm 0.64\%$ and $17.87 \pm 0.70\%$ of the total lung weight in the left and right lungs, respectively. The middle lobes accounted for the smallest proportion of lung weight, comprising $7.41 \pm 0.48\%$ in the left lung and $9.38 \pm 0.48\%$ in the right lung. The accessory lobe represented $8.01 \pm 0.65\%$ of the total weight of the right lung (Table 2).

Table 2
Absolute and relative weights of the pulmonary lobes in the red fox (*Vulpes vulpes*) ($\bar{x} \pm SD$, $n = 5$)

Pulmonary lobe	Left lung, absolute weight, g	Left lung, relative weight, % of total lung weight	Right lung, absolute weight, g	Right lung, relative weight, % of total lung weight	Both lungs, absolute weight, g	Both lungs, relative weight, % of total lung weight
Cranial	8.7 ± 0.9	10.36 ± 0.64	14.9 ± 0.9	17.87 ± 0.70	23.6 ± 1.7	28.23 ± 0.84
Middle	6.2 ± 0.7	7.41 ± 0.48	7.8 ± 0.7	9.38 ± 0.48	14.0 ± 1.4	16.78 ± 0.96
Caudal	20.7 ± 1.1	24.82 ± 0.95	18.2 ± 1.1	21.83 ± 0.52	38.9 ± 2.0	46.64 ± 0.69
Accessory	—	—	6.7 ± 0.9	8.01 ± 0.65	6.7 ± 0.9	8.01 ± 0.65
Total	35.6 ± 1.1	42.79 ± 0.89	47.6 ± 2.1	57.12 ± 1.67	83.2 ± 1.4	100.00

The lungs are composed of two principal morphological components: the conducting airways and the respiratory portion. As in other mammals, the conducting airways of the red fox consist of a branching system of bronchi that collectively forms the bronchial (conducting) tree. The respiratory portion comprises successive branches of the respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli, which together constitute the alveolar tree.

The bronchial tree of the red fox is formed by the right and left principal bronchi, which continue as extrapulmonary lobar bronchi before giving rise to the large intrapulmonary bronchi (Fig. 1). The large bronchi subsequently divide into segmental bronchi, which branch into medium-sized bronchi and then into small bronchi. The latter continue as terminal bronchioles, marking the transition to the respiratory portion of the lung.

Formation of the bronchial tree begins at the tracheal bifurcation, where the trachea divides into the right and left principal bronchi. Upon entering the respective lungs, these bronchi give rise to the lobar bronchi supplying the individual pulmonary lobes (Fig. 1).

The principal bronchus of the right lung gives rise to the bronchus of the cranial lobe at an angle of approximately 30° , immediately distal to the first and second tracheal cartilaginous rings following the tracheal bifurcation. Distal to the third and fourth bronchial cartilaginous rings, the principal bronchus bifurcates into two branches: one supplying the middle lobe and the other supplying both the caudal and accessory lobes (Fig. 1).

Similarly, after the fourth bronchial cartilaginous ring, the left principal bronchus divides into two branches, one entering the caudal lobe and the other supplying the cranial and middle lobes. After two additional bronchial cartilaginous rings, the bronchus of the middle lobe undergoes further branching. The cranial and middle lobes of the

left lung are not completely separated but remain connected by a trapezoid-shaped parenchymal bridge (Fig. 2). The caudal portion of the cranial lobe, which is not fused with the middle lobe, overlaps its cranial region, whereas the caudal part of the middle lobe overlies the cranial portion of the caudal lobe throughout its height.

The histological organization of the principal and lobar bronchi resembles that of the trachea. Microscopically, the bronchial wall consists of three tunics: the mucosa, the fibrous-cartilaginous layer, and the adventitia.

The principal bronchi possess the largest transverse diameter. Their luminal surface is lined by pseudostratified ciliated columnar epithelium. The muscularis mucosae consists of bundles of smooth muscle cells located at the junction between the mucosa and the submucosa. These smooth muscle bundles are arranged into an inner circular layer and an outer longitudinal layer. The fibrous-cartilaginous layer of the principal bronchi is continuous and forms complete bronchial cartilaginous rings.

