

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

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SCIT Seminar
January 29, 2020

Outline

□ Introduction

- Meningeal Lymphatic
- Glymphatic Pathway

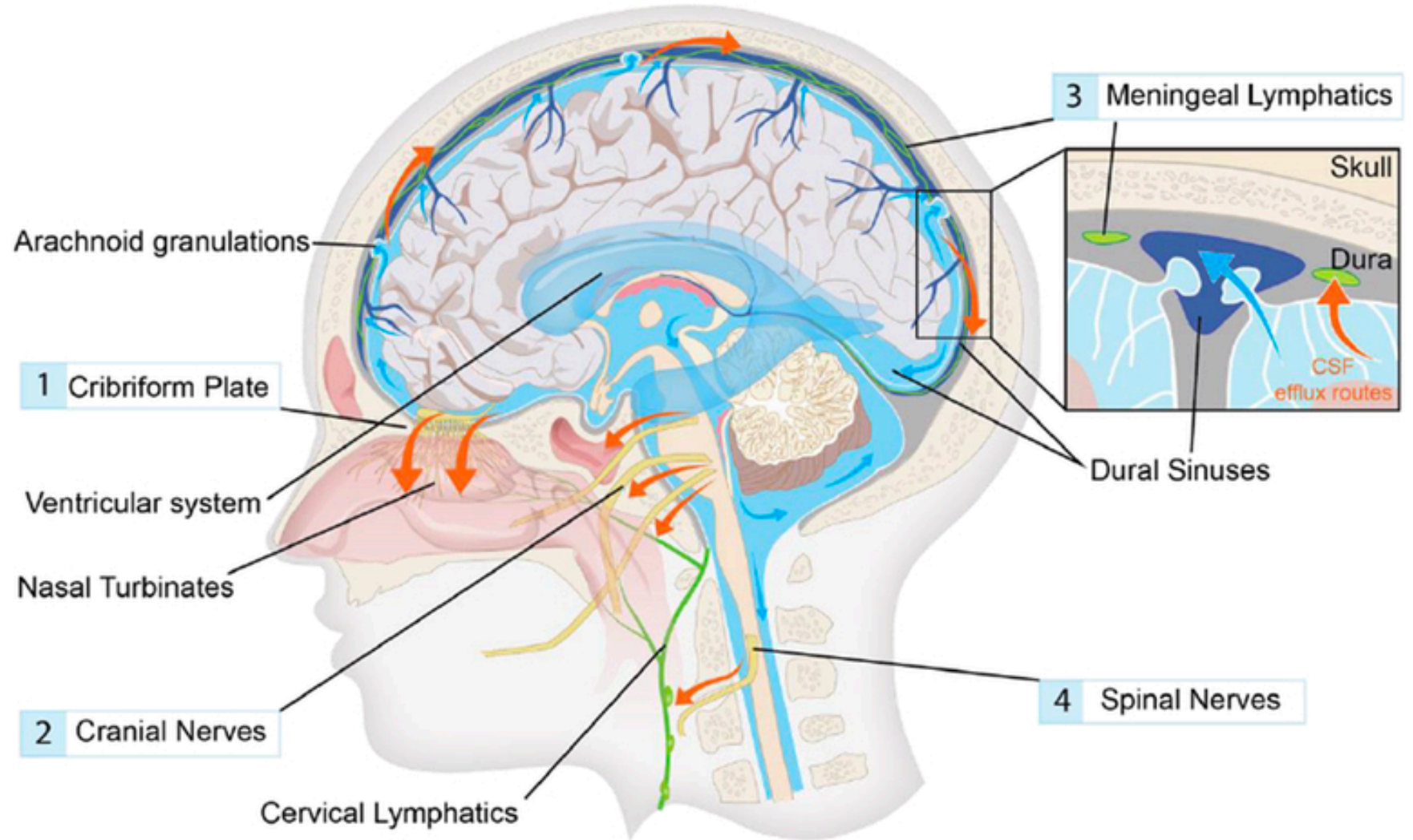
□ Ultrasonic Glymphatic Control

□ Conclusions

□ Future Work

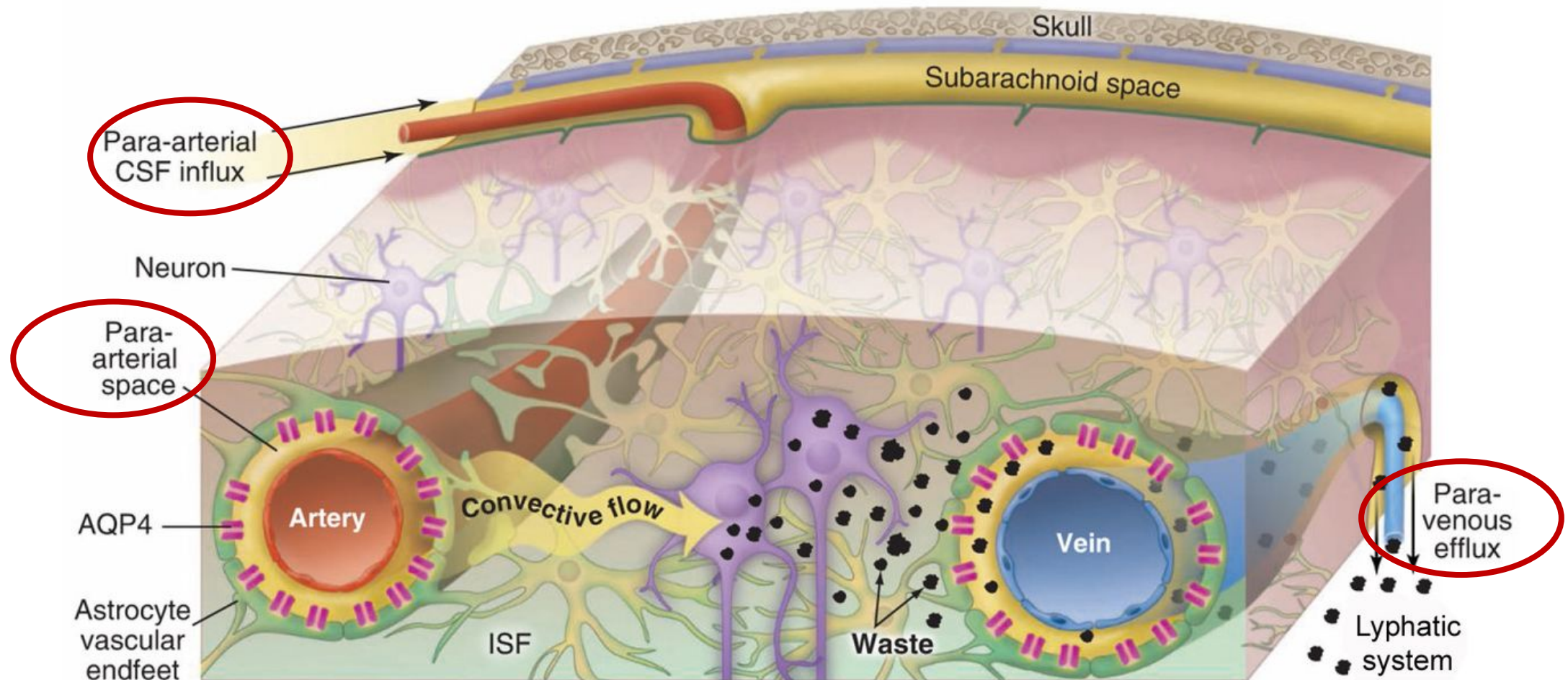
A Garbage Truck of The Brain: Meningeal Lymphatic

- Immune cells
- Cerebral spinal fluid
- Macromolecules



A Garbage Truck of The Brain: Glymphatic Pathway

Proteins (Amyloid-beta ($A\beta$), Tau oligomers)



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 the 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)

