Deposition Distribution of Inhaled Particles Containing Metal in Rat Respiratory System

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Abstract

Particle deposition distributions in single airway bifurcation of rat lung were measured applying micro X-ray fluorescence (μ-XRF) tomography using synchrotron radiation [1]. Previously Wistar rats were placed into an inhalation chamber and inhaled liquid and solid aerosol for several times. Some bifurcations of the lung were selected and cut with the surrounding tissue. Measurements were carried out at the fluorescence beamline of ANKA. In case of liquid aerosol, significantly high particle deposition was found at the carina region. For the solid aerosol different type of deposition patterns were obtained.

Introduction

The location of a particle induced lung disease, for example the place of the tumor, correlates to the deposition maximum places of the particles. On the other hand, the therapeutic effect of aerosol medicines strongly depends on the deposition distribution of the drug particles. For this reason several lung deposition models have been developed, allowing the calculation of the deposition characteristics of the inhaled particles. Most of these models do not take into account the deposition pattern of the particles in a given airway bifurcation and suppose homogeneous deposition. However, the deposition in one airway bifurcation is very inhomogeneous, mostly in the central airway region (first 10, 12 generations). At the peak of the bifurcation, the so-called carina region, the efficiency of impaction is much higher than at other regions of the airway.

Although several three-dimensional measurements were performed on human and animal lungs (CT, Spect, PET), it is difficult to use these results for experimental control of the model calculations. CT method based on X-ray absorption yields detailed morphological images, but the detection of the deposited particles needs more specificity. On the contrary, in case of Spect and PET methods the result shows the distribution of the deposited (radio) aerosols, but does not inform about the morphology. Using micro X-ray fluorescence (μ-XRF) tomography technique it is possible to get information about the particle deposition and the geometry of the airways from the same measurement.

Materials and methods

Liquid aerosol has been generated from a 40 % eosin solution by an OMRON inhaler equipment and large particles were filtered out by a home made labyrinth. Solid aerosol has been generated by resuspension of a ZnO powder in a plastic bag. The generated aerosol has been collected on a surface of a polycarbonate filter for further analysis of its size distribution by scanning electron microscopy.

Following inhalation, the animals were sacrificed and the lungs were fixed and sliced. Some bifurcations of the lung were selected and cut with the surrounding tissue in a cubic form with about 2 mm edge.

Measurements have been carried out at the ANKA FLUO beamline. The sample was fixed to an eucentric goniometer head and placed on a rotation table. The translation and rotation of the sample were controlled by stepping motors. A monochromatic X-ray beam of 18 keV was employed with 21 μm (vertical) × 35 μm (horizontal) spot size.

Several sections of the sample were measured in the vicinity of the carina region. Sinograms for each section were measured by a whole rotation (360°) of the sample. The angular step size was 6°. At each angular position horizontal scans were performed using a translational step size of 40 μm. The characteristic X-ray spectra were recorded by a Si(Li) detector and were evaluated by the AXIL code. The two-dimensional elemental maps were reconstructed from the XRF sinograms using the filtered back-projection method.

Results

Reconstructed bromine and iron maps of the five sections of the first sample are presented in ***Fig. 1***. The distances of the sections from a reference surface are 0, 30, 60, 100, and 130 μm, respectively. High particle depositions were observed in the carina region of the bifurcation (solid arrows). Moreover a second hot spot on the left side of the lower airway could also be detected (open arrows). The second Br hot spot has strong correlation with a Fe hot spot on the lower map sequence. While the hot spots on the Fe maps correspond to the hemoglobin of the blood, one can conclude that the second Br hot spot is in a blood vessel.

In case of the second sample from an animal inhaled solid ZnO aerosol, significant homogeneous particle deposition was detected on the surface of the airway. Deposition maximum on the carina was not found.

Conclusions

The XRF-tomography experiments demonstrated that measuring the particle deposition distribution in a single airway bifurcation

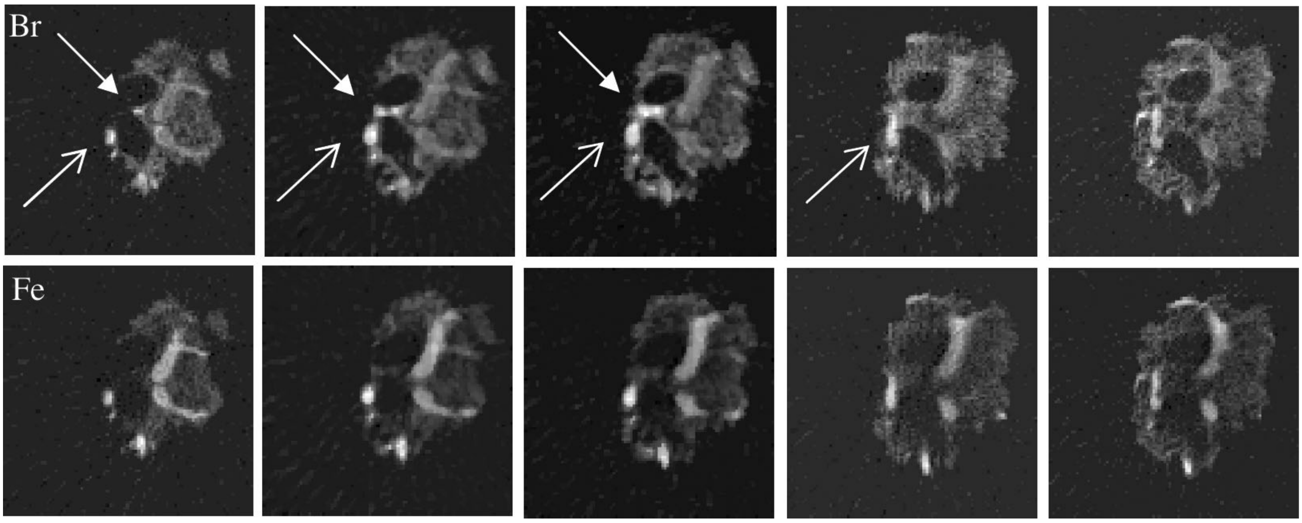

Fig. 1: Br (up) and Fe (down) maps of the five measured sections of a rat lung bifurcation.

is possible with sufficiently high spatial resolution. The results provide information with respect to the particle distribution and the morphology simultaneously. The measured Br deposition corresponds to the expected result from the model calculations. Br had significant migration after the deposition, entering into the tissue and presumably diffused to a blood vessel in close proximity. Solid aerosols have different behavior after the deposition. These could not diffuse into the tissue and, as a result, possibly the mucociliary clearance dissipated them from the surface of the carina.

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