Like the principal bronchi, the walls of the large bronchi consist of three tunics: the mucosa, the fibrous-cartilaginous layer, and the adventitia (Fig. 2a). The muscularis mucosae is well developed and composed of smooth muscle cells arranged in a circular-oblique orientation, extending around the entire circumference of the bronchial wall. Owing to the contraction of these smooth muscle cells, the mucosa forms prominent longitudinal folds that are absent in the principal bronchi. The lamina propria contains numerous aggregates of lymphoid tissue varying in size and shape. Unlike the principal bronchi, the fibrous-cartilaginous layer of the large bronchi is composed of discontinuous elongated hyaline cartilage plates rather than complete cartilaginous rings (Fig. 2a).

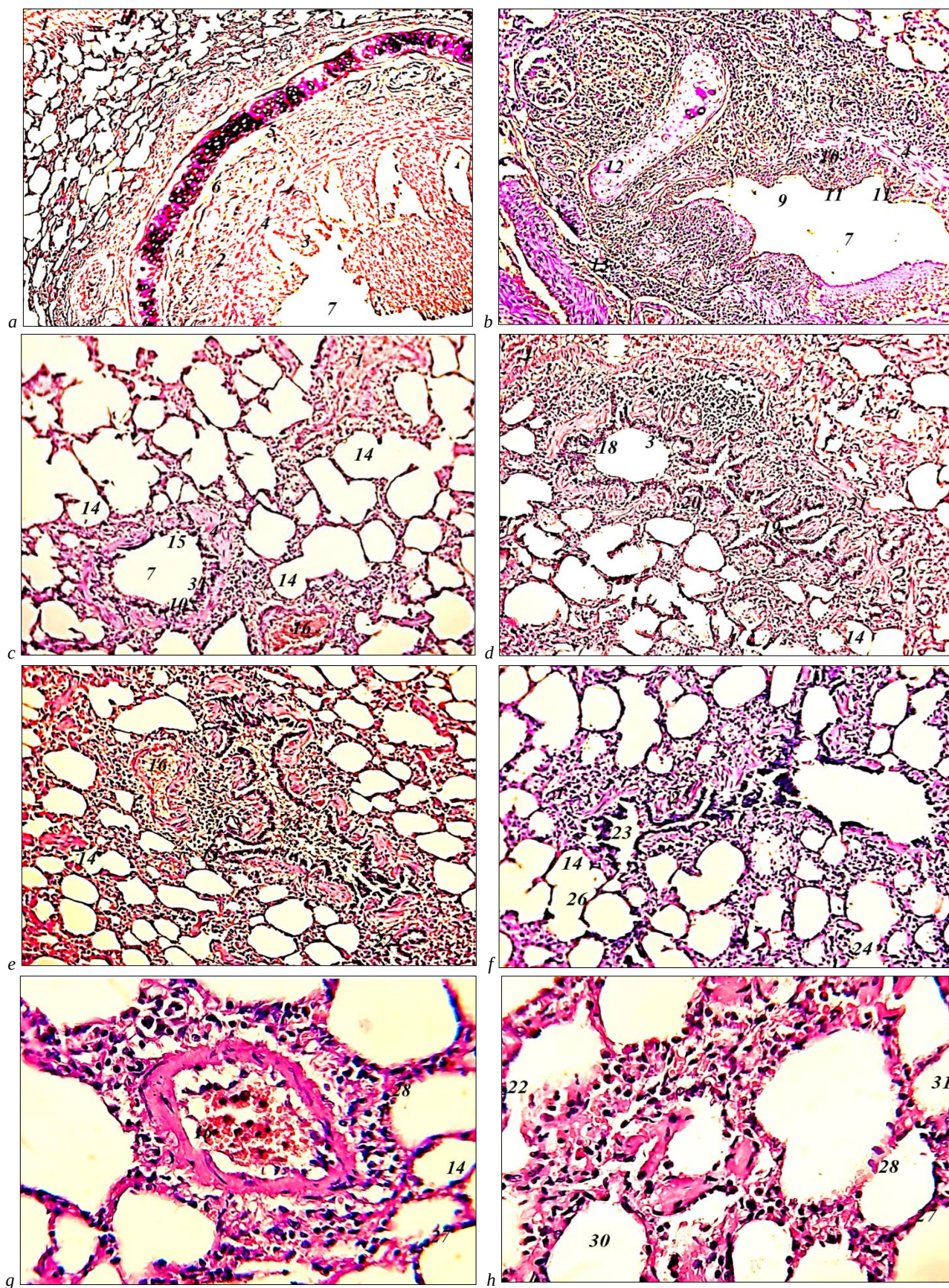


Fig. 2. Histological structure of the lungs of the red fox (*Vulpes vulpes*): *a* – large bronchus; *b–h* – pulmonary tissue. 1 – pulmonary parenchyma; 2 – bronchial wall; 3 – epithelial lining; 4 – muscularis mucosae; 5 – fibrous-cartilaginous layer; 6 – cartilage plate; 7 – bronchial lumen; 8 – adventitia; 9 – medium-sized bronchus; 10 – bronchial mucosa; 11 – mucosal folds; 12 – cartilage islands; 13 – connective tissue stroma; 14 – alveoli; 15 – small bronchus; 16 – blood vessel; 17 – pulmonary parenchyma; 18 – terminal bronchiole (cross-section); 19 – terminal bronchiole (longitudinal section); 20 – bundles of smooth muscle cells; 21 – elastic fibers; 22 – respiratory portion of the lung; 23 – respiratory bronchiole (longitudinal section); 24 – alveolar duct; 25 – bundles of smooth muscle cells; 26 – alveolar sacs; 27 – interalveolar septa; 28 – alveolar epithelial cells (alveolocytes); 29 – large alveolus; 30 – medium-sized alveolus; 31 – small alveolus; hematoxylin and eosin stain

The mucosal lining of the medium-sized bronchi is lined by pseudostratified ciliated columnar epithelium, whereas the muscularis mucosae consists of bundles of smooth muscle cells. The fibrous-cartilaginous layer contains discrete hyaline cartilage plates arranged as isolated cartilage islands (Fig. 2b).

