

## Super-depth Photoacoustic Microscopy

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We develop photoacoustic imaging technologies for early-cancer detection and functional imaging by physically combining non-ionizing electromagnetic and ultrasonic waves. Unlike ionizing x-ray radiation, non-ionizing electromagnetic waves, such as optical and radio waves, pose no health hazard and, at the same time, reveal new contrast mechanisms. Unfortunately, electromagnetic waves in the non-ionizing spectral region do not penetrate biological tissue in straight paths as x-rays do. Consequently, high-resolution tomography based on non-ionizing electromagnetic waves alone, as demonstrated by confocal microscopy and two-photon microscopy as well as optical coherence tomography, is limited to superficial imaging within about one optical transport mean free path (~1–2 mm) of the surface of biological tissue. Ultrasonic imaging, on the contrary, provides good image resolution but has strong speckle artifacts as well as poor contrast in early-stage tumors. We have developed ultrasound-mediated imaging modalities by combining electromagnetic and ultrasonic waves synergistically to overcome the above limitations. The hybrid modalities provide relatively deep penetration at high ultrasonic resolution and yield speckle-free images with high electromagnetic contrast.

In photoacoustic computed tomography, a pulsed broad laser beam illuminates the biological tissue to generate a small but rapid temperature rise, which leads to emission of ultrasonic waves due to thermoelastic expansion. The short-wavelength pulsed ultrasonic waves are then detected by unfocused ultrasonic transducers. High-resolution tomographic images of optical contrast are then formed through image reconstruction. Endogenous optical contrast can be used to quantify the concentration of total hemoglobin, the oxygen saturation of hemoglobin, and the concentration of melanin. Melanoma and other tumors have been imaged in vivo in small animals. Exogenous optical contrast can be used to provide molecular imaging and reporter gene imaging.

In photoacoustic microscopy, a pulsed laser beam is focused into the biological tissue to generate ultrasonic waves. The ultrasonic waves are then detected with a focused ultrasonic transducer to form a depth resolved 1D image directly. Raster scanning yields 3D high-resolution tomographic images.

Thermoacoustic tomography is similar to photoacoustic tomography except that low-energy microwave pulses, instead of laser pulses, are used. Although long-wavelength microwaves diffract rapidly, the short-wavelength microwave-induced ultrasonic waves provide high spatial resolution. Microwave contrast measures the concentrations of water and ions.