To beam or not to beam: Safely scanning mouse lungs for lung disease and therapy research

Lung diseases are among the most important causes of sickness and death in the world. Chronic obstructive pulmonary disease, lung fibrosis and emphysema are examples of such devastating and life-threatening conditions. Doctors can help by relieving symptoms, but effective treatments for these diseases are lacking. Investigators are therefore continuously searching for novel therapies to combat lung diseases. Even when sometimes the cause is obvious (e.g. cigarette smoking…), many aspects of what exactly causes a lung disease to develop remain to be understood in order to find targets for new, effective treatment strategies.

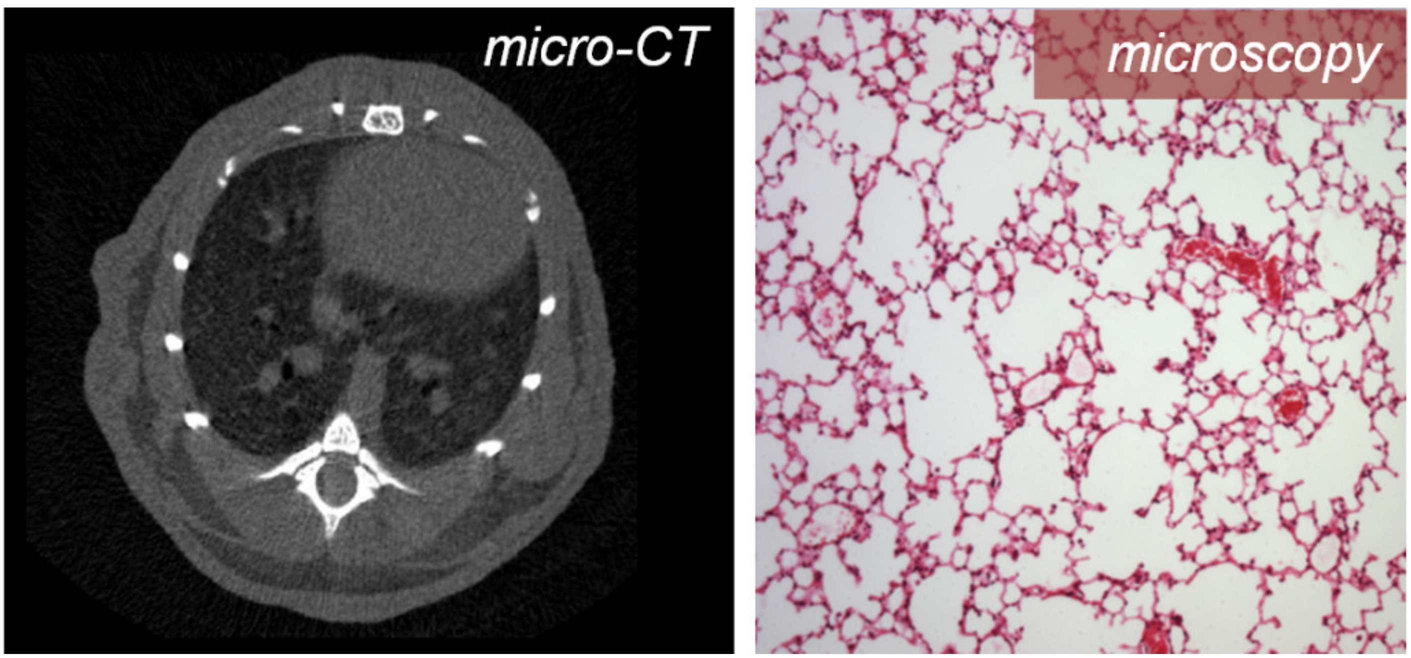

Fig. 1. Longitudinal in vivo microcomputed tomography of mouse lungs: No evidence for radiotoxicity.

To unravel disease processes in the lung and to test novel therapies, investigators typically rely on the analysis of lung tissue samples from indispensable animal models (e.g. rat, mouse, ferret…). Although these techniques provide plenty of opportunities for detailed molecular and microscopic evaluation, they are limited to one measurement per animal, providing only a snapshot of processes that are essentially dynamic in time and space. Any technology that would allow evaluating the lungs of live animals would therefore help a lot to gain better insight in the dynamics of lung disease progression and treatment, but lung function measurements provide too limited information.

Doctors look inside lungs through a computed tomography (CT) scan of their patients' chests. This technology uses x-rays in order to take pictures from different angles around the chest. A computer then reconstructs these pictures into a three-dimensional image of the lung that can be used for diagnosis. This imaging technology would have enormous benefits for the monitoring of dynamic changes regarding lung disease in live animals in a research context, too. Nevertheless, its extension to animals is not that obvious. Especially in small animals such as mice, the lung is particularly challenging to image. As you cannot ask a mouse to hold its breath, the motion caused by its fast respiration poses a technological challenge to reach the high resolution and sensitivity needed in order to obtain meaningful images from an animal that is about a thousand times smaller than a human.

Notwithstanding the challenge, investigators and engineers have worked together to make this imaging technology available for use with small laboratory animals. In recent years, micro-CT has proven to be an excellent tool for monitoring lung disease and therapy repeatedly in a single animal, which is a huge advantage.

But one big hurdle remained before micro-CT could be embraced by the lung research community. Because of the higher resolution and sensitivity needed to provide a good quality mouse lung CT-scan, the x-ray dose would also be higher. Knowing that lungs are particularly sensitive for side effects from radiation, any concerns regarding the possible induction of lung injury because of the x-ray exposure during scanning must be ruled out before calling in micro-CT for animal work. Fortunately, the radiation dose that a mouse is exposed to during a lung micro-CT scan turned out to be much lower than doses used for cancer radiotherapy that are known to cause side-effects. We then excluded any potentially harmful effects when repeatedly scanning the same mouse, thereby demonstrating the safety of micro-CT. This was done for different scanning protocols that involve scans once or twice a week up to three months in a row, long enough to cover a typical preclinical study.

As it is now clear that lung micro-CT studies provide high-quality data while being safe for the animal, this work has paved the way for the routine use of micro-CT in preclinical lung research, thereby reducing manifold the amount of animals needed for this type of investigations.

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