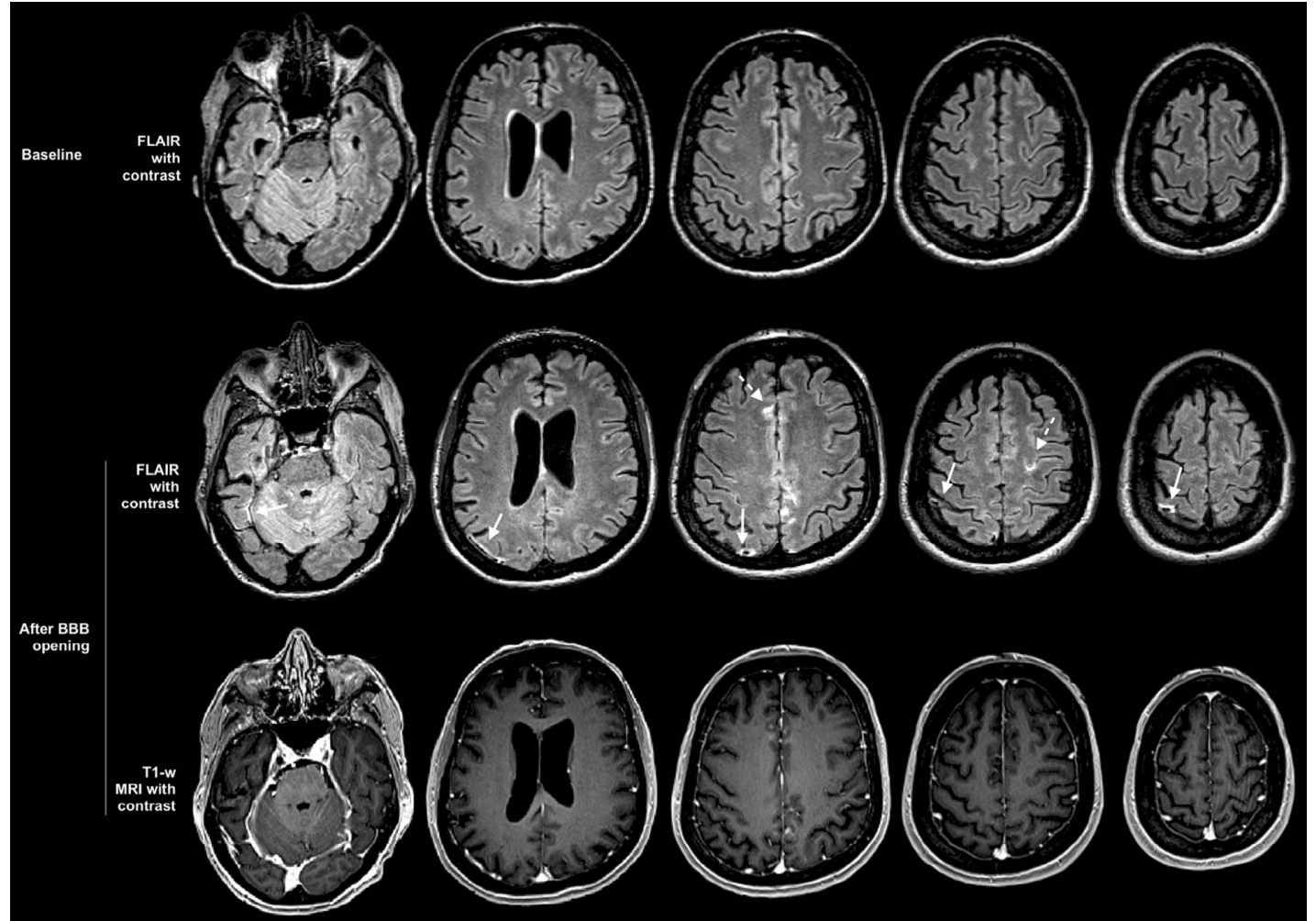
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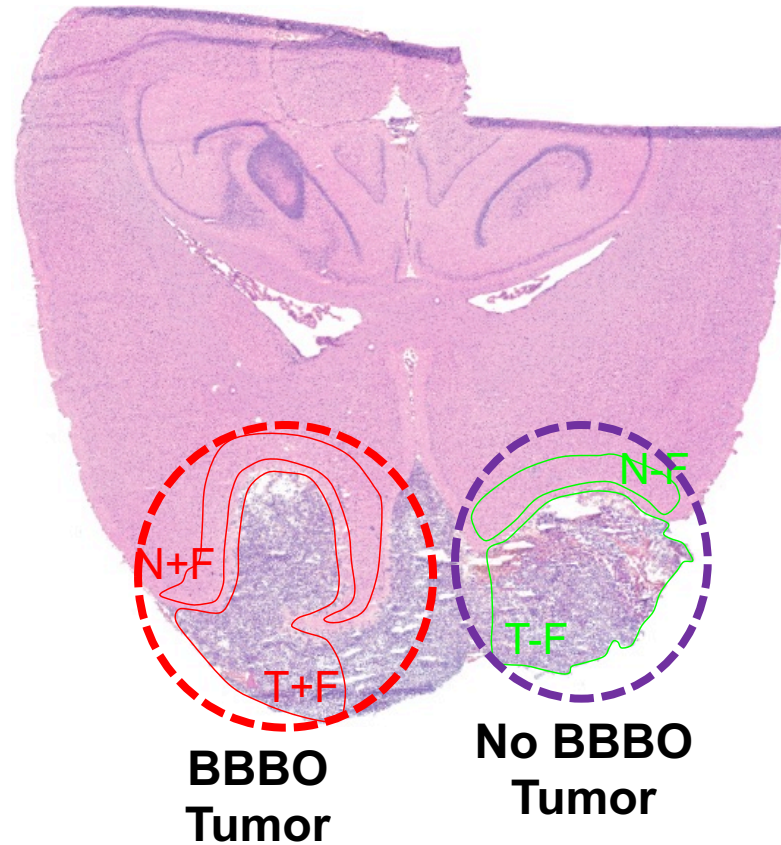
Limitations of BBBO

