High-Resolution 4D *In Vivo*-CT for Visualization of Cardiovascular and Respiratory Motion of Small Animals

We have constructed a high-resolution, computed tomography (CT) system that can visualize the motion and deformation of the heart, coronary arteries and small airways of live small animals (rat and mouse), which are most often used as models for human diseases [1].

In the past five years, several systems based on micro-CT have been proposed and developed for imaging the heart and lungs of live small animals, but none had enough resolution to detect the motion of coronary arteries and small airways. To obtain high-resolution CT images, the animal needs to be as still as possible. In the visualization of a live animal, breathing and cardiac motion cause serious motion artifacts in the reconstructed images, including blurring of the lung and heart. When imaging the heart, the movement of the lung needs to be minimized, and vice versa. Thus, the images need to be collected under a certain well-controlled condition.

The *in vivo*-CT system was constructed in the medical imaging beamline **BL20B2**. This system consists of a precision rotation stage, a high-resolution image detector (1 pixel=12 μm), an X-ray shutter, a mechanical ventilator, an electrocardiogram (ECG) recorder, and PCs. To avoid the artifacts caused by breathing and heartbeats, the projection images were acquired prospectively in synchrony with respiratory and cardiac gatings. The sample rodent was anaesthetized, put onto a ventilator, and connected to the ECG recorder. To visualize the lung, we acquired data at controlled iso-airway pressures between heartbeats. To visualize the heart and arteries, a contrast agent was injected into the tail vein, and image acquisition was timed at the end of breath expiration. In both imaging procedures, the total scan time was approximately 10 min.

We are the first to visualize the deformation of the coronary arteries, aortic valves (Fig. 1), and small airways down to 125 μm in diameter (Fig. 2) of a live

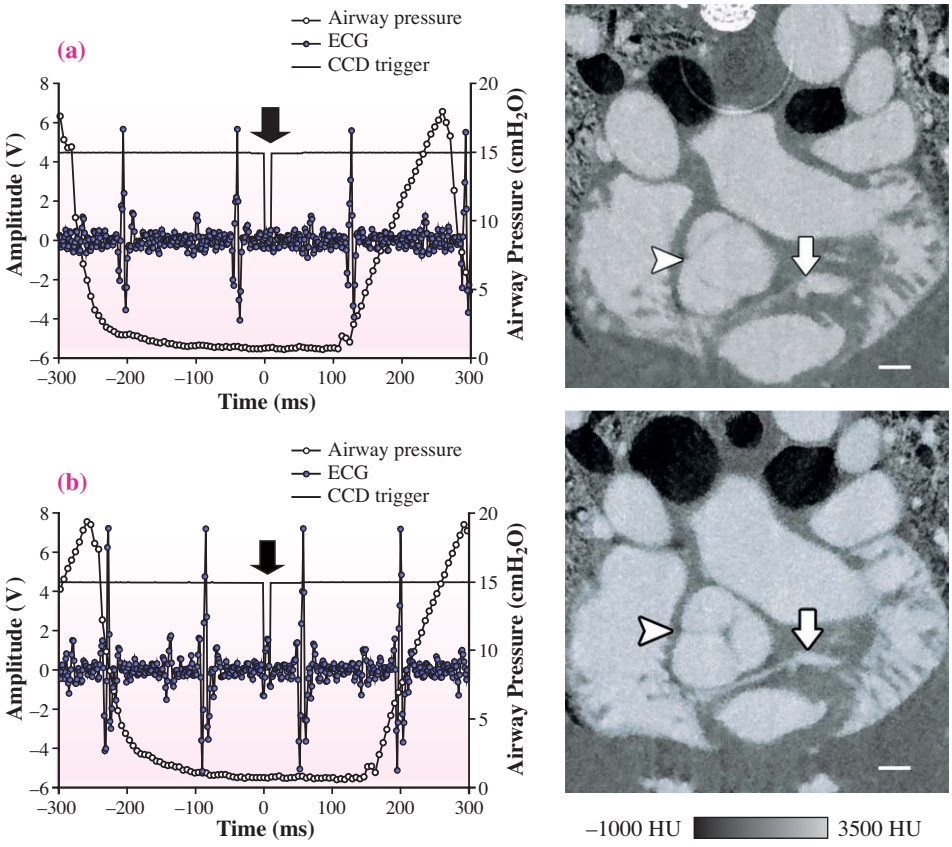

Fig. 1. Left: Timing charts of the time-resolved CT imaging. The airway pressure was controlled using a ventilator and repeated every 560 ms. The heart was beating spontaneously and the ECG was monitored. The X-ray exposure was made at a selected time (indicated by the black arrows) in the respiratory and cardiac cycles, which was at 45 ms **(a)** or 95 ms **(b)** after the R peak in the ECG. The exposure time was 10 ms. Right: axial images of the coronary arteries (arrows) and aorta valves (arrow heads) of a mouse recorded at the time shown in the timing diagrams. The diameters of the coronary arteries are 444 μm in **(a)** and 288 μm in **(b)**. Bar: 500 μm.