The walls of the small bronchi and terminal bronchioles consist exclusively of the mucosa and adventitia, as the fibrous-cartilaginous layer is absent. The mucosal epithelium of the small bronchi is lined by ciliated pseudostratified epithelium, whereas the muscularis mucosae is well developed and composed of smooth muscle cells (Fig. 2c).

The mucosa of the terminal bronchioles is lined by simple ciliated cuboidal epithelium resting on a distinct basement membrane. The lamina propria contains longitudinally arranged elastic fibers interspersed with bundles of smooth muscle cells (Fig. 2d).

Morphometric analysis demonstrated that the mean external diameter of the large bronchi was $3478.4 \pm 28.9 \mu\text{m}$, whereas the internal diameter measured $1750.2 \pm 12.4 \mu\text{m}$. The mean wall thickness was $864.1 \pm 9.3 \mu\text{m}$, including the mucosa ($367.8 \pm 7.8 \mu\text{m}$), the fibrous-cartilaginous layer ($404.6 \pm 4.8 \mu\text{m}$), and the adventitia ($91.7 \pm$

$1.6 \mu\text{m}$, Table 3). The morphometric parameters of the medium-sized bronchi ($P < 0.01$) and terminal bronchioles ($P < 0.001$) were significantly smaller than those of the large bronchi. The external and internal diameters of the medium-sized bronchi were 1233.4 ± 13.4 and $618.4 \pm 9.9 \mu\text{m}$, respectively. The mean wall thickness measured $307.4 \pm 8.6 \mu\text{m}$, comprising the mucosa ($136.9 \pm 3.7 \mu\text{m}$), the fibrous-cartilaginous layer ($140.2 \pm 3.3 \mu\text{m}$), and the adventitia ($30.3 \pm 0.8 \mu\text{m}$, Table 3).

The smallest morphometric dimensions were observed in the small bronchi and terminal bronchioles, reflecting the absence of a fibrous-cartilaginous layer within their walls (Table 3). The external diameter of the small bronchi averaged $604.1 \pm 9.9 \mu\text{m}$, whereas the internal diameter measured $306.7 \pm 7.5 \mu\text{m}$. Their total wall thickness was $148.7 \pm 3.6 \mu\text{m}$, including the mucosa ($129.6 \pm 1.3 \mu\text{m}$) and the adventitia ($19.1 \pm 0.6 \mu\text{m}$). The terminal bronchioles had an external diameter of $424.9 \pm 9.1 \mu\text{m}$ and an internal diameter of $275.3 \pm 4.9 \mu\text{m}$. The total wall thickness was $74.8 \pm 0.9 \mu\text{m}$, consisting of a mucosal layer measuring $68.3 \pm 1.5 \mu\text{m}$ and an adventitial layer measuring $6.5 \pm 0.3 \mu\text{m}$ (Table 3).

