@ rdance MEDICAL

Focused Ultrasound Mediated Blood-Brain Barrier Penetrance to Enable Cell-Free DNA as a Liquid Biopsy in Recurrent Primary Brain Tumors

Bhaskar Ramamurthy¹, Alexandra Miller², Luke Pike², Mallika Keralapura¹, Jack Marshall¹, Marvin Jones¹, Chi-Yin Lee¹, Chandra Karunakaran¹, Jonathan Hofius¹, Alexander Jonsson¹, Cameron Brennan², Thomas Kaley², Ingo Mellinghoff², Ryan Dittamore¹

¹ Cordance Medical, Inc., Mountain View, CA www.cordancemedical.com ² Memorial Sloan Kettering Cancer Center, New York, NY



Objectives

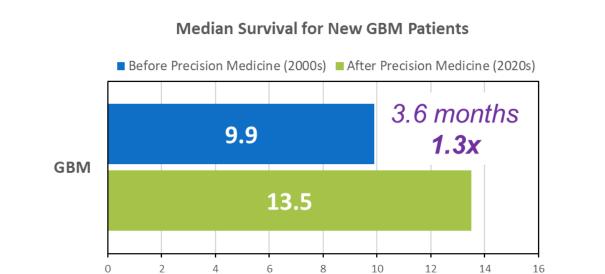
• Develop a Focused Ultrasound (FUS) device to enable precision medicine in brain tumor patients that can 1) guide ultrasound non-invasively to enable brain-wide safe opening of the BBB; 2) Correct for patient specific properties (physical and acoustic); 3) Ensure the device fits within the current workflow of **community practices** for treating cancer; 4) is **compact & portable**.

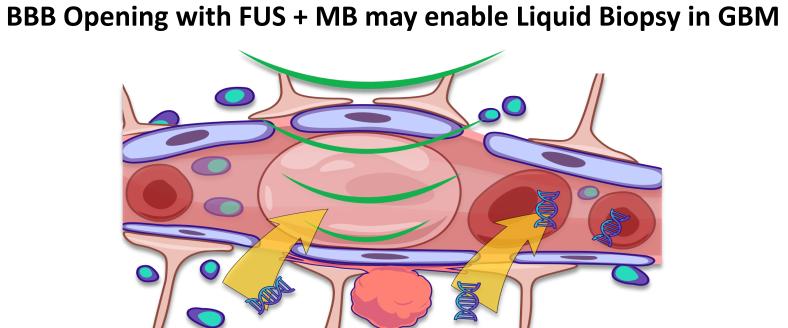
• As a first indication, enable improvements in liquid biopsy detection and analysis to facilitate precision medicine in brain tumor patients.