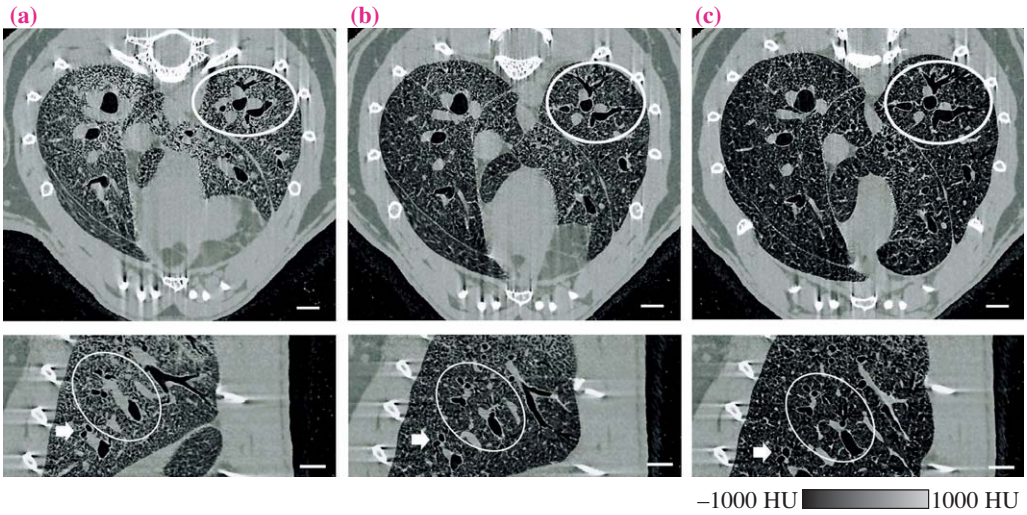

Fig. 2. Representative axial (top) and sagittal (bottom) images of a mouse chest recorded at different airway pressures: 0 cmH_2O (minimum pressure, **a**), 5 cmH_2O (during inspiration, **b**), 15 cmH_2O (maximum pressure, **c**). The circles and arrows show the deformation of the same airways. Bar: 1 mm.

mouse with acceptable radiation risk. To test the applicability of this 4D *in vivo*-CT system, we measured the airway diameters at different pressures. The results (Fig. 3) show that the change in diameter is large for small airways, and indicate that airways do not behave homogeneously *in vivo*. These high-resolution images taken at different phases of dramatic motions will allow the calculation of gas exchange in small airways, and of shear stress in blood vessels.

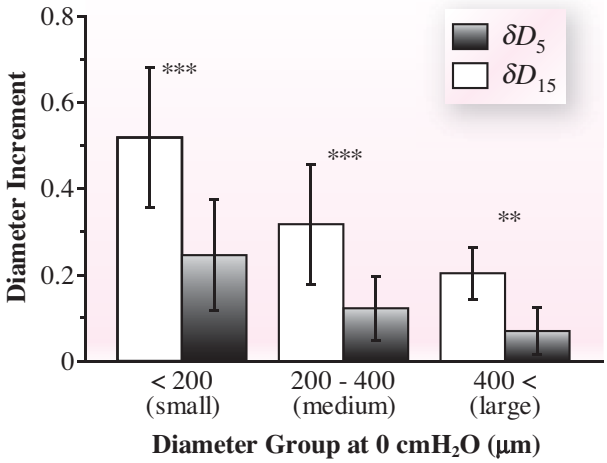

Fig. 3. Changes in the airway diameters of a mouse lung during inspiration. The airways were classified into three groups according to their diameters at an airway pressure of 0 cmH_2O: small (smaller than 200 μm), medium (between 200 and 400 μm), and large (larger than 400 μm). Relative increases in the diameter of each airway were measured at 5 cmH_2O (dark bars) and 15 cmH_2O (white bars). The airways with small diameters expand more than those with large diameters.

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References

[1] *T. Sera, H. Yokota, K. Fujisaki, H. Tachibana, K. Uesugi, N. Yagi, R. Himeno: Physics in Medicine and Biology* ***53*** *(2008) 4285.*