Table 3

Histomorphometric characteristics of the components of the bronchial tree in the lungs of the red fox (*Vulpes vulpes*) ($\bar{x} \pm \text{SD}$)

Parameter	Large bronchi	Medium-sized bronchi	Small bronchi	Terminal bronchioles
External diameter, μm	3478.4 ± 28.9	1233.4 ± 13.4	604.1 ± 9.9	424.9 ± 9.1
Internal diameter, μm	1750.2 ± 12.4	618.4 ± 9.9	306.7 ± 7.5	275.3 ± 4.9
Wall thickness, μm	864.1 ± 9.3	307.4 ± 8.6	148.7 ± 3.6	74.8 ± 0.9
Mucosal thickness, μm	367.8 ± 7.8	136.9 ± 3.7	129.6 ± 1.3	68.3 ± 1.5
Fibrous-cartilaginous layer thickness, μm	404.6 ± 4.8	140.2 ± 3.3	—	—
Adventitial thickness, μm	91.7 ± 1.6	30.3 ± 0.8	19.1 ± 0.6	6.5 ± 0.3

The pulmonary lobules, which constitute the respiratory portion of the lungs, are pyramidal or conical in shape. Histologically, each lobule is composed of numerous pulmonary acini separated by connective tissue septa forming the pulmonary stromal framework.

According to Van Gieson staining, the pulmonary stroma consists of loose connective tissue containing blood and lymphatic vessels (Fig. 2e). The pulmonary acini originate from the terminal bronchioles and subsequently undergo dichotomous branching into respiratory bronchioles, alveolar ducts, and alveolar sacs, thereby forming the alveolar tree (Fig. 2f). These branching structures are accompanied by blood vessels, nerve fibers, and delicate strands of loose connective tissue.

The mucosa of the respiratory bronchioles is lined by simple cuboidal epithelium resting on a basement membrane, with ciliated epithelial cells occurring only occasionally. The muscularis is thin and is subdivided into discontinuous circular bundles of smooth muscle cells. The connective tissue fibers of the adventitia gradually merge with the pulmonary interstitial connective tissue. The walls of the alveolar ducts and alveolar sacs are formed by numerous alveoli.

The pulmonary alveoli are sac-like structures separated by thin interalveolar septa composed of delicate loose connective tissue containing vessels of the hemomicrocirculatory bed (Fig. 2g).

The inner surface of the alveolar wall is lined by simple squamous epithelium resting on a basement membrane. The alveolar epithelium is composed of alveolar epithelial cells (alveolocytes), including respiratory (type I) pneumocytes, secretory (type II) pneumocytes, and alveolar macrophages. Alveoli of different sizes, including large, medium-sized, and small alveoli, were identified throughout the pulmonary parenchyma (Fig. 2h).

Histomorphometric analysis demonstrated that the respiratory portion accounted for $52.74 \pm 0.62\%$ of the lung parenchyma, whereas the connective tissue stroma comprised $47.26 \pm 0.75\%$. The mean alveolar volume was $90.4 \pm 1.55 \times 10^3 \mu\text{m}^3$ (Table 4).

Table 4

Histomorphometric characteristics of the lungs of the red fox (*Vulpes vulpes*) ($\bar{x} \pm \text{SD}$)

Parameter	Morphometric value
Respiratory portion of the lung, %	52.74 ± 0.62
Connective tissue stroma, %	47.26 ± 0.75
Mean alveolar volume, $\times 10^3 \mu\text{m}^3$	90.40 ± 1.55

Discussion

Investigation of the morphofunctional organization of animal organs remains one of the principal areas of modern morphological research in biology (Richter & Wirkner, 2014; Ribitsch et al., 2020). Particular attention has been devoted to comprehensive studies of the respiratory system, especially the lungs, which perform essential physiological functions in vertebrates, the most fundamental of which is pulmonary gas exchange (Bide et al., 2000; De Backer et al., 2009; Fröhlich, 2024).