Background

The BBB Stops Our Most Effective Cancer Tools for GBM Patients Liquid Biopsy



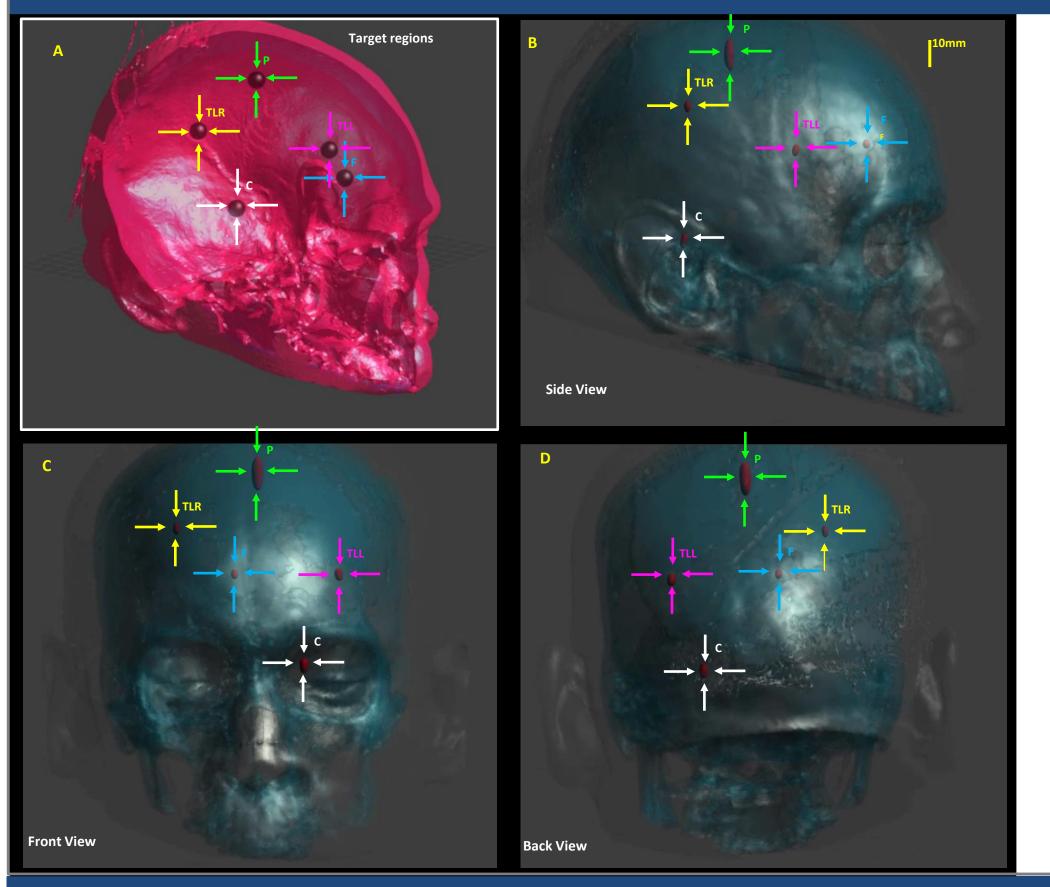




Sonobiopsy= FUS + MB facilitated liquid biopsy

Pacia et al. Theranostics 2021

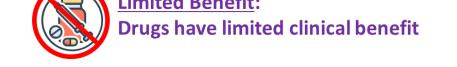
Cordance Guidance Accurately Targets All Regions of the Brain



P: Parietal Lobe Target TLR: Temporal Lobe Right Target TLL: Temporal Lobe Left Target F: Frontal Lobe Target C: Cerebellum Target

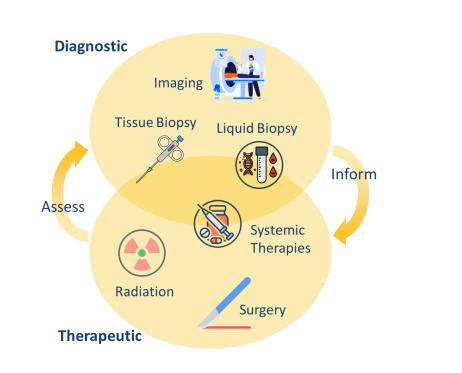
- Targets are defined in Figure A.
- Red ellipsoid shapes in Figures B-D indicate the accuracy and resolution we can achieve with Cordance Guidance Algorithm when compared with the target definitions in Figure A.

• We can reach all major areas of the brain (brain-wide access)



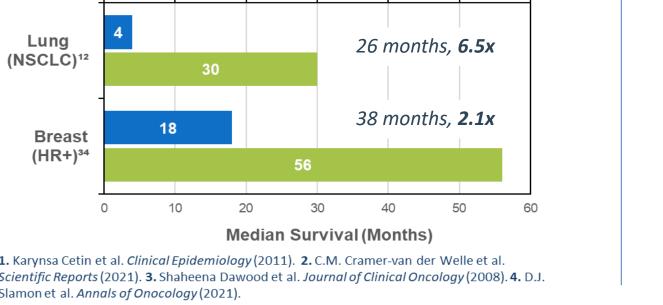
R. Helseth et al. Acta Neurolgoica Scandinavica (2010); Lina Marenco Hellembrand et al. Journal of Neuro-Oncology (2020s

Precision Medicine Has Driven Survival Benefits in non-CNS Solid Tumors



Before Precision Medicine (2000s) After Precision Medicine (2020s)

