Noninvasive and Targeted Brain Drug Delivery using Transcranial Focused Ultrasound

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Outline

- **Existing Approaches for Brain Drug Delivery**
  1. Vascular Opening
     (Focused Ultrasound + Microbubbles)
  2. Without Vascular Opening
     (Focused Ultrasound + Nanodroplets)

- **New Approach for Brain Drug Delivery**

- **Conclusions**
1. Cerebrospinal fluid: 10%
2. Blood vasculature: 10%
3. Interstitial fluid: 12-20%
4. Intracellular fluid: 60-68%
Brain’s Fluid Compartments and Barriers

1. Cerebrospinal fluid: 10%
2. Blood vasculature: 10%
3. Interstitial fluid: 12-20%
4. Intracellular fluid: 60-68%
However, those vascular barriers, the BBB, and the BCSFB limit drug delivery for neurological disorders.
Approaches for Brain Drug Delivery

- Invasive
- Trans-Nasal Delivery
- Biopharmaceutical
- New: Focused Ultrasound

- Direct Injection
- Implantable devices
- Intrathecal/Intraventricular Injection
- BBBD via arterial injection of osmotic solution
Vascular Opening

A. BBB Disruption

Blood Vessel

Ultrasound Contrast Agent (Microbubble)

Red Blood Cell

Drug

Noninvasive, Localized, Repetitive

FUS

Stanford University
Vascular Opening

A. BBB Disruption

Blood Vessel

Noninvasive, Localized, Repetitive

Ultrasound Contrast Agent (Microbubble)
Red Blood Cell
Drug

✔ FDA approved for phase 0/1 trial in brain cancer and alzheimer
Without Vascular Opening

B. No BBB Disruption

Blood Vessel

- Polymers (PEG/PLGA)
- Perfluoropentane
- Red Blood Cell
- Drug

Noninvasive, Localized, Repeatable
Without Vascular Opening

B. No BBB Disruption

Polymers (PEG/PLGA)
Perfluoropentane
Red Blood Cell
Drug

✓ Preclinical models for neuroscience and cancer applications

Zhong et al., Biomaterials. 2019
Aryal* & Wang* et al., Neuron. 2018, * equally contributed
Note: black colored stars & ns: two tailed paired t-test between left (non-treated) and right (treated) hemisphere of the brain in FUS cohorts
blue colored stars & ns: two tailed unpaired t-test between Control and FUS Cohort of right hemispheres
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