Over the past decades, numerous studies have examined the morphology of the lungs in domestic and laboratory animals under both physiological and experimental conditions (Gehr et al., 1981; Hyde et al., 2009; Meeusen et al., 2009; López & Martinson, 2017). By contrast, information regarding the gross and microscopic anatomy, as well as the organometric and histomorphometric characteristics of the lungs in wild mammalian species, remains limited.

Therefore, the present investigation of the morphotopography and the gross and microscopic structure of the lungs of the red fox provides valuable data for comparative morphology. These findings contribute to a better understanding of the anatomical organization of the respiratory system in wild carnivores and provide a basis for comparative analyses of structural adaptations that have evolved among different taxonomic groups in response to environmental conditions and evolutionary pressures.

The present study demonstrated that the morphology, shape, and topographical organization of the lungs are closely associated with the spatial arrangement of the thoracic organs, major blood vessels, thoracic musculature, and the configuration of the diaphragmatic dome.

Consistent with the shape of the thoracic cavity, the lungs of the red fox exhibit the morphology of a laterally compressed truncated cone. Similar observations have been reported by other investigators, who concluded that the conical shape of mammalian lungs reflects their anatomical accommodation within the thoracic cavity (Krause & Leeson, 1973; Hsia et al., 2013; Hsia et al., 2016; Blagojević et al., 2018). Consequently, the lungs, together with the heart and other thoracic organs, including the aorta, esophagus, and thymus, collectively conform to the overall configuration of the thoracic cavity (Weibel, 2001; Neagu et al., 2019).

Several authors have suggested that the lobar organization of the lungs is highly conserved among mammals and exhibits relatively

limited species-specific variation (Krause & Leeson, 1973; Duncker, 2004). In contrast, other studies have demonstrated the existence of species-dependent and individual differences in pulmonary lobation (Pantoja et al., 2020; Palchuk et al., 2023), which is consistent with the findings of the present study. Our results indicate that the distinct lobation of the right and left lungs in the red fox is closely related to the structural organization of the thoracic cavity and to species-specific physiological adaptations characteristic of mammals, particularly those associated with the mechanical demands imposed on the lungs during respiration.

In the red fox, both lungs are divided by deep cranial and caudal interlobar fissures into cranial, middle, and caudal lobes. In addition, the right lung possesses a fourth, accessory lobe, resulting in asymmetry between the right and left lungs. A distinctive anatomical feature observed in this species is that the interlobar fissures extend to the level of the principal bronchus, producing complete separation of all pulmonary lobes. The only exception is the cranial and middle lobes of the left lung, which remain connected by a parenchymal bridge in the dorsal region.

In addition, our observations demonstrated that the dorsal border of both the right and left lungs is not rounded along the first four to five thoracic vertebrae, as is commonly described in anatomical literature, but rather exhibits a distinct sharp crest. This morphological feature appears to result from the lateral compression of the thoracic cavity, which creates a narrow space between the ribs and the bodies of the cranial thoracic vertebrae occupied by the longissimus dorsi muscle. Consequently, the dorsal border of the lung is confined within this restricted space and assumes a relatively sharp, crest-like configuration. The cranial and ventral margins of the cranial pulmonary lobes display irregular contours. Moreover, the right cranial lobe possesses two nipple-like projections that occupy the available spaces between the heart, esophagus, trachea, and the major blood vessels, including the aorta, brachiocephalic trunk, cranial vena cava, and caudal vena cava.

The ventral and basal borders of the lungs are sharp and closely conform to the spaces formed between the thoracic viscera, the ribs, and the diaphragmatic dome. Owing to the high elasticity of the pulmonary parenchyma, the lung tissue extends into these confined spaces without increasing in thickness, resulting in the formation of characteristically sharp pulmonary borders. Furthermore, the caudal portion of the left cranial lobe overlaps the cranial region of the middle lobe, whereas the caudal margin of the middle lobe overlaps the cranial portion of the caudal lobe.