- 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*

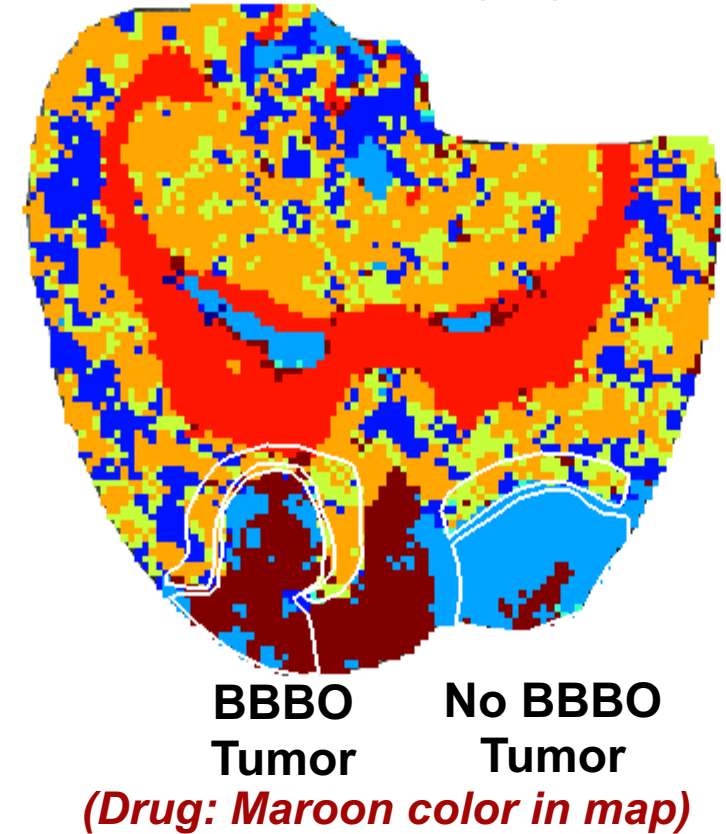
Supportive Data

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

