Breaking of the fundamental barriers of time and space resolutions in Biomedical Ultrasound

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In the last fifteen years, the introduction of plane or diverging wave transmissions rather than line by line scanning focused beams broke the resolution limits of ultrasound imaging. By using such large field of view transmissions, the frame rate reaches the theoretical limit of physics dictated by the ultrasound speed and an ultrasonic map can be provided typically in tens of micro-seconds (several thousands of frames per second). Interestingly, this leap in frame rate is not only a technological breakthrough but it permits the advent of completely new ultrasound imaging modes, including shear wave elastography[1,2], electromechanical wave imaging, ultrafast Doppler, ultrafast contrast imaging, and even functional ultrasound imaging of brain activity (fUltrasound) introducing Ultrasound as an emerging full-fledged neuroimaging modality.

At ultrafast frame rates, it becomes possible to track in real time the transient vibrations – known as shear waves – propagating through organs. Such "human body seismology" provides quantitative maps of local tissue stiffness whose added value for diagnosis has been recently demonstrated in many fields of radiology (breast, prostate and liver cancer, cardiovascular imaging, ...).

For blood flow imaging, ultrafast Doppler permits high-precision characterization of complex vascular and cardiac flows. It also gives ultrasound the ability to detect very subtle blood flow in very small vessels. In the brain, such ultrasensitive Doppler paves the way for **fUltrasound** (functional ultrasound imaging) of brain activity with unprecedented spatial and temporal resolution compared to fMRI (figure 1).
It provides the first modality for imaging of the whole brain activity working on awake and freely moving animals with unprecedented resolutions [3,4,5].

Finally, we recently demonstrated that it can be combined with 3 µm diameter microbubbles injections in order to provide a first *in vivo* and non-invasive imaging modality at microscopic scales deep into organs (figure 2) combined with contrast agents by localizing the position of millions of microbubbles at ultrafast frame rates.
This ultrasound localization microscopy technique solves for the first time the problem of *in vivo* imaging at microscopic scale the whole brain vasculature [6]. Beyond fundamental neuroscience or stroke diagnosis, it will certainly provide new insights in the understanding of tumor angiogenesis.

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