Organometric analysis represents one of the principal approaches for evaluating the morphological development and functional status of organs and organ systems, providing quantitative information at both the organ and tissue levels throughout ontogenetic and phylogenetic development, as well as under the influence of environmental factors (Horalskyi et al., 2024). Among organometric parameters, absolute and relative organ weights are widely recognized as reliable indicators of morphological and functional maturity (Lee et al., 2007). In the present study, the mean absolute lung weight was 83.2 ± 1.4 g, whereas the relative lung weight reached $1.01 \pm 0.03\%$. The absolute weights of the left and right lungs were 35.6 ± 1.1 g and 47.6 ± 2.1 g, respectively, indicating that the right lung was 1.34-fold heavier than the left. The greatest absolute weights were recorded in the caudal lobes, followed by the cranial, middle, and accessory lobes. The calculated right-to-left lung asymmetry coefficient was 1:1.33.

Compared with other vertebrate classes, including amphibians, reptiles, and birds, the lungs of mammals exhibit a substantially higher degree of structural specialization for efficient oxygen uptake and carbon dioxide elimination (Ramchandi et al., 2001; Oizumi et al., 2017). Throughout mammalian evolution, pulmonary lobation and the general pattern of bronchial branching have remained remarkably conserved (Monteiro & Smith, 2014; Hsia et al., 2016; Han et al., 2022). Nevertheless, one of the principal distinguishing features of the mammalian lung is the advanced differentiation of the conducting airways into the bronchial tree, consisting of the principal, large, medium-sized, and small bronchi. In mammals, bronchial branching follows a monopodial (major-axis) pattern throughout most levels of

the bronchial tree, whereas the terminal intralobular branches exhibit dichotomous branching (Patra, 1986; Nakakuki, 1994; Mouton et al., 1999; Einstein et al., 2008; Monteiro & Smith, 2014).

According to our findings, the bronchi of the red fox lungs vary in both size and structural organization. They are classified into extrapulmonary bronchi (the principal and lobar bronchi) and intrapulmonary bronchi, which branch extensively within the lungs to form the bronchial tree. The lobar bronchi give rise to segmental bronchi of different calibers, which are further classified according to their orientation into dorsal and ventral segmental bronchi. In each lung, the principal bronchus branches successively into large, medium-sized, and small bronchi, followed by terminal bronchioles. This branching pattern proceeds caudally along the basal region of the rounded dorsal border of the lungs.

The bronchial tree and the alveolar tree function as an integrated structural and functional unit, collectively ensuring pulmonary gas exchange between inspired air and the bloodstream (Wang & Kraman, 2004). This function is achieved through the intimate anatomical relationship between the pulmonary parenchyma and the pulmonary vascular network (Valerius, 1996; Lindstedt & Schaeffer, 2002). During mammalian phylogenetic evolution, however, both the gross and microscopic organization of the lungs have undergone varying degrees of structural specialization according to species-specific ecological and physiological adaptations (Maina & Gils, 2001; Majumdar et al., 2005).

The present study demonstrated that, although the microscopic structure of the bronchi varies throughout the bronchial tree of the red fox, all bronchial segments share common histological features.

The mucosa, which forms the innermost layer of the bronchial wall, resembles that of the trachea and is lined by pseudostratified ciliated columnar epithelium. The height of this epithelium gradually decreases along the bronchial tree, changing from tall columnar cells in the larger bronchi to low cuboidal epithelial cells in the distal airways.

The lamina propria contains numerous longitudinally arranged elastic fibers that facilitate expansion of the bronchial lumen during inspiration and contribute to elastic recoil during expiration.

The bronchial mucosa forms prominent longitudinal folds produced by contraction of the obliquely and circumferentially arranged bundles of smooth muscle cells comprising the muscularis mucosae, which separates the mucosa from the submucosa.

The submucosa contains terminal portions of mixed seromucous glands arranged in groups, particularly in regions where cartilaginous tissue is absent. Their excretory ducts open onto the mucosal surface, where the secretions trap and coat inhaled dust particles and other foreign material, thereby facilitating their removal through the mucociliary clearance mechanism. In contrast, submucosal glands are absent in the small bronchi.

The fibrous-cartilaginous layer undergoes progressive structural modification with decreasing bronchial caliber. In the principal bronchi, it is represented by complete cartilaginous rings, which are replaced by discontinuous cartilage plates in the lobar, zonal, and segmental bronchi, and finally by isolated cartilage islands in the medium-sized bronchi.

In the medium-sized bronchi, elastic cartilage gradually replaces hyaline cartilage. By contrast, the fibrous-cartilaginous layer is completely absent in the small bronchi.

The outer adventitia consists of dense fibrous connective tissue that gradually merges with the interlobular connective tissue of the pulmonary parenchyma.