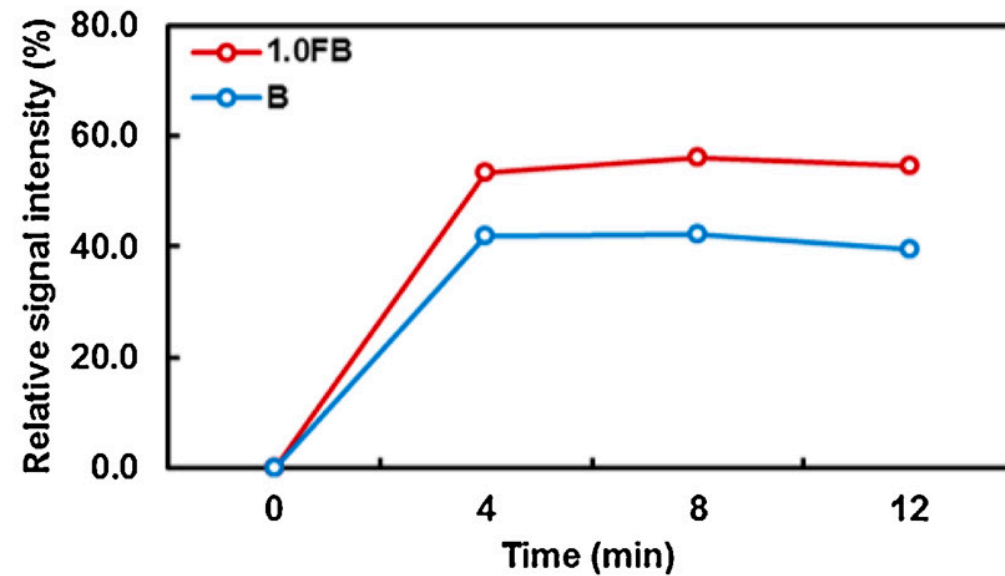
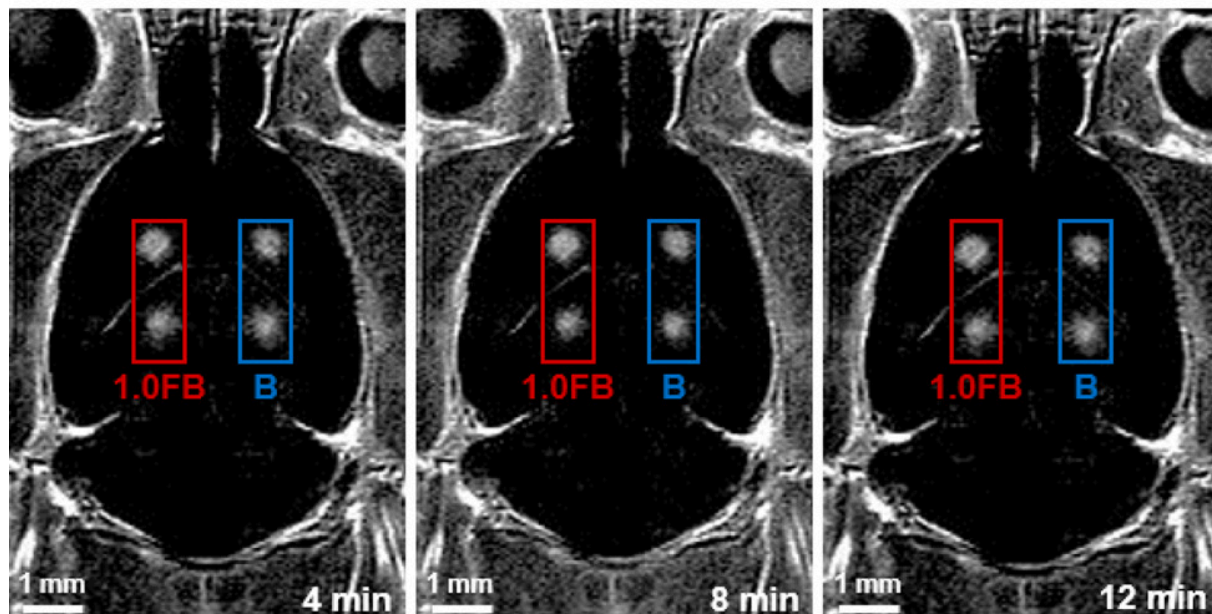
Hematoxylin and Eosin Staining



