Generation of acinar skeletons in high resolution 3D-visualizations of terminal airways in mammals

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Introduction

Up to now the generation of skeletons of the gas-exchanging airways was limited by the resolution of the available 3D-imaging methods.
We developed [1] and applied wide field synchrotron radiation based X-ray tomographic microscopy (WF-SRXTM) to generate large high resolution three dimensional datasets of heavy metal stained and paraffin embedded rat lung samples [2] at an isometric voxel length of 0.74 µm.

Materials and Methods

At the beamline TOMCAT [4] at the Swiss Light Source (Paul Scherrer Institut, Switzerland) we obtained tomographic datasets of the apex tip of the right lower lung lobe of samples obtained at post-natal days 4, 10, 21, 36 and 60.
Acini have been extracted using a region growing algorithm. Using a distance transformation-based skeletonization technique [3] we calculated airway skeletons whose three dimensional topology correspond to the extracted acinus. All calculations and visualizations have been realized with MeVisLab (Version 1.6.1, MeVis Research GmbH, Bremen, Germany).

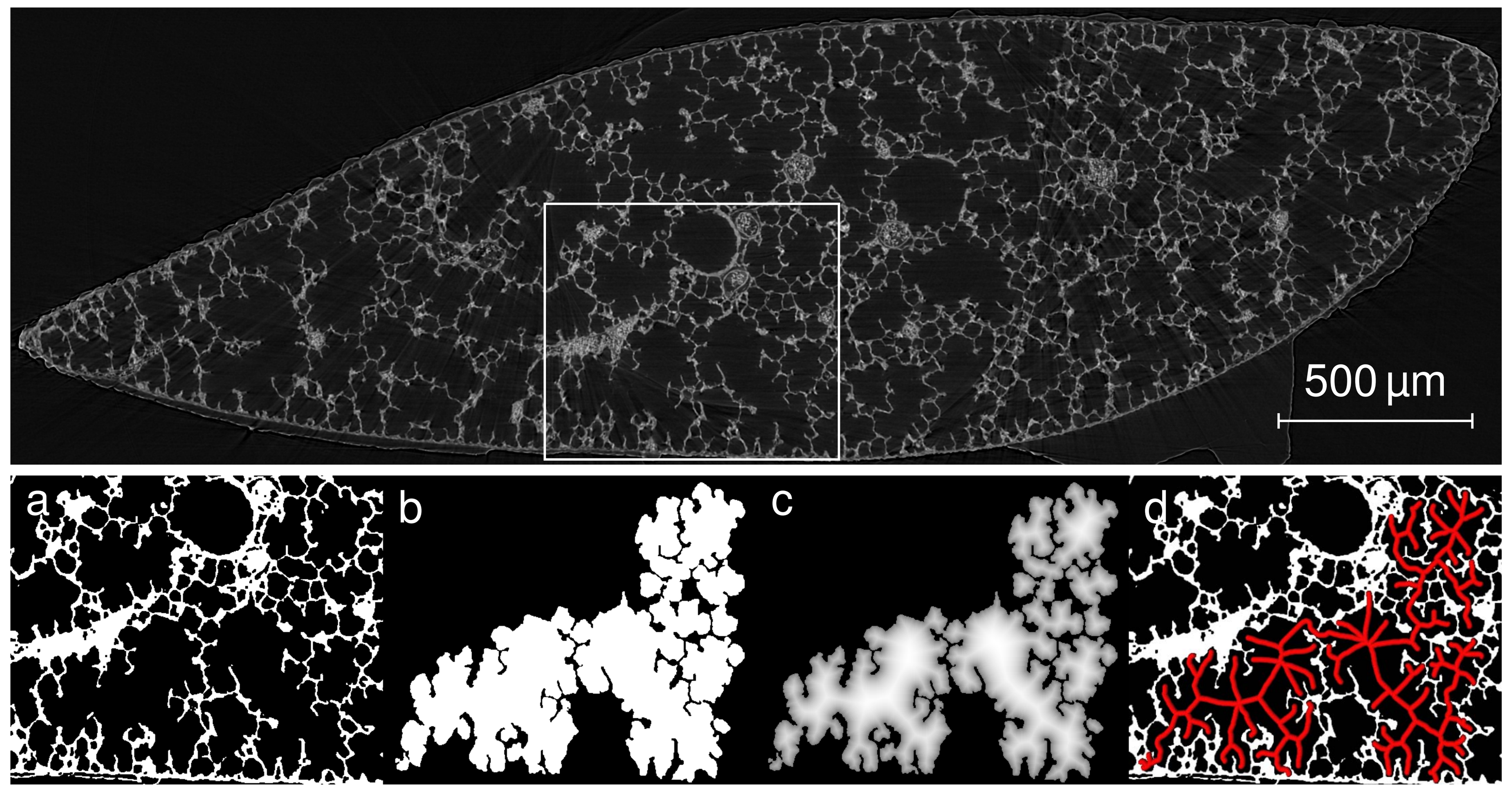


Figure 1: *Two-dimensional skeletonization process. Top: Wide field scanned tomographic slice from rat lung sample obtained at postnatal day 21. The inset frame corresponds to the region of the images shown in the bottom row. Bottom: a) Binarized region of interest (ROI). b) Filled structure inside the ROI, conforming to one connected airspace in two dimensions. c) Distance transformation. d) The local maxima of the distance transformation constitute the skeleton overlayed over the binarized lung structure.*

Results

Tomographic datasets covering a cylindrical field of view with a height of 1.4 mm and a diameter of approximately 4 mm have been obtained. We extracted three independent central terminal airway segments from all samples and the skeletons of these segments have been calculated and visualized as shown in figures 2 and 3.