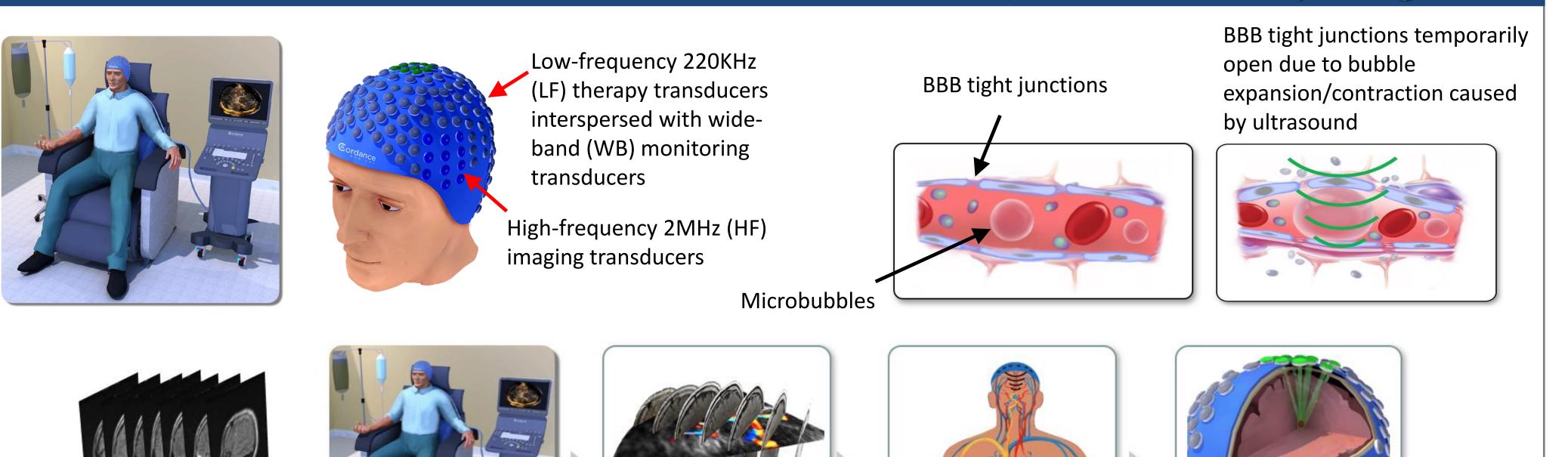
Median Survival for New Metastatic Patients



