High resolution three dimensional lung imaging for the extraction of the airway skeleton

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Introduction

LARGE parts of the mammalian airways and gas-exchange area are formed by branching morphogenesis. The branching pattern of the airways, as well as the size, shape and localization of the terminal airspaces – the alveoli – are important parameters for lung ventilation and particle deposition. With the extracted skeleton of the airways we are able to supply these parameters. We also aim to supply the structural data of the gas-exchange region as a basis for the modeling of airflow and particle deposition by computational fluid dynamics.

Materials & Methods

THE lung of a 60 day old Sprague-Dawley rat was embedded in EPON™ [1] and shaped to a rod with a diameter of 1.2 mm on a watchmakers lathe.

A three-dimensional stack of images has been obtained using high resolution synchrotron radiation x-ray tomographic microscopy at the TOMCAT beamline [2] of the Swiss Light Source at the Paul Scherrer Institut (PSI) in Villigen, Switzerland. The energy of the beam was tuned to 12.6 keV, the sample was scanned with the 10x-lens and the images were recorded with a 2x2 binning resulting in isotropic voxels of 1.4 μm sidelength (Fig. 1).

In order to bypass the problem of choosing a correct threshold to generate an isosurface of an airway segment, we chose a snake-based segmentation algorithm implemented in itk-SNAP 1.4 (`http://itksnap.org/`) to extract an airway segment from the original dataset (Fig. 2a and 2b).

The skeleton of the segmented airway part has been obtained with a homotopic thinning algorithm published by Cornea et al. [3] (Fig. 2d, 3c and 3d). Cornea et al. published the algorithm source code which has been adapted into an in house product.

The visualization of the data has been done either with amira® 4.1 (Visage Imaging, Inc., `http://amira.com/`, Fig. 1 and 3) or MeVisLab 1.5.2 (MeVis Research GmbH, `http://mevislab.de/`, Fig. 2c and 2d).

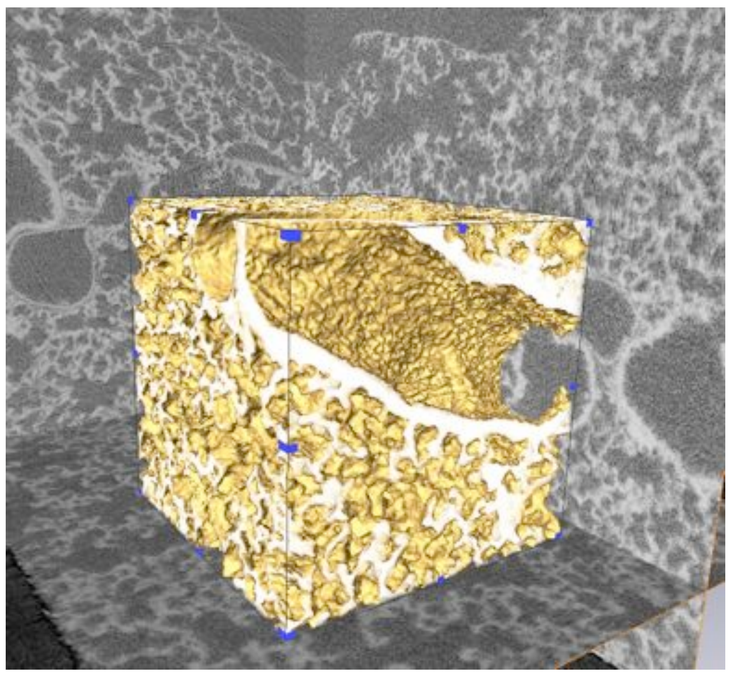

Figure 1: *Isosurface visualization of lung tissue (yellow/white) surrounded by three orthogonal slices. The original dataset is an isotropic cube of 1024 pixels sidelength, the tissue has been cropped to a sidelength of 256 pixels for easier visualization.*