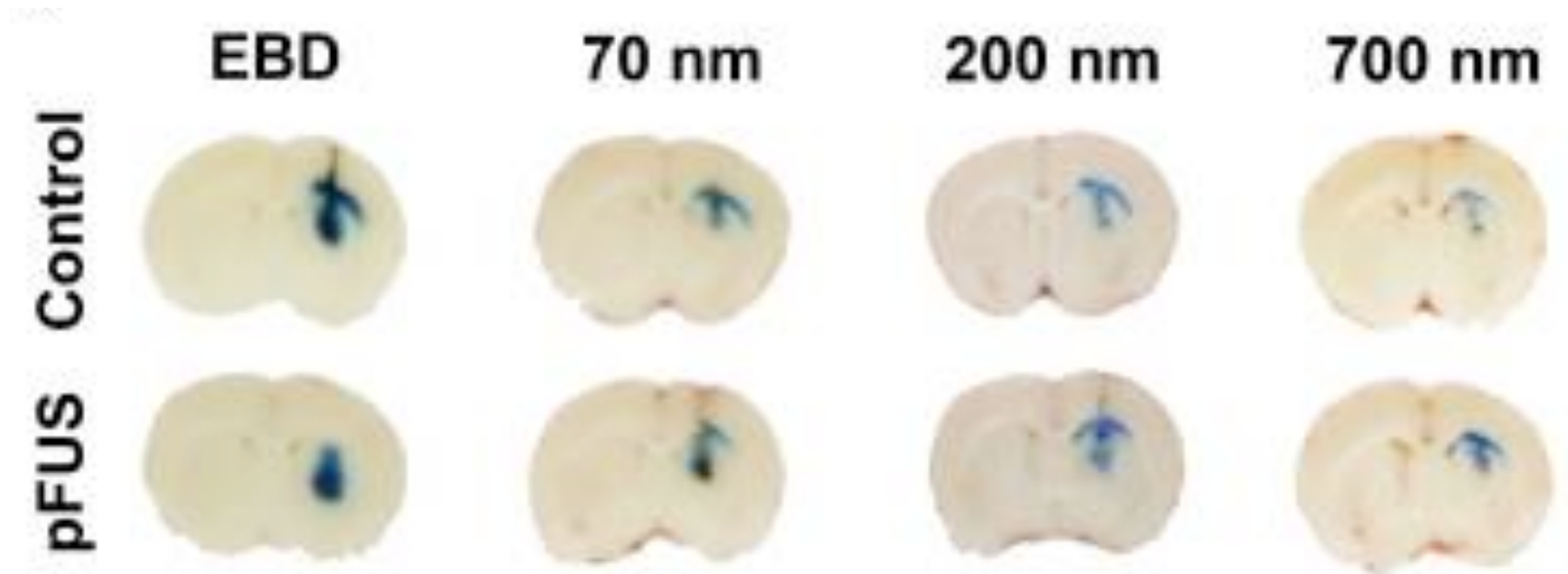
Segmentation map of MALDI-MS imaging



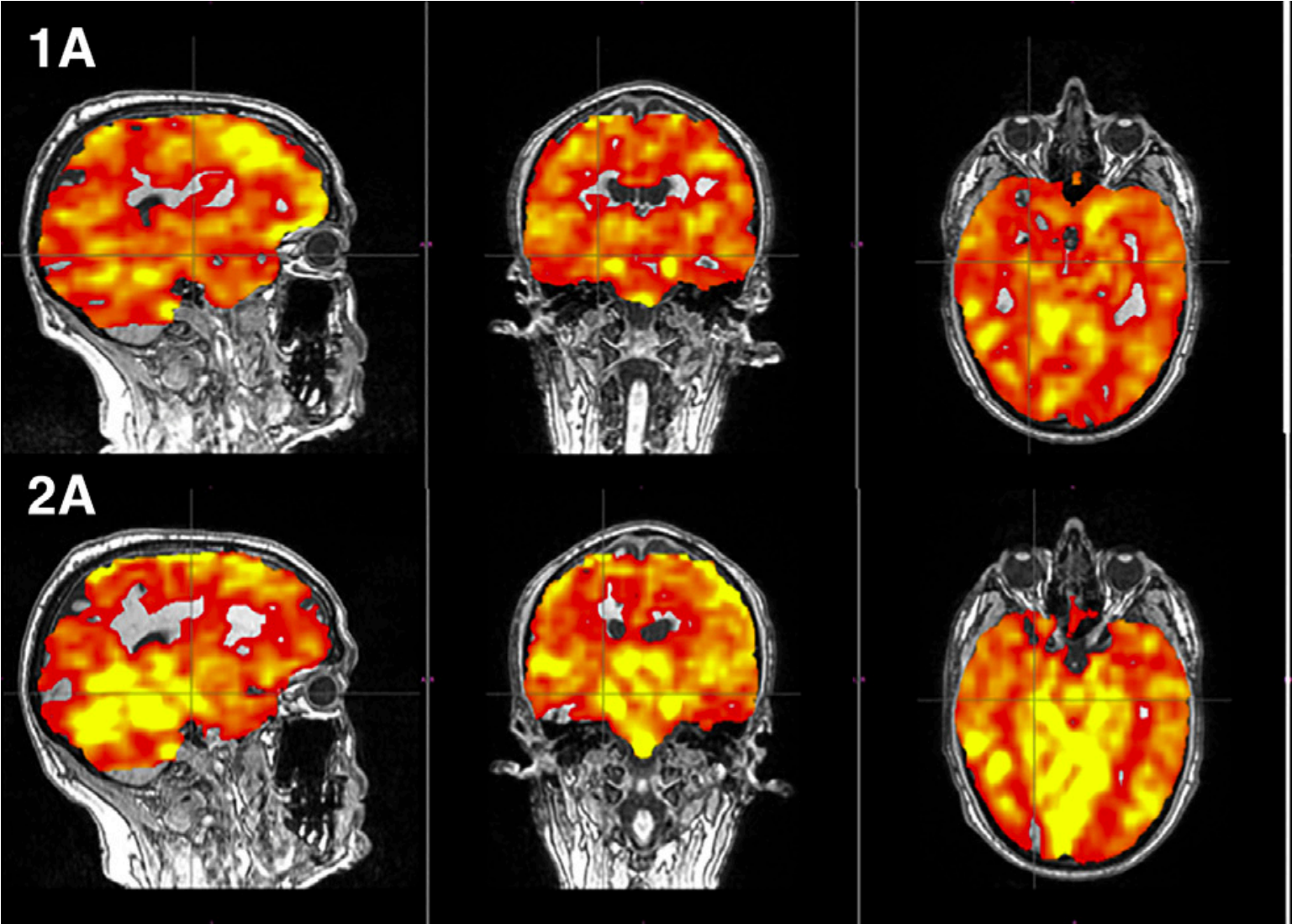
Supportive Data