FUS increases cfDNA & ctDNA in GBM models & human patients

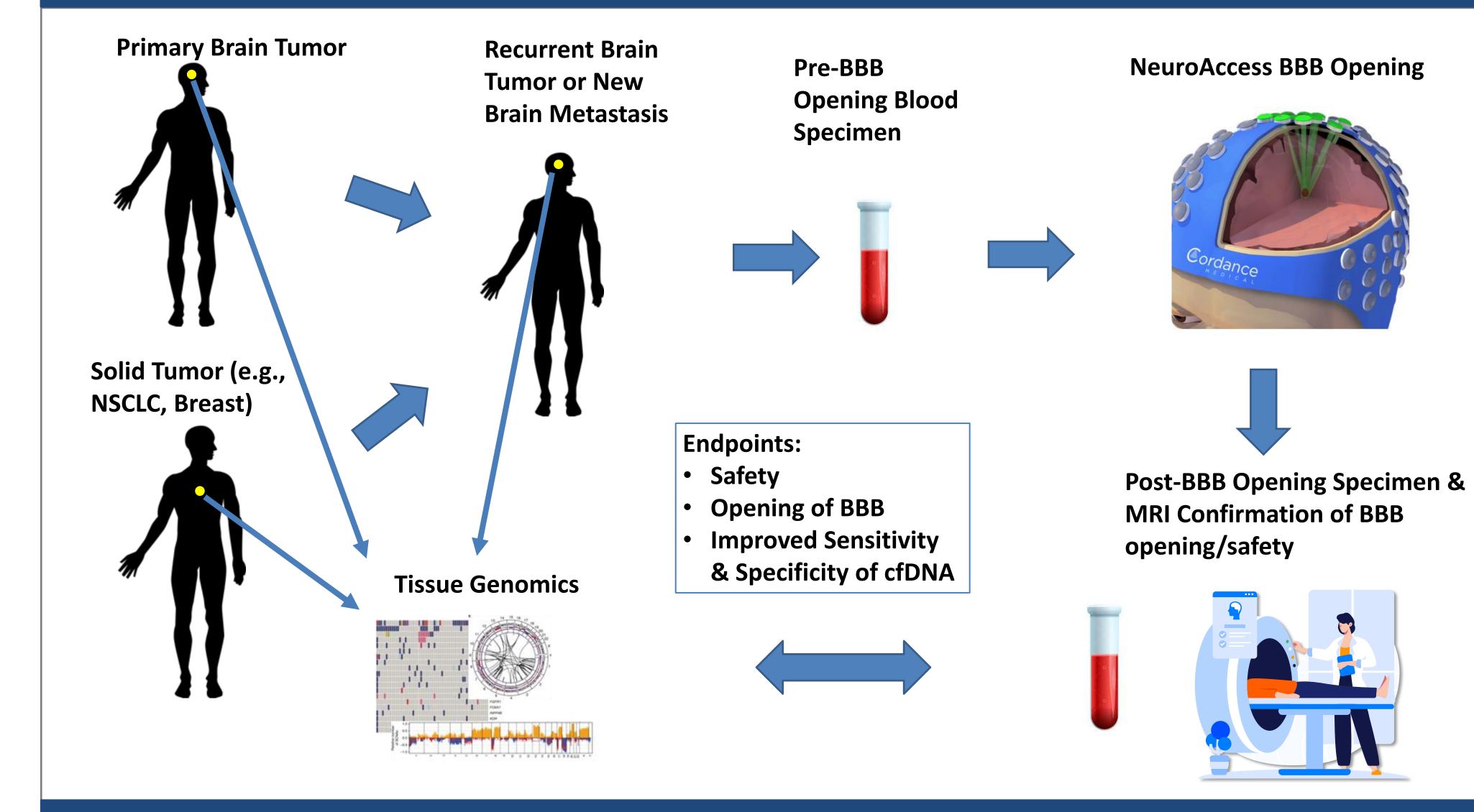
Meng, Ying, et al. Neuro-oncology (2021)

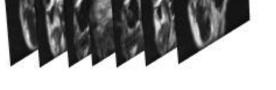
The Cordance NeuroAccess[™] Device: Non-invasive, Painless BBB-Opening



• We can accommodate the physical and acoustic properties of the patient's brain

Clinical Trial Schema to Facilitate Improved Liquid Biopsy Results in Brain Tumor Patients





Us of a diagnostic MR





of target location(s)



administered

BBB opening, enabling liquid biopsy or drug delivery

• The Cordance cap contains three types of transducers:

• Low-frequency (220KHz) for providing therapy (i.e., opening the BBB).

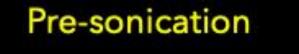
Post-sonication

Patient puts on cap

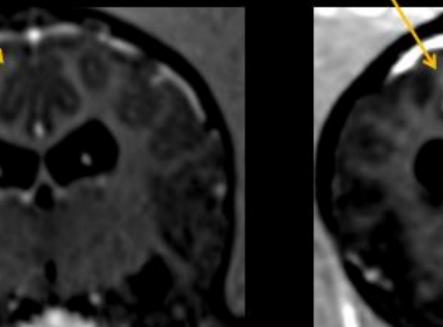
- High-frequency (2MHz) for imaging through the temporal lobe (used for non-invasive alignment with diagnostic MRI).
- Wide-band monitoring transducers.

• Acoustic coupling and conformability to physical shape are provided by a fillable, disposable jacket between the cap and head.

