



2019 AAPM Annual Meeting
SAM Ultrasound Symposium
Advances in Image-Guided
Focused Ultrasound Applications
TU-III-303-4

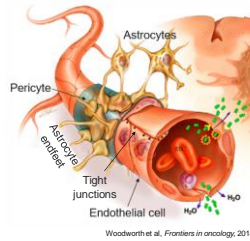
Image-guided focused ultrasound-mediated brain drug delivery

Hong Chen, Ph.D.

Assistant Professor
Department of Biomedical Engineering
Department of Radiation Oncology
Washington University in St. Louis
Email: hongchen@wustl.edu
<http://chemultrasoundlab.wustl.edu/>



Blood-brain barrier (BBB) and brain drug delivery

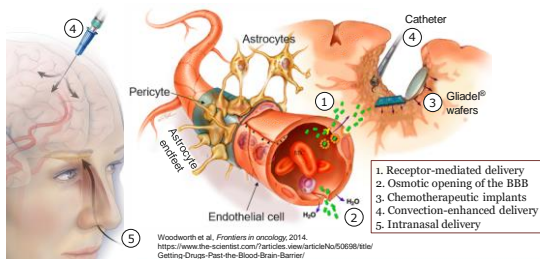


Woodworth et al. *Frontiers in oncology*, 2014.



Department of Biomedical Engineering
Department of Radiation Oncology

Blood-brain barrier (BBB) and brain drug delivery



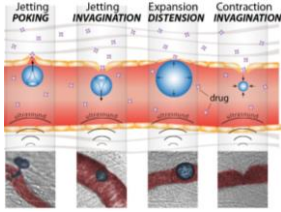
Woodworth et al. *Frontiers in oncology*, 2014.
<https://www.the-scientist.com/?articles.view/articleNo/50698/title/Getting-Drugs-Past-the-Blood-Brain-Barrier>



Department of Biomedical Engineering
Department of Radiation Oncology

Cavitation is the physical mechanism for FUS-BBBD

Ultra-high speed photomicrography (time scale: ns; spatial scale: μm)



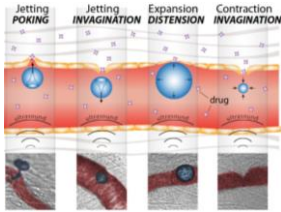
Chen et al. Phys. Rev. Lett. 2011

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology

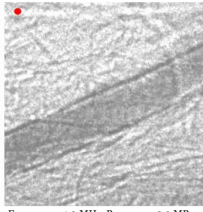
Cavitation is the physical mechanism for FUS-BBBD

Ultra-high speed photomicrography (time scale: ns; spatial scale: μm)



Chen et al. Phys. Rev. Lett. 2011

Washington University in St. Louis

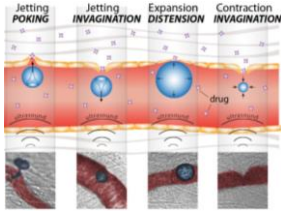


Frequency = 1.0 MHz; Pressure = 0.9 MPa;
Vessel diameter = 20 μm

Department of Biomedical Engineering
Department of Radiation Oncology

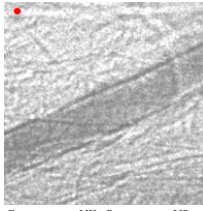
Cavitation is the physical mechanism for FUS-BBBD

Ultra-high speed photomicrography (time scale: ns; spatial scale: μm)



Chen et al. Phys. Rev. Lett. 2011

Washington University in St. Louis

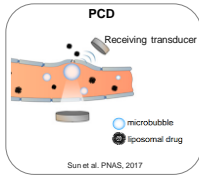


Frequency = 1.0 MHz; Pressure = 0.9 MPa;
Vessel diameter = 20 μm

Department of Biomedical Engineering
Department of Radiation Oncology

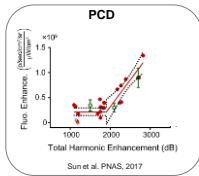
Treatment monitoring by passive cavitation detection

- Passive cavitation detection (PCD) uses a single element ultrasound sensor to monitor cavitation activity during FUS-BBBD.



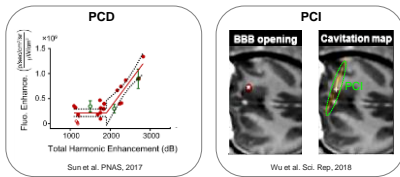
Treatment monitoring by passive cavitation detection

- Passive cavitation detection (PCD) uses a single element ultrasound sensor to monitor cavitation activity during FUS-BBBD.



Treatment monitoring by passive cavitation imaging

- Passive cavitation imaging (PCI) provides spatial maps of cavitation activity during FUS-BBBD.



Treatment monitoring by passive cavitation imaging

Can PCI predict FUS-BBBD drug delivery **location** and **concentration**?

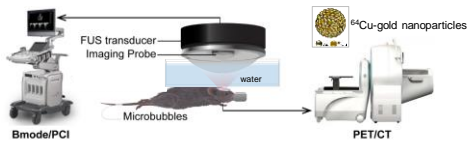
Treatment monitoring by passive cavitation imaging

Can PCI predict FUS-BBBD drug delivery **location** and **concentration**?

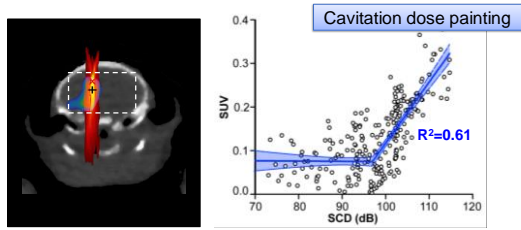
Passive cavitation imaging (PCI)
Spatial distribution of microbubble
cavitation activity



Positron emission tomography (PET)
Spatial distribution of radiolabeled
therapeutic agents



Spatial correlation between PCI and PET

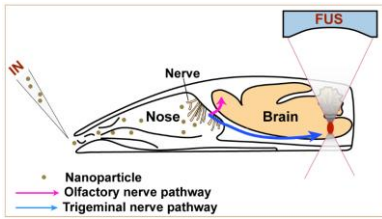


Yang et al. *Sci Rep.* 2019

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology

Focused ultrasound-mediated intranasal delivery (FUSIN)

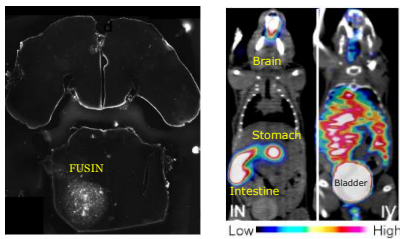


Chen et al. *PLoS One* 2014; Chen et al. *Sci. Rep.* 2016; Ye et al. *J. Control. Release* 2018

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology

FUSIN: Localized brain drug delivery with minimized systemic exposure



Ye et al. *J. Control. Release* 2018

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology

Conclusions

- Focused ultrasound-mediated brain drug delivery techniques provide noninvasive and localized strategies to circumvent the BBB.
- Passive cavitation imaging (PCI) can spatially “paint” the delivered nanoparticle concentration, named as **cavitation dose painting**.
- FUS-enhanced intranasal delivery (FUSIN) is a promising technique for localized brain drug delivery with minimized systemic exposure.

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology

Acknowledgements



NIH: R01MH116981
 NIH: R01EB027223
 NSF: #1727412
 ONR: N00014-19-1-2335

Washington University in St. Louis

Department of Biomedical Engineering
Department of Radiation Oncology