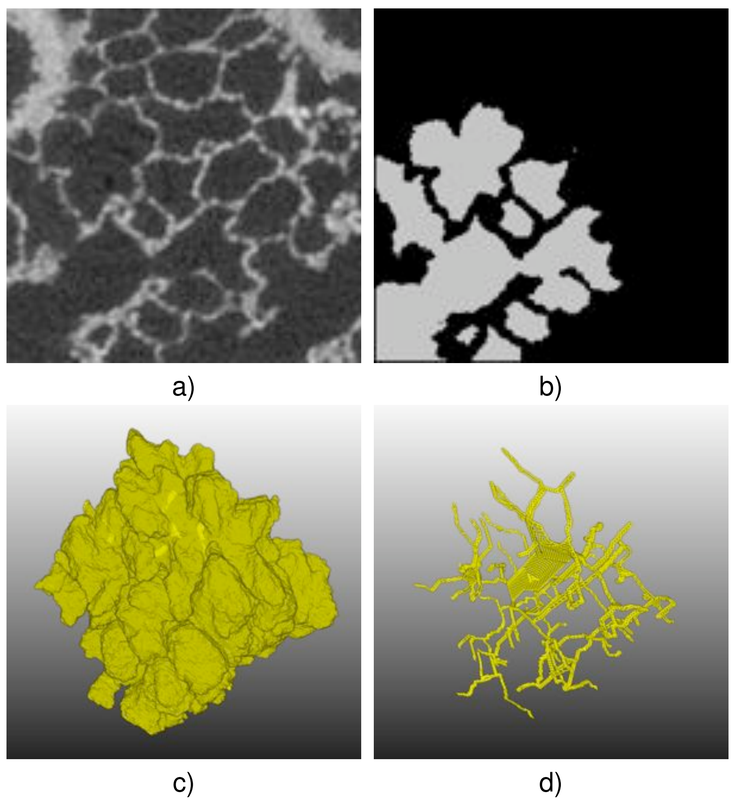

Figure 2: *Workflow from original image to skeletonization of the airway structure: a): one slice of a 256 pixel sidelength wide crop of the original data. b): one slice of segmented airway structure. For demonstration purposes we segmented only a part of one terminal airway. c): Volume rendering of segmented airway structure. d): Volume rendering of homotopically thinned airway structure.*

