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論　文　内　容　の　要　旨

氏　名　（肖　蘿　莎）	
論文題名	Micro-CT-based morphological measurement and analysis of pulmonary acinar cluster in mouse using a semi-automatic segmentation algorithm（半自動領域抽出法を用いた三次元マイクロCT画像に基づくマウス肺細葉の形態計測および分析）

論文内容の要旨

The mammalian pulmonary acinus is the essential and functional unit of the respiratory airways for gas exchange, which is a vital component for breathing and the development of lung disease. With decreasing scale of airways, the acini originate in the terminal purely conductive airways, and a group of acini stemming from the same conducting airway is defined as a cluster of acini, which may be regarded as a secondary pulmonary lobule. Such hierarchical architecture allows the alveoli to be ventilated by air in sequence. Therefore, quantifying such morphological characteristics in three-dimensional is critical for exploring the respiratory function or disease processes.

In the first part of the thesis, based on the multiscale and hierarchical architecture of the lungs, a semi-automatic segmentation algorithm was developed for extracting the complete structure of individual acini and acinar cluster from synchrotron micro-CT (computed tomography) images of the mouse lungs. The segmentation consists of two stages: the extraction of terminal bronchiole and the segmentation of acinus. In principle, the segmentation of the airway structure at each scale is performed by controlling the number of repetition of 3D erosion and dilation operators. Applying this segmentation algorithm, a great amount of acini and their cluster were collected to establish a database.

A quantitative approach was proposed to measure the morphological characteristics of pulmonary acini. In this thesis, a portion of the collected acini, including the individual acini and the clustered acini stemming from the same terminal conducting airway, were picked up for the morphological estimation and analysis. The volume and surface area of 50 individual acini belonging to five clusters were estimated based on the voxel and surface mesh of segmented acini. The acinar volume was 0.09 ± 0.07 mm^3 (mean ± SD), and the surface area was 6.82 ± 4.49 mm^2, in agreement with previous studies. The volume of the acinar clusters was 0.89 ± 0.34 mm^3, and the surface area was 68.18 ± 17.66 mm^2. As for the acinar cluster, the largest volume acinus per cluster was found in the distal region of the terminal conducting airway, and apparent respiratory bronchioles were observed only in large-volume acini. The pathway length and width were estimated for one cluster including 15 acini based on the skeleton of segmented acini. The generation number of pathway per acinus was 8 ± 2 (range: 6 to 12). The pathway length at lower generations (generation 2 to 6) was increased with the generation in a single cluster, while did not significantly change at lower generations in some acinar groups. The pathway width of alveolar ducts increased with increasing generations from 0.052 ± 0.003 mm to 0.132 mm with a mean of 0.081 mm. The estimated results indicate that the acinar morphology is also heterogeneous in small scale. Based on the estimated data, this thesis discussed the impact of location and size variation in acinar cluster from the viewpoint of oxygen transport. As a result, it was found that even if the largest acini located at the distal region of the terminal conducting airway, which is a disadvantageous condition for gas transport, the oxygen transport ability is enough to cover the large volume.

The developed semi-automatic segmentation algorithm opens up the possibility to efficiently investigate pulmonary acini statistically. The quantitative approach is well suited for characterizing the morphology of pulmonary acinar clusters. The statistical analysis provided the distribution of each morphological characteristic that indicates the lung heterogeneity at acini level. All measured and analyzed results (e.g., volume, surface area, length and width) can be used for further investigating the impact of the structure on the lung functions (e.g., ventilation and gas exchange) by means of biomechanical analysis. Combining with biomechanical analysis, the approaches proposed in this thesis may open up opportunities for quantitatively assessing the acinar structure and functions in healthy and even diseased lungs.

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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

本論文は，気道系末梢に位置し，肺のガス交換機能を担う肺胞および肺胞道から構成される肺細葉の形態を計測し，その解剖学的特徴を明らかにしたものである．そのために，まず，シンクロトロン放射光CT装置で撮影されたマウス肺画像から肺細葉を抽出するアルゴリズムを開発した．肺胞空間を隔てる肺胞壁には小孔が存在し，個々の肺細葉を抽出するにはそれらを除去する必要がある．本研究では肺細葉構造のマルチスケール性を利用し，解剖学的データに基づいて対象領域を適切に縮小および復元させる独自の画像処理法を提案し，半自動的に個々の肺細葉およびその集合体を短時間で抽出できるようにした．こうした半自動化アルゴリズムを開発することにより，マニュアルによる処理を多く含む従来の手法を大きく改善し，複数の肺細葉を抽出して，統計学的にその形態の特徴を評価することが可能となった．

次に，開発した手法を用いて，5頭のマウス肺から得られた50個の肺細葉に対して，体積や表面積，気道の分岐数，直径，長さなどの統計学的データを取得した．また，一本の終末細気管支につながる複数の肺細葉から形成される5つのクラスター構造を調べ，ガス輸送面から考えると不利な条件となる遠位部に体積の大きな肺細葉が存在することを示した．これほど多くの肺細葉やその集合体の形態はこれまでに報告されておらず，得られた結果は，肺細葉の解剖学的特徴を理解する上で極めて貴重なデータである．さらに，肺細葉クラスターにおいて，一次元拡散モデルを適用して各肺細葉への酸素輸送能を評価した結果，正常な呼吸状態においてはいずれの肺細葉でもガス交換機能が維持されることが示された．不均一は肺細葉構造に対するこのようなバイオメカニクス解析による理解は，肺細葉レベルの構造変化から引き起こされる肺気腫などの肺疾患の機能不全や発症メカニズムの解明にもつながるものであり，医工学的にも意義が大きい．

以上の点から，博士（工学）の学位論文として価値のあるものと認める．