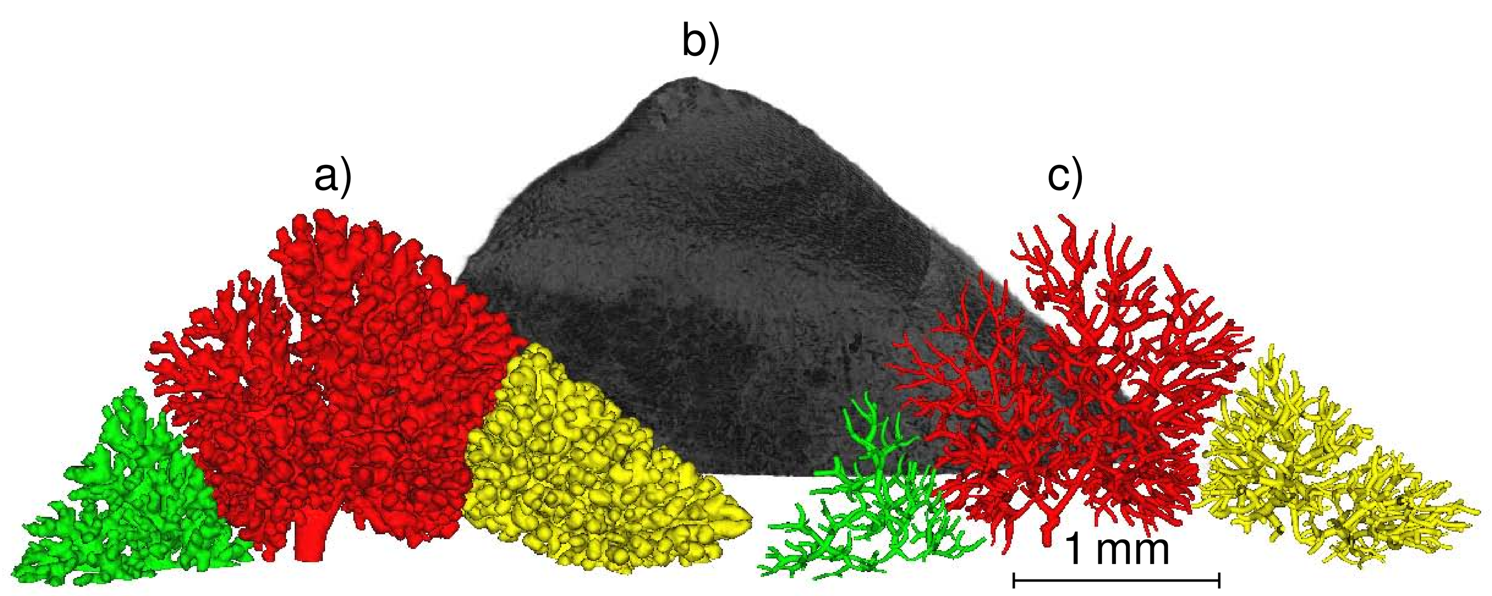
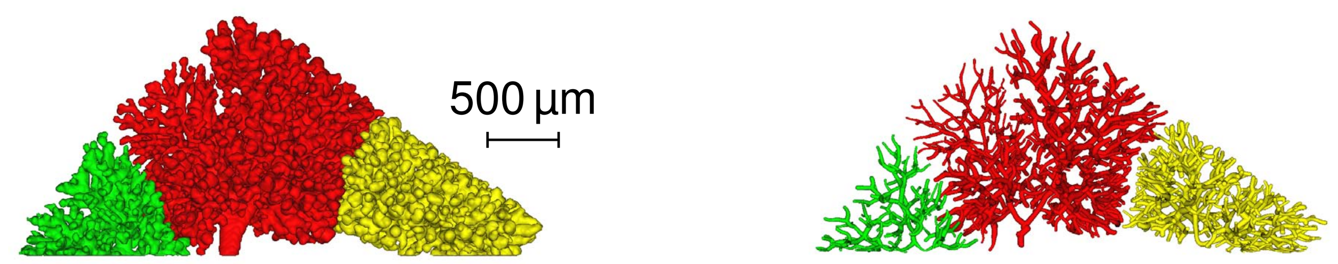
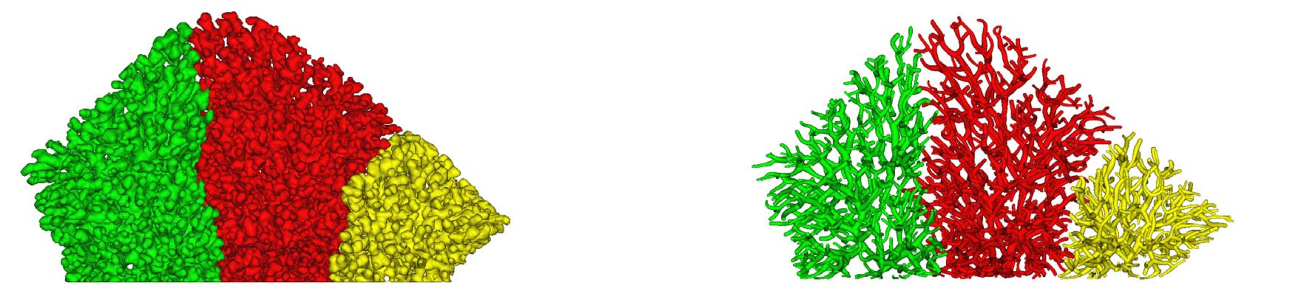


Figure 2: *Overview of a three-dimensional dataset of a Sprague Dawley rat lung sample obtained at postnatal day 4. a) Three independent airway segments extracted using a region growing algorithm. The green segment contains one partially cut acinus, the red segment contains two entire acini and the yellow segment contains one complete and one partially cut acinus. b) Three-dimensional view of the full sample. c) Skeletons of segmented acini.*

We have successfully extracted airway segments corresponding to acini from multiple datasets as shown in figure 3. We can thus map the acinar tree and locate any alveolus of interest within the acinus in three dimensions.