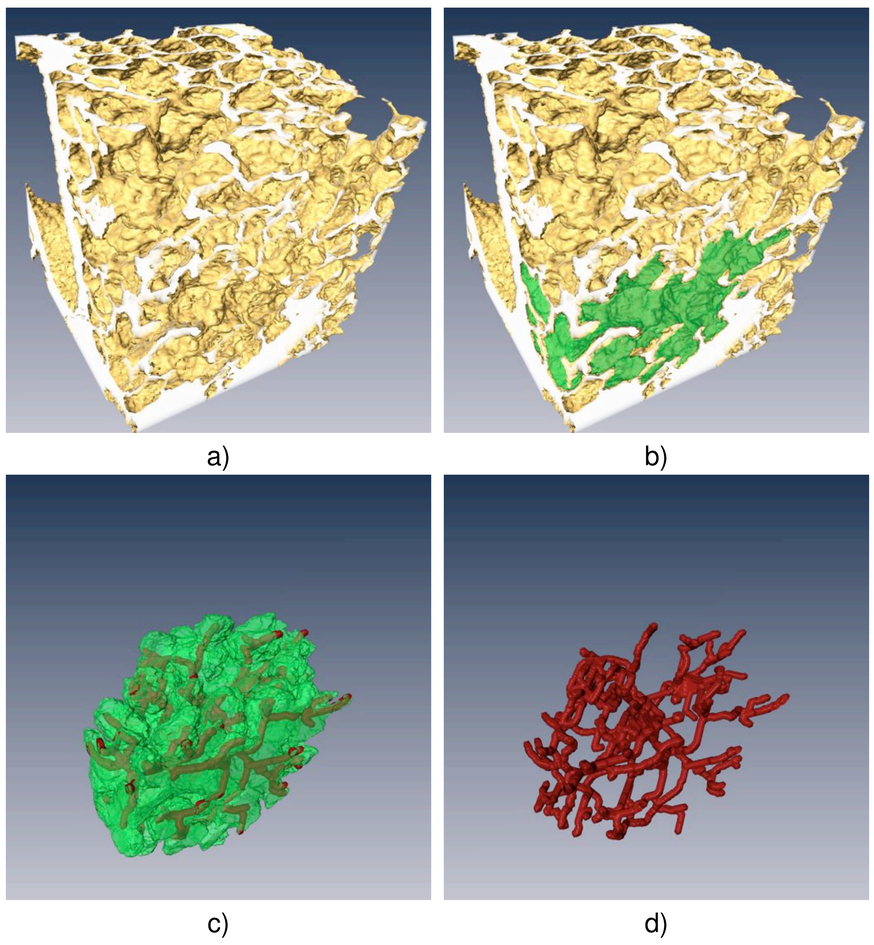

Figure 3: *Homotopic thinning of segmented airway: a): Isosurface visualization of a 256 pixel sidelength wide crop of the original data. b): Isosurface visualization of lung tissue with segmented airway part (transparent green isosurface). c): Segmented airway part with its homotopically thinned skeleton (red). d): 3D-rendering of homotopically thinned airway structure. The extracted skeleton has been dilated (3D maximum dilatation with a neighborhood of 26) for the purpose of visualization, since a homotopically thinned structure is generally only one pixel wide, which is too thin for the visualization in this context. This dilation leads to a protrusion of the skeleton out of the segmented airway in subfigure c).*

Conclusion

- We have developed a method for the extraction of a homotopic skeleton of an arbitrary structure and are able to extract and visualize the skeleton of segmented terminal airways.
- The skeleton captures the features of the segmented lung structure and is the basis for an upcoming quantitative analysis of the mammal terminal airway structure which can then be used for the simulation of airflow and particle deposition in the lung.
- Homotopic skeletonization of segmented airway structure is not limited to the sample shown here; we applied our workflow to rat, mice, primate and human lung samples which have been scanned with high resolution synchrotron radiation x-ray tomographic microscopy.
- The three dimensional reconstruction of these scanned samples permits us to obtain fully three dimensional reconstructions of the lung tissue. In comparison to conventional Electron Microscopy (with a resolution down to several nm) our technique allows us to have a real three dimensional dataset, permitting us to have a look inside the sample. This allows the visualization of an arbitrary part and location in the sample – down to the imaging of single alveoli.
- Skeletonization has been done for whole lungs on a much larger scale, with much lower resolution; we are able to provide structural information of the terminal airways at very high resolution.

Acknowledgments

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References

[1] J. C. Schittny, M. Paulsson, C. Vallan, P. H. Burri, N. Kedei, and D. Aeschlimann. Protein cross-linking mediated by tissue transglutaminase correlates with the maturation of extracellular matrices during lung development. *Am J Respir Cell Mol Biol*, 17(3):334–343, Sep 1997.

[2] M. Stampanoni, A. Groso, A. Isenegger, G. Mikuljan, Q. Chen, D. Meister, M. Lange, R. Betemps, S. Henein, and R. Abela. Tomcat: A beamline for TOmographic Microscopy and Coherent rAdiology experimenTs. *AIP Conference Proceedings*, 879(1):848–851, 2007. doi: 10.1063/1.2436193. URL `http://link.aip.org/link/?APC/879/848/1`.

[3] N.D. Cornea, D. Silver, and P. Min. Curve-skeleton applications. In *Visualization, 2005. VIS 05. IEEE*, pages 95–102, 23-28 Oct. 2005. doi: 10.1109/VISUAL.2005.1532783.