# Ultrafast ultrasound predicts ischemic stroke outcome in mouse model

Vincent Hingot[1,*], Camille Brodin[2,*], Baptiste Heiles[1], Cyrille Orset[2,3], Denis Vivien[2,3], Mickael Tanter[1], Thomas Deffieux[1,**], Olivier Couture[1,**]
1. Institute Physics for Medicine Paris, Inserm U1273, ESPCI Paris, CNRS FRE 2031, PSL University
2. Normandie Univ, UNICAEN, INSERM, UMR-S U1237, Physiopathology and Imaging of Neurological Disorders (PhIND), Caen, FRANCE.
3. CHU Caen, Department of Clinical Research, Caen University Hospital, Avenue de la Côte de Nacre, Caen, FRANCE.
*, **, those authors contributed equally.

## Background, Motivation and Objective

Every year, 42 million people suffer a stroke worldwide, representing the 2nd cause of death and the first cause of disabilities. Cerebral arterial recanalization and tissue reperfusion are the major prognostic factors of good functional outcomes. However, efficient methods to image cerebral perfusion lack for both clinical and preclinical studies. The introduction of ultrafast ultrasound led to the development of ultrafast Doppler [Deffieux & al. Current Opinion in Neurobiology, 2018] and Ultrasound Localization Microscopy (ULM), [Couture & al. IEEE UFFC 2018]), two methods with excellent sensitivity to small blood flows. In this study, we combine both methods to provide a longitudinal monitoring of whole brain perfusion in a relevant model of stroke with recombinant tissue Plasminogen Activator (rtPA)-induced reperfusion.

## Statement of Contribution/Methods

After anesthesia and injection of 1 µL of thrombin (1UI) to form a clot *in situ* in the middle cerebral artery, 2 groups of 10 mice were either treated with rtPA or saline. Ultrafast Doppler was done on a Verasonics system with a 15 MHz probe (Vermon) that was mounted on a translational motor so it could scan 24 coronal planes over 8 mm of the mouse brain every 40 s. For each Doppler image, 200 compounded frames were acquired at 500 Hz. Scanning was performed for 5 minutes before occlusion, for the following 2 hours and again at 24 hours. ULM was performed in one same plane before and after the occlusion, and after 1, 2 and 24 hours. After injecting 100 µl of Sonovue intravenously, 180.000 frames were acquired at 1 kHz. After high pass filtering, the centroids were localized on the filtered images using a weighted average method and microbubbles tracks were formed using SimpleTracker (MathWorks).

## Results/Discussion

Ultrafast Doppler enabled 3D identification of hypoperfused areas. In both groups we measured hypoperfusion volumes of 18 ± 4 $mm^3$ directly after occlusion. While we didn't see any recanalization in saline treated mice, complete recanalization happened around 90 minutes in the rtPA treated group. Fine differences in tissue reperfusion could be observed with ULM. Constant registration with T2 MRI reveals tight correlation between early reperfusion and tissue protection (Figure 1).

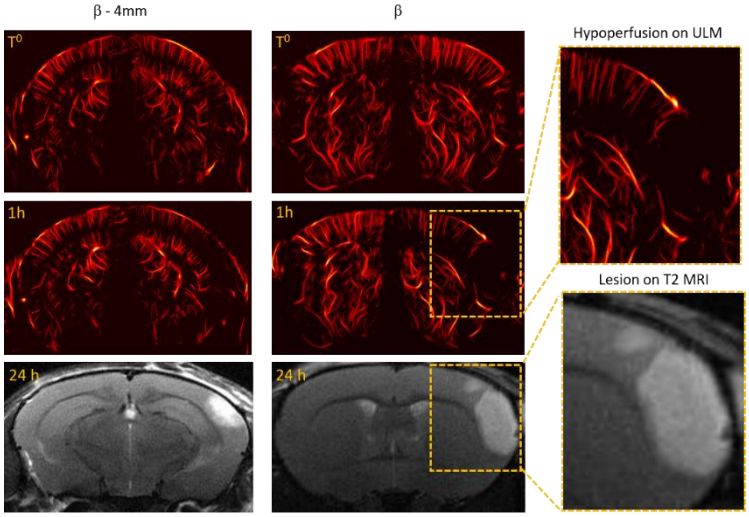


**Figure 1**: Ultrasound Localization Microscopy over two coronal planes of a mouse brain before ischemia and 1 hour after and T2 MRI at 24 h over the corresponding coronal planes reveal correlation between hypoperfusion at 1 hour and lesion at 24 hours.