Opto-acoustic mesoscopy visualizes tumor tissue patterns

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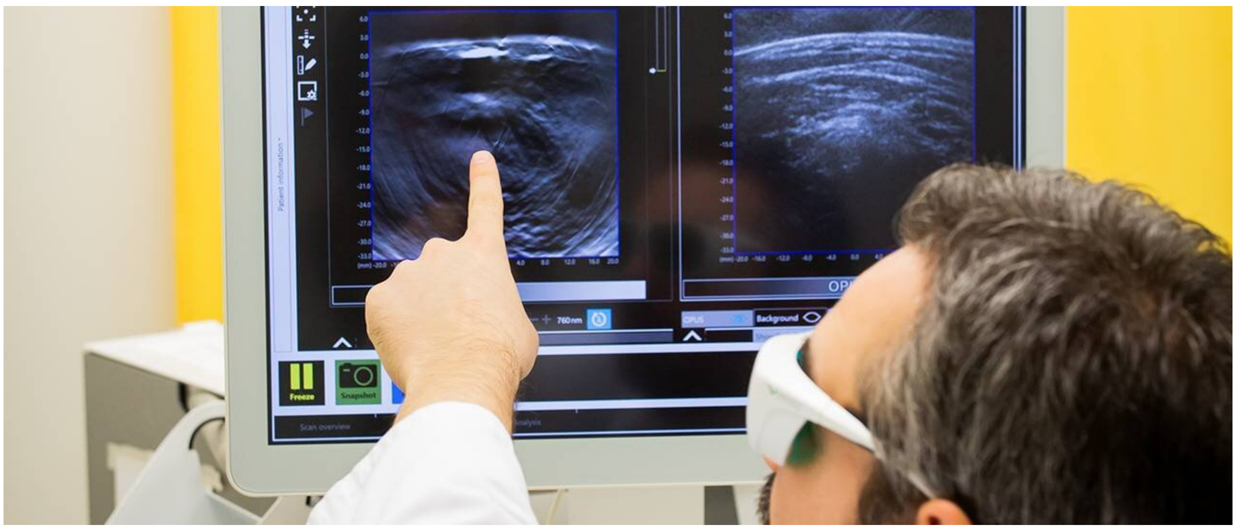

Prof. Vasilis Ntziachristos demonstrates an imaging method similar to multi-spectral optoacoustic mesoscopy. Credit: M. Jooss

Breast cancer is the most common cancer in women. But individual tumors can vary significantly, presenting different spatial patterns within their mass. Researchers at the Technical University of Munich (TUM) and Helmholtz Zentrum München have now visualized spatial changes within tumors by means of optoacoustics. This method may be helpful for the future development of new drugs.

Malignant tumors consume nutrients and oxygen faster than healthy cells. To do so, they recruit blood vessels in their environment. Depending on tumor type and genetic profile, there are differences on how tumors look internally. Typically, tumors present different patterns across their volume. The role of this spatial heterogeneity is not well understood or studied in living tumors. Typically used to understand biological functions in tumors, optical microscopy, for example, gives limited insights into the spatial heterogeneity of tumors as it only accesses volumes of less than a cubic millimeter.

High resolution with new imaging method

A new technique developed by Munich researchers, known as multi-spectral optoacoustic mesoscopy (MSOM), has now been shown capable of resolving optical contrast through tumor volumes that are at least 1,000 times larger than those possible with optical microscopy, enabling high-resolution visualization of tumor heterogeneity patterns. With this imaging method, the tumor is first excited from all sides with pulses of infrared laser light. "Tumor and tissue components that absorb this excitation light undergo a tiny, transient temperature increase, which leads to a small local volume expansion, followed by a contraction. This expansion and contraction process generates a weak ultrasound signal, which we collect with a detector," says guest researcher Dr. Jiao Li.

The data collected is mathematically processed to form light absorption images which indicate different tumor patterns reflecting tumor oxygenation and vascularization. "For the first time, MSOM offers optical images that reach inside tumors to depths of ten millimeters and more with a resolution of less than 50 micrometers," says Dr. Li.

Understanding functional variety in tumors

"MSOM imaging of solid tumors allowed us to see tumors in a new light," says Prof. Vasilis Ntziachristos, holder of the Chair of Biological Imaging at TUM and Director of the Institute for Biological and Medical Imaging at Helmholtz Zentrum München. "MSOM allows us to understand how tumor functionality varies across the tumor, clearly moving the reach of optical observations well beyond the depth penetration limitations of optical microscopy".

In the pictures taken from mamma carcinomas of mice, researchers can see patterns indicating the presence or absence of blood vessels, and thus study blood supply patterns. MSOM can also resolve hemoglobin levels, and indicate whether oxygen is bound to hemoglobin or not. Furthermore, MSOM images were used to determine permeability of the vessel walls relative to nanoparticles. Using the mouse model, the scientists were already able to track how tiny gold particles were transported.

3-D tumor pictures without surgical biopsy

In contrast to conventional histology, where tissue has to be removed, cut up and examined under the microscope by a pathologist, MSOM allows a three-dimensional analysis of entire living tumors without the need for surgical biopsies. This further supports longitudinal studies so that tumor growth or recession under different drugs can be studied with greater accuracy. All of which paves the way for an improved understanding of biological function and drug efficacy during drug development for humans.

More information: Jiao Li et al, Spatial heterogeneity of oxygenation and haemodynamics in breast cancer resolved in vivo by conical multispectral optoacoustic mesoscopy, *Light: Science & Applications* (2020). DOI: 10.1038/s41377-020-0295-y

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