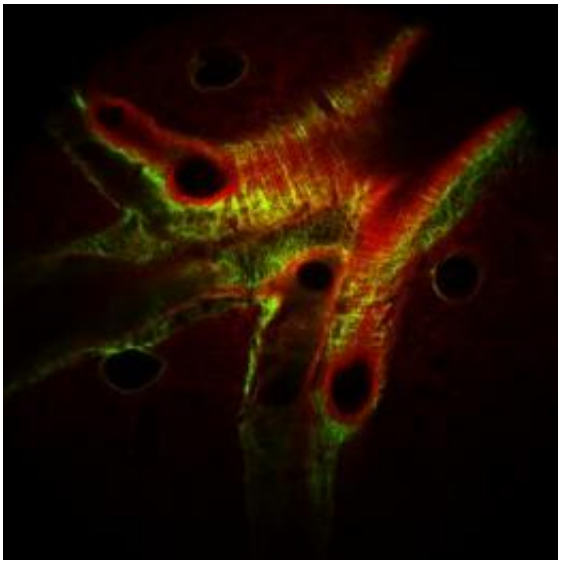
Scientists create 3-D models of whole mouse organs (w/ Video)

June 24 2010



Collagen fibers (in green) outline the bronchiole pathways against a background of elastin tissue (in red) in this high-resolution image of a mouse lung. Credit: Michael Levene/Yale University

Yale University engineers have for the first time created 3D models of whole intact mouse organs, a feat they accomplished using fluorescence microscopy. The team reports its findings in the May/June issue of the *Journal of Biomedical Optics*, in a study published online this week.

Combining an imaging technique called multiphoton microscopy with "optical clearing," which uses a solution that renders tissue transparent,

the researchers were able to scan mouse organs and create high-resolution images of the brain, small intestine, large intestine, kidney, lung and testicles. They then created 3D models of the complete organs—a feat that, until now, was only possible by slicing the organs into thin sections or destroying them in the process, a disadvantage if more information about the sample is needed after the fact.

With traditional microscopy, researchers are only able to image tissues up to depths on the order of 300 microns, or about three times the thickness of a human hair. In that process, tissue samples are cut into thin slices, stained with dyes to highlight different structures and cell types, individually imaged, then stacked back together to create 3D models. The Yale team, by contrast, was able to avoid slicing or staining the organs by relying on natural fluorescence generated from the tissue itself.

When combined with optical clearing, multiphoton microscopy—so called because it uses photons to excite naturally fluorescent cells within the tissue—can image a larger field-of-view at much greater depths and is limited only by the size of the lens used. Once the tissue is cleared using a standard solution that makes it virtually transparent to optical light, the researchers shine different wavelengths of light on it to excite the inherently fluorescent tissue. The fluorescence is displayed as different colors that highlight the different structures and tissue types (in the lung, for example, collagen is depicted as green while elastin shows up as red).

"The intrinsic fluorescence is just as effective as conventional staining techniques," said Michael Levene, associate professor at the Yale School of Engineering & Applied Science and the team leader. "It's like creating a virtual 3D biopsy that can be manipulated at will. And you have the added benefit that the tissue remains intact even after it's been imaged."

The Yale team was able to reach depths in excess of two millimeters—deep enough to image complete mouse organs. Typical tissue samples taken during patient biopsies are about this size as well, meaning the new technique could be used to create 3D models of biopsies, Levene said. This could be especially useful in tissues where the direction of a cancerous growth may make it difficult to know how to slice tissue sample, he noted.

In addition, the technology could eventually be used to trace fluorescent proteins in the mouse brain and see where different genes are expressed, or to trace where drugs travel in the body using fluorescent tagging, for example.

"Fluorescence microscopy plays such a key role throughout biology and medicine," Leven said. "The range of applications of this technique is immense, including everything from improved evaluation of patient tissue biopsies to fundamental studies of how the brain is wired."

Provided by Yale University