Transcranial Ultrasound Localization Microscopy reveals sub-resolution blood dynamics in aneurysms and stenosis in the adult human brain

Charlie Demene [1], Justine Robin [1], Mathieu Pernot [1], Fabienne Perren[2], Mickael Tanter[1],
[1]Physics for Medicine Paris, Inserm, ESPCI Paris, CNRS, PSL Research University, 17 rue Moreau, 75012, Paris., [2]Clinical Neuroscience Department, LUNIC (Laboratory of Ultrafast-ultrasound Neuroimaging in Clinics), Université de Genève, Hôpitaux Universitaires de Genève, Switzerland

Background, Motivation and Objective

Human brain vascular imaging is key for management of cerebrovascular and neurological pathologies. Very challenging across modalities, it requires contrast injection, ionizing (CT) or expensive (MRI) imaging devices, overlooks the local blood flow time-dynamics and gives limited resolution (CT 0.6 mm, MRI 1 mm). Ultrasound (US), conversely, is poorly used for neuroimaging due to limited sensitivity and resolution. US Localization Microscopy (ULM) has been shown able to increase sensitivity and to reach sub-resolution precision in the rat brain [1]. Combined here with ultrafast diverging wave transmissions, skull aberration corrections and tissue motion compensation, we show that ULM pushes the boundaries of clinical neuroimaging both in terms of resolution and very local blood flow dynamic description.

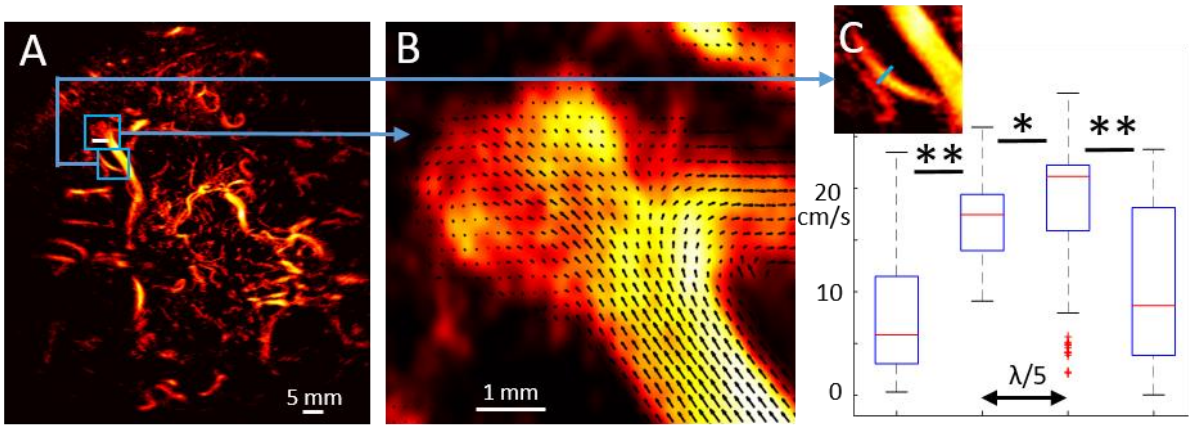
Statement of Contribution/Methods

Experiments complied with the Declaration of Helsinki and patients gave informed and written consent (protocol 2017-00353 Geneva CCER). They were injected intravenously boluses of 0.3 mL of Sonovue before imaging through the temporal window with a 3-MHz phased array (pitch 0.2 mm) and an ultrafast scanner. Ultrafast US sequences consisted in 4 diverging waves fired at 4800 Hz, repeated at 800 Hz during 1s, looped every 2s, during 2 minutes. Tissue was filtered out using spatiotemporal SVD filtering, aberration corrections were calculated for isoplanatic patches thanks to local coherence optimization on isolated bubbles RF signatures before beamforming and motion compensation. Bubbles geometric centers were estimated using quadratic fitting, tracked and assigned to super-resolution trajectories using Hungarian algorithm.

Results/Discussion

With only 2 minutes of examination we could obtain an image with a ~100 µm resolution (compared to the typical ~3 mm lateral and ~0.8 mm axial for transcranial US), at depth up to 120 mm (~whole brain), with quantitative data on blood flow dynamics at a sub-resolution level. Vortex flow in a 1.5 mm-wide aneurysm, accelerated flow in a 0.9mm-wide stenosis and parabolic speed profile on a 0.8 mm vessel section could be observed, which is impossible with any other neuroimaging modality. Complex flow pattern in a Moya-Moya syndrome could be observed, overstepping the partial information given by luminal-only clinical vascular imaging modalities.

[1] Errico et al, *Nature*, 2015



Legend: A. ULM image obtained transcranially on a patient presenting a middle cerebral artery aneurysm. B. Zoom on the 1.7 mm-wide sub-resolution aneurysm exhibiting a vortex flow, as visible on the speed vector field reconstructed from bubble trajectories. C. A subwavelength analysis of the bubble speeds on the cross section (blue line) of a ~0,8mm diameter vessel show significant differences (* p-value < 0,01, ** p-value <0,005), revealing a typical parabolic profile.