Noninvasive Focused Ultrasound Accelerates Glymphatic Transport to Bypass the Blood-Brain Barrier

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Outline

- Introduction
  - Meningeal Lymphatic
  - Glymphatic Pathway

- Ultrasonic Glymphatic Control

- Conclusions

- Future Work
A Garbage Truck of The Brain: Meningeal Lymphatic

- Immune cells
- Cerebral spinal fluid
- Macromolecules

Louveau et al., Nature 2015.
A Garbage Truck of The Brain: Glymphatic Pathway

Proteins (Amyloid-beta (Aβ), Tau oligomers

Nedergaard et al., Science 2013.
Glymphatic Dysfunction and Therapeutics

- Clearance efficacy can decay
  - Healthy aging
  - Alzheimer
  - Traumatic brain injury,
  - Subarachnoid hemorrhage
  - Strokes (Hemorrhagic, Ischemic)
  - Idiopathic normal pressure hydrocephalus
  - Diabetes Mellitus Type 2
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- **Glymphatic Transport**: novel therapeutic target to optimize and maintain brain health
Approaches to Accelerates Glymphatic Flow

- Physical exercise
- Changes in body posture
- Intake of omega-3 polyunsaturated fatty acids
- Low dose alcohol (0.5 g/kg)

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Limitations of BBBO

- Spatial Resolution is limited for neurodegenerative diseases that needs global treatment like Alzheimer’s and infiltrating/metastatic tumor and for other
- Disrupting the BBB by FUS induces sterile inflammation, Kovacs et al. *PNAS* 2017
- BBB breakdown is an early biomarker of human cognitive dysfunction, Nation et al. *Nature medicine* 2019
Supportive Data

- BBBO helps to distribute drug homogeneously in tumor
- Ultrasound is accelerating the bulk flow of interstitial fluid

Hematoxylin and Eosin Staining

Segmentation map of MALDI-MS imaging

BBBO Tumor
No BBBO Tumor

(Drug: Maroon color in map)
Supportive Data
Supportive Data

Hersh et al., PLoS One. 2018,
Supportive Data
Biological Agent Delivery via BBBO

- **Panitumumumab**: Epidermal growth factor receptor inhibitor cancer drug (biological therapy)
- **Optically-labeled** **Panitumumumab**: Pan800
- **Test**: BBBO-based drug delivery efficacy

Preliminary Results
Thank you