Washington University in St. Louis
Office of Technology Management

# ULTRASOUND "PAINTING" FOR PRECISE, TARGETED DRUG DELIVERY TO THE BRAIN

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T-018953

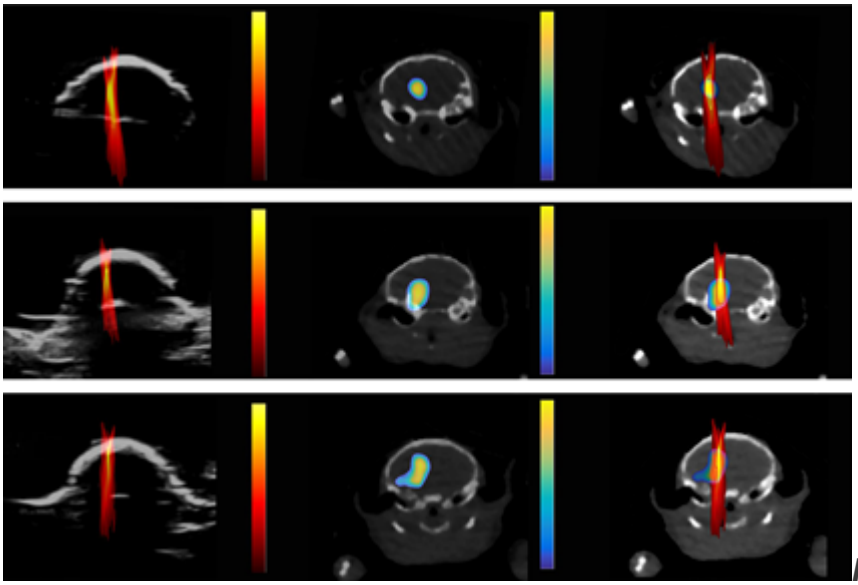
## Technology Description

Researchers in Prof. Hong Chen's laboratory have developed a safe, convenient monitoring technique to precisely deliver drugs to the brain by integrating ultrasound imaging with ultrasound therapy (focused ultrasound-blood-brain-barrier delivery, "FUS-BBBD").

FUS-BBBD is a promising non-invasive approach for localized drug delivery. It utilizes the ultrasound effects on microbubble contrast agents to control the release of drugs across the blood brain barrier. However, it is currently difficult to precisely control, modulate, detect and measure the delivery without knowing the exact location of the microbubbles during focused ultrasound treatment. This technology, called "cavitation dose painting", solves that problem using passive cavitation imaging ("PCI") to track both the location and concentration of drugs during the FUS-BBBD procedure. By spatially "painting" to verify where the drug is, higher doses can be delivered to the precise treatment area while avoiding off target effects to healthy tissue. This type of intraprocedural monitoring and real-time feedback is not possible with alternative imaging techniques (MRI, PET, SPECT). The methods and algorithms for cavitation dose painting could open new horizons for spatially targeted ultrasound drug delivery.

## Stage of Research

*Proof-of-concept* – The inventors performed in vivo imaging studies on mice with $^{64}$Cu-Au nanoclusters. This demonstrated that "cavitation dose painting" with ultrasound is capable of predicting the location and concentration of nanoclusters delivered by FUS-BBBD - the PCI images were correlated with PET imaging of the nanoclusters on a pixel-by-pixel level.



***Passive cavitation imaging (PCI) compared to PET:*** *PCI/B-mode images (left column), PET/CT images (middle column), and PCI and PET overlaid images (right column) for three representative cases.*

## Applications

- **Therapeutic ultrasound** – methods and algorithms for treatment monitoring of FUS-BBBD drug delivery to the brain

## Key Advantages

- **Convenient:**
  - real-time feedback control of FUS parameters
  - ultrasound used to both control drug delivery and monitor FUS treatment, no other imaging modality is needed
- **Precise, controlled drug delivery of FUS-BBBD**
  - predicts where the drug is delivered (spatial distribution) and the concentration
  - allows higher doses to be delivered to treatment area while avoiding side effects to healthy tissue
  - enables intraprocedural monitoring of the FUS treatment which is not possible with other imaging techniques (MRI, PET, SPECT)
- **Safe, low-cost:**
  - tracers for alternative PET imaging are expensive and subject the patient to radioactivity
  - non-invasive delivery is safer than surgical procedures

## Publications


- Yang, Y., Zhang, X., Ye, D., Laforest, R., Williamson, J., Liu, Y., & Chen, H. (2019). Cavitation dose painting for focused ultrasound-induced blood-brain barrier disruption. *Scientific reports*, 9(1), 2840.
- A new method for precision drug delivery: painting, theSOURCE, Feb. 27, 2019


## Patents

- Provisional patent application filed

## Website

- Chen Lab