

HIGH RESOLUTION MICROTOMOGRAPHY OF HUMAN LUNG TISSUE SPECIMENS: OBSERVATION OF NORMAL ANATOMY AND THREE-DIMENSIONAL RECONSTRUCTION

To precisely understand lung function, it is necessary to accurately visualize detailed lung architecture. We used a novel X-ray tomographic technique [1] to study the morphology of human lung at a high resolution.

Postmortem lungs were inflated and chemically fixed by Heitzman's method. Lung samples were sectioned at a 15-mm thickness. Utilizing the present synchrotron radiation computed tomography (CT) system, the entire sample must be contained within the field to enable visualization of multiple viewing angles in a cylinder, 8 mm in diameter. We, therefore, reduced the sample size by carefully removing the edges of the block, yielding a column specimen containing the target site. During this process, we were careful to retain one terminal bronchiole to include the peripheral structure in the column specimen.

The CT images were obtained at **BL20B2** using a phosphor X-ray detector with a cooled CCD camera at an X-ray energy of 9 keV. Synchrotron radiation CT images effectively captured the alveolar wall, the air spaces, and small airways. Alveolar septa were visualized at an effective spatial resolution of approximately 24 μm , experimentally determined in the present synchrotron radiation CT system. Detailed correlation between the synchrotron radiation microtomography and histology can be achieved by precise spatial registration [2].

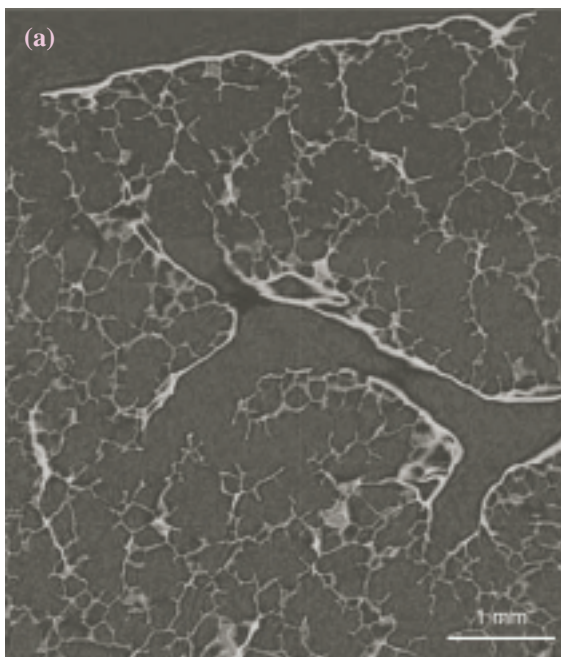


Fig. 1(a). Planar reformatted image.

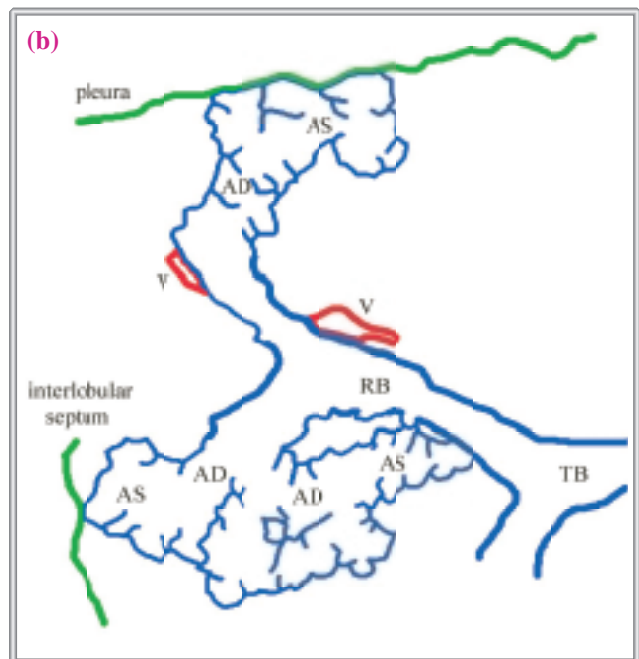


Fig. 1(b). TB = terminal bronchiole
RB = respiratory bronchiole
AD = alveolar duct
AS = alveolar sac
V = pulmonary vessel

Using the nearly-parallel, synchrotron radiation beam, comprehensive isotropic volumetric data can be obtained in multiple cross-sectional planes, throughout the full three-dimensional volume of the tissue. Serial analysis of these synchrotron radiation CT images allowed us to identify the terminal bronchiole, the respiratory bronchiole, the alveolar duct, and the alveolar sac. We reformatted the para-sagittal planar image from the three-dimensional isotropic volumetric data with a high resolution (Fig. 1a) to systematically confirm the structural sequence; the respiratory bronchiole originates from the terminal bronchiole (TB), sequentially branches off into alveolar ducts (AD) and terminates in the alveolar ducts abutting on either the pleura or the interlobular septum (Fig. 1b).

An alveolar duct, distal to the bronchiole-alveolar duct junction, communicates with all alveoli in the ventilatory unit defined in our studies. For each voxel within the air spaces, we calculated the

distance to the nearest voxel on the boundary, assigning this value to the voxel as the density value. A subsequent volume rendering technique allowed interactive viewing of the segmented structure in the appropriate viewing perspective without hidden structures (Fig. 2). This three-dimensional imaging technique, possessing a high isotropic spatial resolution, offers a new mechanism to analyze the acinar geometry, necessary to accurately define the physiology of the human lung.

Three-dimensional, super-resolution imaging of the inflated and fixed human lung, utilizing the combination of synchrotron radiation and histology, establishes a novel, fundamental approach allowing greater understanding of the human lung. Deeper understanding of the normal lung architecture and the consequent morphological modifications resulting from physiopathological conditions will hopefully allow advances in biomedicine.

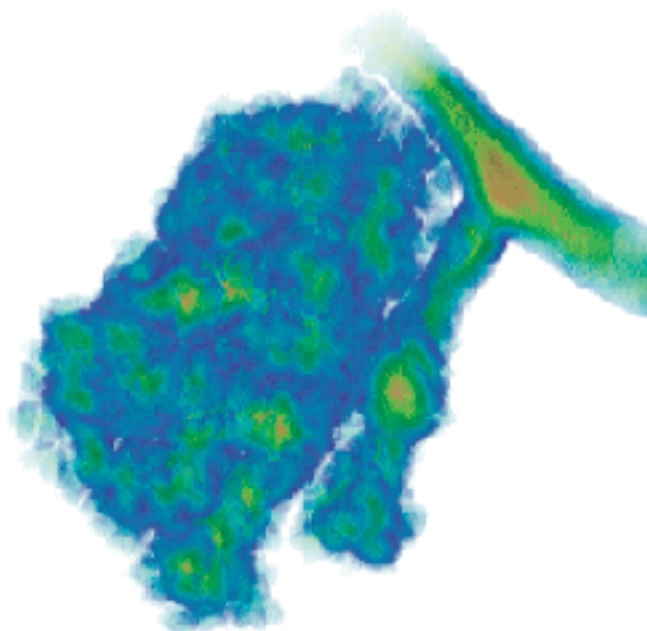


Fig. 2. Three-dimensional reconstruction of the sub-acinus.

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