Histomorphometric analysis plays an essential role in evaluating the development and morphofunctional status of the lungs by providing quantitative information at the tissue level (Horalskyi et al., 2019). In the present study, the external and internal diameters of the large bronchi were 3478.4 ± 28.9 μm and 1750.2 ± 12.4 μm , respectively, with a mean wall thickness of 864.1 ± 9.3 μm . Considerably smaller morphometric values were recorded for the medium-sized bronchi, small bronchi, and terminal bronchioles. The corresponding external diameter, internal diameter, and wall thickness were 1233.4 ± 13.4 , 618.4 ± 9.9 μm , and 307.4 ± 8.6 μm for the medium-sized bronchi;

604.1 ± 9.9, 306.7 ± 7.5, and 148.7 ± 3.6 µm for the small bronchi; and 424.9 ± 9.1, 275.3 ± 4.9, and 74.8 ± 0.9 µm for the terminal bronchioles.

The pulmonary acinus represents the structural and functional unit of the mammalian respiratory system (Habberthür et al., 2021). It comprises a system of alveoli arising from the walls of the respiratory bronchioles, alveolar ducts, and alveolar sacs, where gas exchange occurs between alveolar air and the pulmonary capillary blood (Vasilescu et al., 2012; Habberthür et al., 2021; Knudsen et al., 2023).

In the red fox, as in other mammalian species, each pulmonary acinus originates from a terminal bronchiole, which gives rise to first-order respiratory bronchioles. These branch dichotomously into second-order respiratory bronchioles, which subsequently divide into third-order respiratory bronchioles. The walls of the respiratory bronchioles are lined by simple cuboidal epithelium. The third-order respiratory bronchioles give rise to successive generations of alveolar ducts, which branch into alveolar sacs whose walls are formed by numerous alveoli, thereby establishing the alveolar tree. Histologically, these structures are accompanied by blood vessels, nerve fibers, and delicate strands of loose connective tissue.

Histomorphometric evaluation demonstrated that the mean alveolar volume in the red fox was $90.4 \pm 1.6 \times 10^3 \mu\text{m}^3$. The respiratory portion constituted $52.74 \pm 0.62\%$ of the lung parenchyma, whereas the connective tissue stroma accounted for $47.26 \pm 0.75\%$.

Conclusion

The lungs of the red fox (*Vulpes vulpes*) exhibit a distinct lobar organization. The left lung consists of three lobes (cranial, middle, and caudal) whereas the right lung comprises four lobes: cranial, middle, caudal, and accessory. The mean absolute lung weight was 83.2 ± 1.4 g, and the relative lung weight was $1.01 \pm 0.03\%$. The left lung was slightly smaller than the right, with absolute weights of 35.6 ± 1.1 and 47.6 ± 2.1 g, respectively. The right-to-left lung asymmetry coefficient (right lung weight/left lung weight) was 1:1.33. The lungs measured 14.9 ± 0.4 cm in total length, 13.1 ± 0.3 cm in width, and 6.8 ± 0.3 cm in thickness. The lung development index was $114.00 \pm 0.35\%$, indicating an elongated-expanded morphological type.

The bronchial tree originates from the right and left principal bronchi, which continue as extrapulmonary lobar bronchi before branching into large intrapulmonary bronchi. These subsequently divide into segmental, medium-sized, and small bronchi, which further branch into terminal bronchioles, marking the transition to the respiratory portion of the lungs. The pulmonary lobules constituting the respiratory portion of the lungs are pyramidal or conical in shape. Histologically, each lobule is composed of pulmonary acini separated by connective tissue septa forming the pulmonary stroma. The internal histological organization of the lungs is characterized by pulmonary lobules of pyramidal or conical shape separated by connective tissue septa. The connective tissue stroma accounted for $47.26 \pm 0.75\%$ of the lung tissue and consisted of loose connective tissue containing elastic fibers, blood vessels, and lymphatic vessels.

The respiratory parenchyma constituted $52.74 \pm 0.62\%$ of the lung tissue and was composed of respiratory bronchioles, alveolar ducts, and alveolar sacs, the walls of which contained alveoli with a mean volume of $90.4 \pm 1.6 \times 10^3 \mu\text{m}^3$.

The authors declare that they have no conflict of interest.

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