Supportive Data

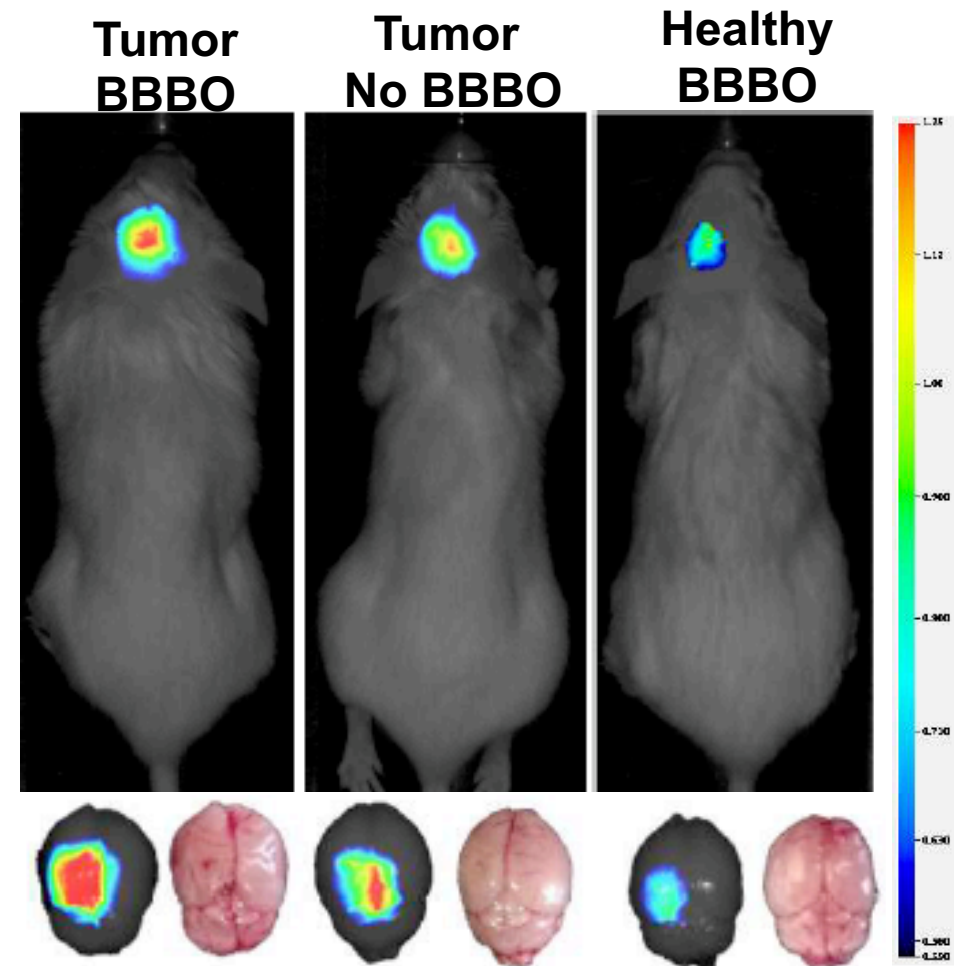


Supportive Data



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