**Fast and Robust Super-Resolution Ultrasound Microvessel Imaging via Microbubble Separation** Chengwu Huang<sup>1</sup>, Matthew R. Lowerison<sup>1,2,3</sup>, Joshua D. Trzasko<sup>1</sup>, Armando Manduca<sup>4</sup>, Yoram Bresler<sup>2,3,5</sup>, Shanshan Tang<sup>1</sup>, Ping Gong<sup>1</sup>, U-Wai Lok<sup>1</sup>, Pengfei Song<sup>1,2,3</sup>, Shigao Chen<sup>1</sup>, <sup>1</sup>Department of Radiology, Mayo Clinic College of Medicine and Science, Mayo Clinic, Rochester, MN, <sup>2</sup>Beckman Institute, University of Illinois at Urbana-Champaign, Urbana, IL, <sup>3</sup>Department of Electrical and Computer Engineering, University of Illinois at Urbana-Champaign, Urbana, IL, <sup>4</sup>Department of Physiology and Biomedical Engineering, Mayo Clinic College of Medicine and Science, Rochester, MN, <sup>5</sup>Coordinated Science Laboratory, University of Illinois at Urbana-Champaign, Urbana, IL

## **Background, Motivation and Objective**

Super-resolution ultrasound microvessel imaging (SR-UMI), based on localization and tracking of individual microbubbles, has been proposed to break the ultrasound diffraction limit. Dilute microbubbles are typically used to ensure microbubble signals are spatially isolated for accurate bubble localization, which significantly extends the data acquisition time to collect sufficient isolated bubble signals for a full reconstruction of microvasculature. To break this fundamental tradeoff between acquisition time and bubble concentration, we propose a microbubble separation method based on the spatial-temporal hemodynamics of microbubbles for fast and robust SR-UMI.

## Statement of Contribution/Methods

Ultrasound data were acquired from a chick embryo chorioallantoic membrane (CAM) and a xenograft renal tumor using a Verasonics Vantage system (L35-16vX linear array, 15-ange plane wave compounding, frame rate = 500 Hz), and a chick embryo brain using a Visualsonics Vevo 3100 system (MX250s linear array, focused imaging, frame rate = 301 Hz) after 1 bolus (about 70  $\mu$ L) injection of microbubbles (Bracco, 5 times the standard concentration). After tissue clutter rejection, a 3D Fourier transform was applied to convert the spatial-temporal data into the k-f domain. Microbubbles with different speeds/directions correspond to energies concentrated in different regions of the k-f domain, which can then be separated into multiple subsets of data (15 subsets for this study) with sparser microbubble concentration by properly filtering in k-f space. Localization and bubble tracking (Song *et al. IEEE TUFFC* 2018) were then performed for each subset separately, and the final SR-UMI was generated by combining signals from all the subsets.

## **Results/Discussion**

SR-UMI of the CAM and tumor derived from 2160 frames of data (4.32s acquisition time), and brain from 5000 frames (16.6 s) with and without the microbubble separation are shown in Fig. 1. A significantly larger amount of tiny vessels (from several  $\mu$ m to tens of  $\mu$ m diameter) can be resolved with the proposed method (right side of each subfigure). Separation of microbubbles that spatially overlap enables better localization and thus more robust SR imaging. This method could significantly reduce the acquisition time for full reconstruction of microvasculature and thus has great potential for successful clinical translation.

