Ultrafast Imaging in Biomedical Ultrasound:

Applications in pediatric imaging

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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 has broken the conventional barriers 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].

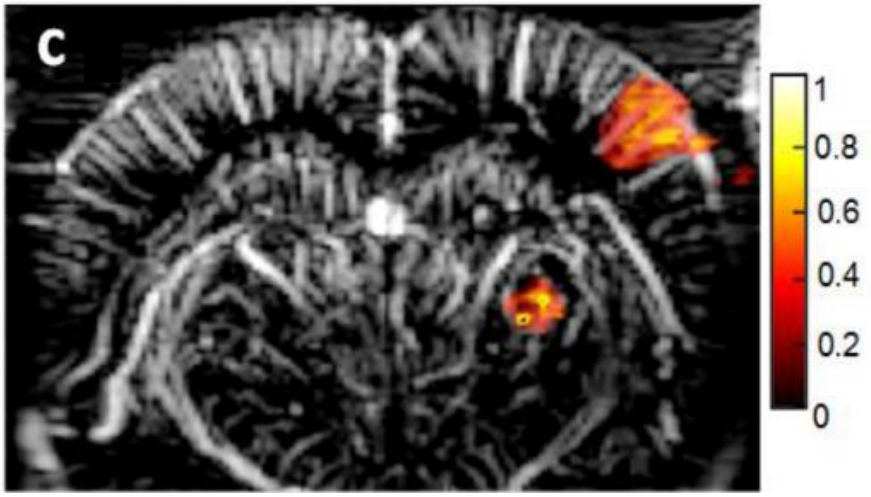

Figure 1. Functional ultrasound imaging of the rat brain activity during whisker stimulation (from Mace et al, Nature Methods 2011; see also Sieu et al, Nature Methods 2015)

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].

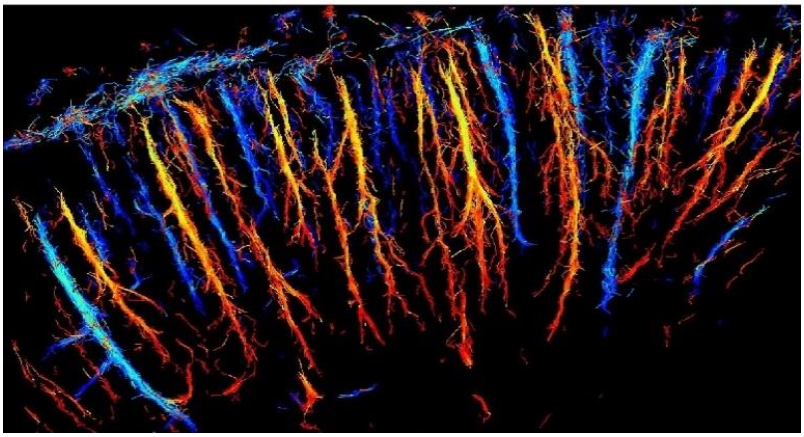

Figure 2. Superresolution Ultrasound: Blood flow quantification of the vascular network in the rat brain cortex at micrometric resolution using Ultrasound Localization Microscopy (Errico et al, Nature 2015).

All these innovations could lead in a near future to major applications in pediatric imaging : Shear Wave Elastography provides an easy, portable, non-invasive, real time and cost effective way to map elastic properties of liver of brain tissues at bedside on newborns or preterm babies for a better characterization of tissue.

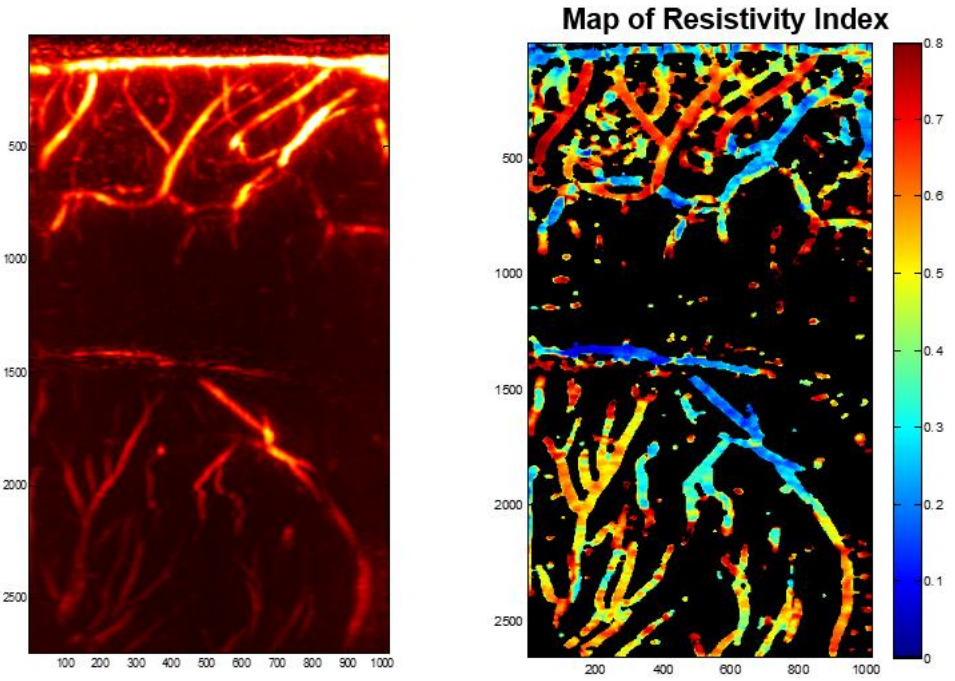

Figure 3. Left image : cerebral blood volume of a human newborn measured by ultrafast Doppler. Right image: corresponding 2D map of the resistivity index of vessels estimated within one single cardiac cycle based on ultrafast Doppler imaging. (from Demene et al[7], JCBFM 2015)

Ultrasensitive Doppler imaging provides very high sensitivity maps of brain vasculature in small vessels (up to 1 mm/s) without any contrast agents injection. The ultrafast acquisitions lead to the full 2D mapping of cerebral resistivity index (figure 3) within a single cardiac cycle for hemodynamic pathologies.

Finally, evidence of functional ultrasound imaging of brain activity (fUltrasound imaging) is demonstrated at bedside for newborns with unprecedented spatiotemporal resolution resolutions.

1. Tanter et al, **Ultrasound in Medicine and Biology**, 34(9), 2008
2. M.E. Fernandez-Sanchez et al, **Nature**, July 2015
3. Mace et al., **Nature Methods**, Jun. 2011
4. Osmanski et al, **Nature Comm**., Oct. 2014
5. L.A. Sieu et al, **Nature Methods**, Jul. 2015
6. C.Errico et al, **Nature**, Dec. 2015
7. Demene et al, **JCBFM**, 201