Triple modality transmission-reflection optoacoustic ultrasound (TROPUS) computed tomography of small animals

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Introduction – Rapid progress in the development of multispectral optoacoustic tomography techniques has enabled unprecedented insights into biological dynamics and molecular processes *in vivo* and noninvasively at penetration and spatiotemporal scales not covered by modern optical microscopy methods [1]. Ultrasound imaging provides highly complementary information on elastic and functional tissue properties and further aids in enhancing optoacoustic image quality [2]. We devised a hybrid transmission-reflection optoacoustic ultrasound (TROPUS) small animal imaging platform that combines optoacoustic tomography with both reflection- and transmission-mode ultrasound computed tomography. The system features full-view cross-sectional tomographic imaging geometry for concomitant noninvasive mapping of the absorbed optical energy, acoustic reflectivity, speed of sound and acoustic attenuation in whole live mice with submillimeter resolution and unrivaled image quality (Fig. 1) [3].

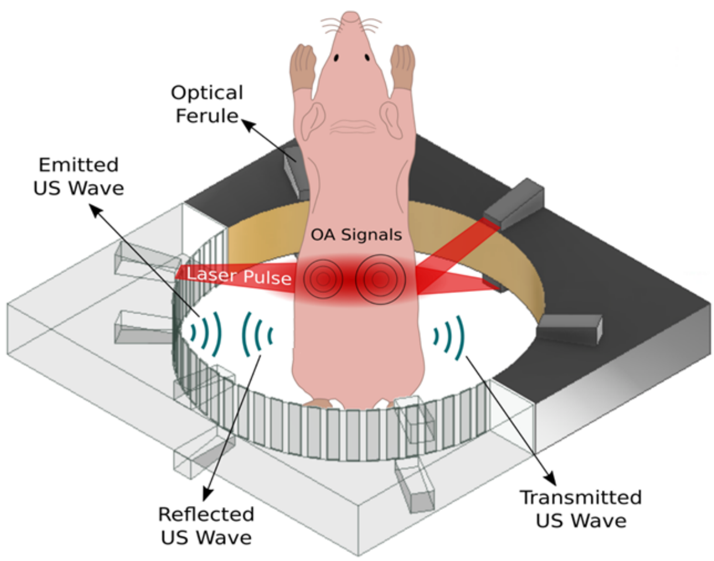

Figure 1. The tri-modal transmission reflection optoacoustic ultrasound (TROPUS) imaging platform featuring laser excitation and acquisition in the optoacoustic (OA) imaging mode, reflection ultrasound computed tomography (RUCT) mode and transmission ultrasound computed tomography (TUCT) speed of sound (SoS) imaging mode.

Methods – The hybrid TROPUS imaging system consist of four main components, namely, a circular transducer array (512 elements, 40 mm radius, 5 MHz central frequency), a nanosecond pumped laser source, a data acquisition system (DAQ) and a workstation for data saving/processing. The laser wavelength was tuned between 700 and 1000 nm with step size of 20 nm for multispectral OA acquisition. OA images were reconstructed using GPU-accelerated 3D filtered back-projection algorithm [4]. Ultrasound (US) data acquisition was performed using synthetic transmit aperture (STA) technique as elaborated elsewhere [5]. Reflection ultrasound computed tomography (RUCT) images were beamformed by delay and sum algorithm and then compounded to create final high contrast image. Transmission ultrasound computed tomography (TUCT) images representing speed-of-sound (SoS) in tissues were reconstructed from transmitted US waves through the body using full wave inversion method [6].

Results – *In vivo* mouse imaging experiments revealed fine details on the organ parenchyma, vascularization, tissue reflectivity, density and stiffness (Fig. 2). We further used the speed of sound maps retrieved by the transmission ultrasound tomography to improve optoacoustic reconstructions via two-compartment modeling. We further demonstrated the capabilities of TROPUS imaging for detection and assessment of non-alcoholic fatty liver disease (NAFLD), which refers to the early stage of liver fibrosis resulting from accumulation of lipid and scarring in liver tissues. Early detection and treatment of NAFLD is paramount in preventing long-term liver damage. Both *ex vivo* and *in vivo* results show that TROPUS system can be used for detection and assessment of NAFLD development in liver tissues. Specifically, the regions of interest were segmented from RUCT images and the lipid content of liver tissues was quantified by multispectral OA images. In addition, SoS images provided quantitative readings of lipid accumulation ratios in liver tissues.

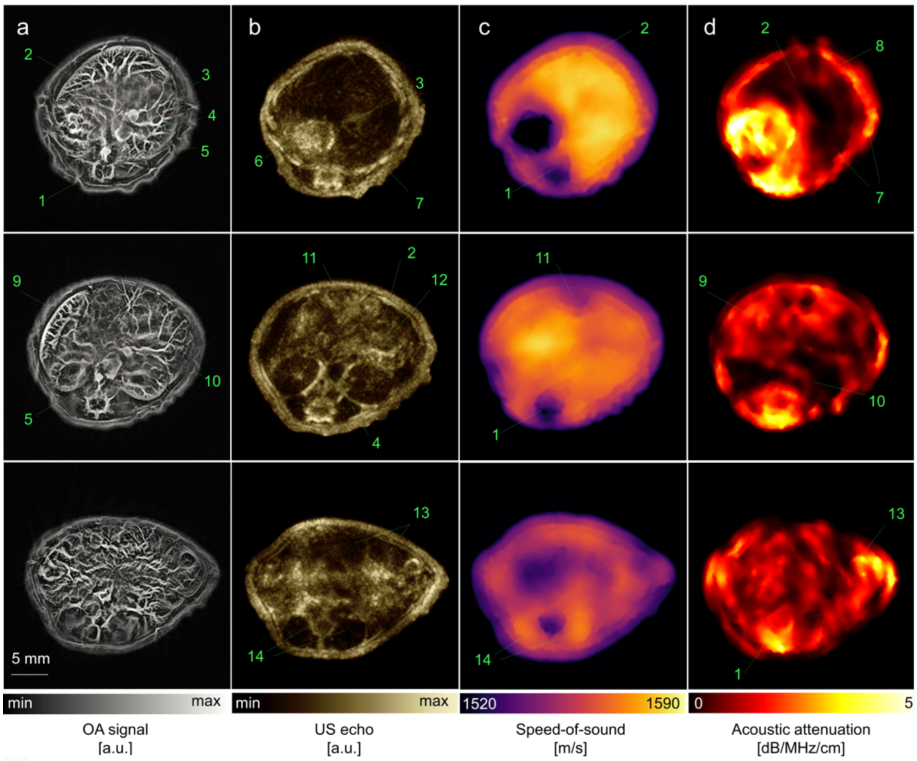

Figure 2. Hybrid transmission-reflection optoacoustic ultrasound (TROPUS) whole-body mouse imaging. **(a)** Representative cross-sections acquired in the optoacoustic mode. **(b)** The corresponding reflection-mode ultrasound images. **(c), (d)** The corresponding transmission-mode ultrasound images showing the distribution of the speed of sound and acoustic attenuation, respectively. Annotations: 1: spinal cord; 2: liver; 3: vena porta; 4: vena cava; 5: aorta; 6: stomach; 7: ribs; 8: skin/fat layer; 9: spleen; 10: right kidney; 11: cecum; 12: pancreas; 13: intestines; 14: muscle.

Conclusions – The newly developed synergistic multimodal TROPUS combination offers unmatched capabilities for imaging multiple tissue properties and biomarkers with high resolution, penetration and contrast. The results further indicate that the proposed approach is suitable for assessing the NAFLD development in preclinical models.

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