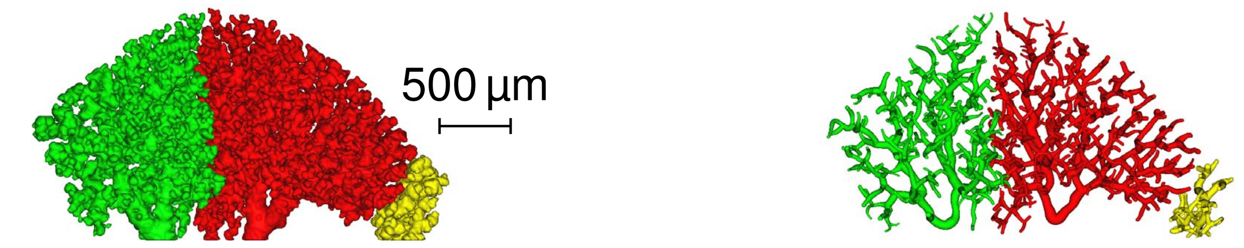


(a) Day 4

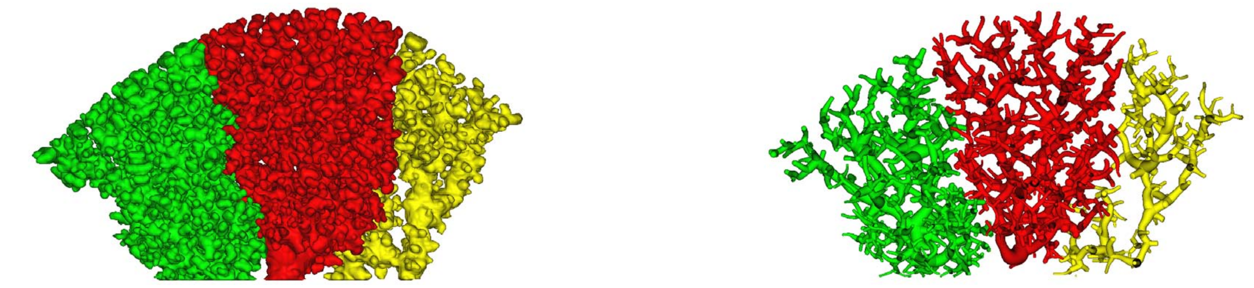


(b) Day 10

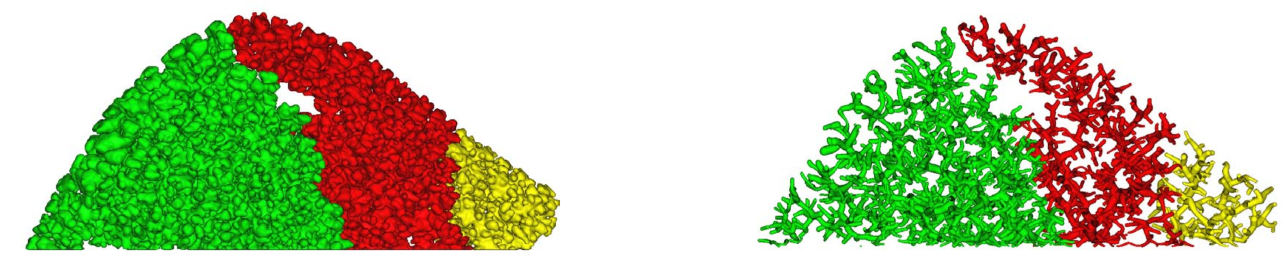
Figure 3: *Segments and corresponding skeletons*



(c) Day 21



(d) Day 36



(e) Day 60

Figure 3: *Segments and corresponding skeletons (continued)*

Analyzing the complexity of the skeleton structure including the amount and positions of the nodal points of the skeleton branches permits compare then to the volume of the segments.

Discussion

Wide field SRXTM allows the generation of acinar skeletons which we would like to use for the analysis of the 3D-structure of the gas-exchanging airways and air flow in the terminal airways. Using this method, we can divide the acinar tree into proximal and distal regions and are able to map the distribution of nanoparticle deposition and retention within the acinus for different regions in the terminal airway tree in the mammalian lung.

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