Pulsatility mapping using time-resolved ultrasound localization microscopy in the rodent's brain in vivo

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Background, Motivation and Objective

Cognitive impairment is often prodromal to dementia in patients with risk factors for cardiovascular diseases. The increased stiffness of aging arteries is associated with an increased pulsatility in downstream vessels, which could potentially lead to microvessel and brain structural damage. Hence, brain-wide pulsatility maps could become a powerful biomarker for neurodegenerative diseases. However, mapping pulsatility in an entire brain remains challenging, even in small animals: MRI's spatiotemporal resolution is insufficient, and optical microscopy is limited to the brain's surface. Ultrasound Localization Microscopy (ULM) can probe the smallest vessels of the rodent's brain but is typically used to map the vascular tree itself or mean velocities averaged over multiple cardiac cycles[1]. The objective of this work was to show the feasibility of performing ULM pulsatility mapping (ULM-PM) in a rodent's brain.

Statement of Contribution/Methods

Rat brains were imaged following craniotomy using a Vantage system (L22-14, Verasonics, WA). 102 400 frames at 1000 fps were acquired in groups of 400, each gated on the ECG and the respiratory pause, were obtained over 8.5 minutes following the injection of a 5-µL microbubble solution (Definity, Lantheus, MA). After singular value decomposition, the positions of microbubbles were measured using their centroid and tracked with the Hungarian algorithm. The median velocity profile of vessels was measured during both systole and diastole and used to map the pulsatility index.

Results/Discussion

Distinct velocities were measured during systole and diastole throughout a 2-D slice of the rat brain. Looking at individual plunging vessels, the pulsatility index was observed to decrease downstream, as expected. Data (Fig. 1) show a vessel of about 93 µm in diameter with pulsatility decreasing from 0.36 to 0.25 at 0.9 mm downstream. To our knowledge, this study demonstrates for the first time the feasibility of mapping pulsatility with ULM in small vessels in the rodent's brain. Upon further validation, ULM-PM could characterize the development and progression of vascular diseases. Future work will include a larger sample size and pathological animal models. We acknowledge the support of IVADO, TransMedTech, and the Canada First Research Excellence Fund (Apogée/CFREF).

1. Couture et al., *IEEE TUFFC*, (65)8-1304, 2018.

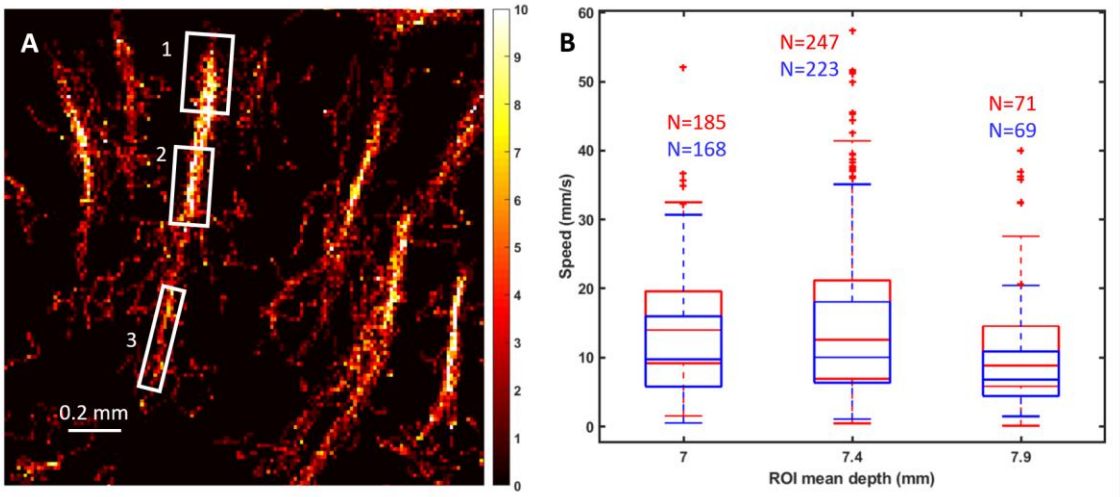

Fig. 1. Pulsatility index changes with depth within a vessel. A. Map of density count of microbubbles: 3 regions of interest (ROI) are selected within a vessel, B. Velocity profiles associated with each ROI, for systole (in red) and diastole (in blue). The central mark indicates the median ; the bottom and top edges indicate the 25th and 75th percentiles, respectively ; the whiskers extend to the most extreme data points not considered outliers. The number of microbubble events N detected during a systole or a diastole within a ROI is indicated in red and blue, respectively. The pulastility indexes calculated for each ROI are 0.36, 0.22 and 0.25 respectively.