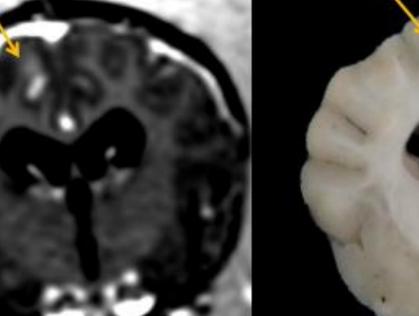
Pre-Clinical Opening of the BBB in a Large Animal



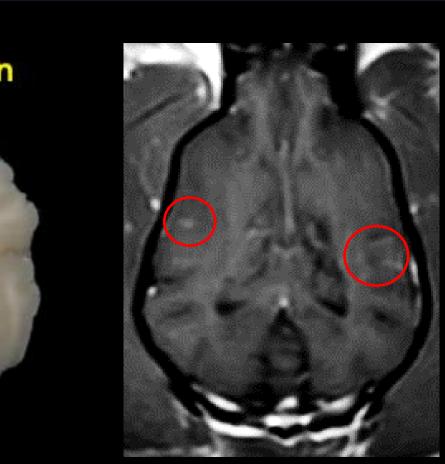
Brain section post sonication



Reference



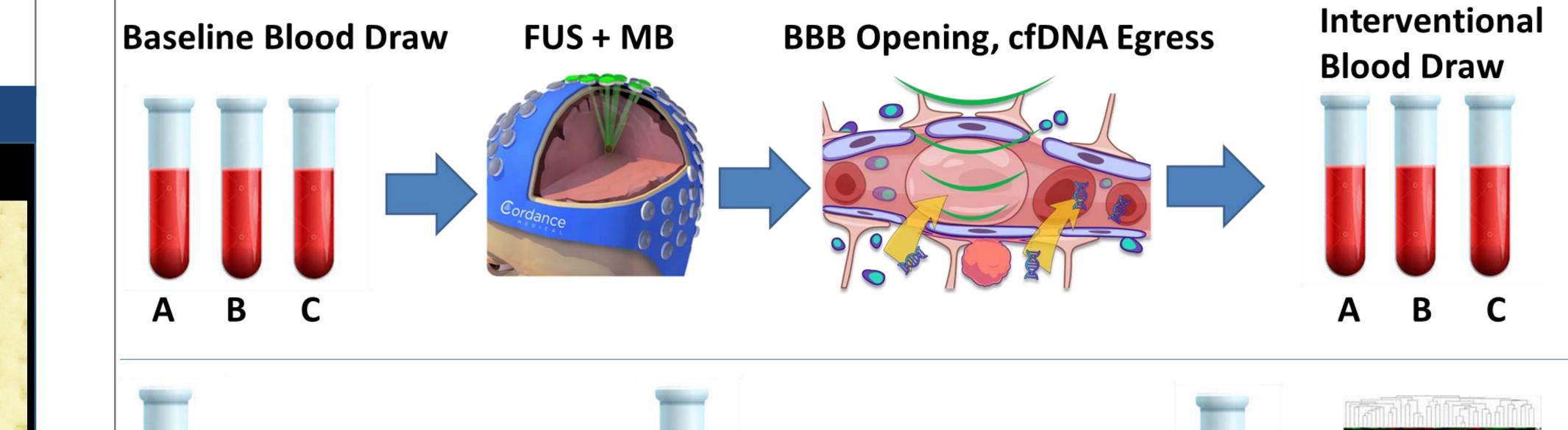
Gadolinium diffusion through open BBB



Post-sonication MR Evans Blue Stain

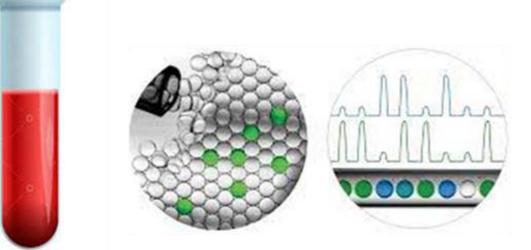
Impact of Cordance Guidance in Improving Accuracy

Process for Analysis of Blood Specimens

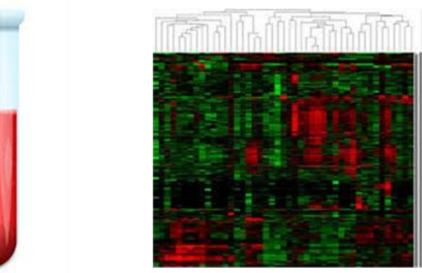




A Oncology NGS Panel



B Tumor informed ddPCR

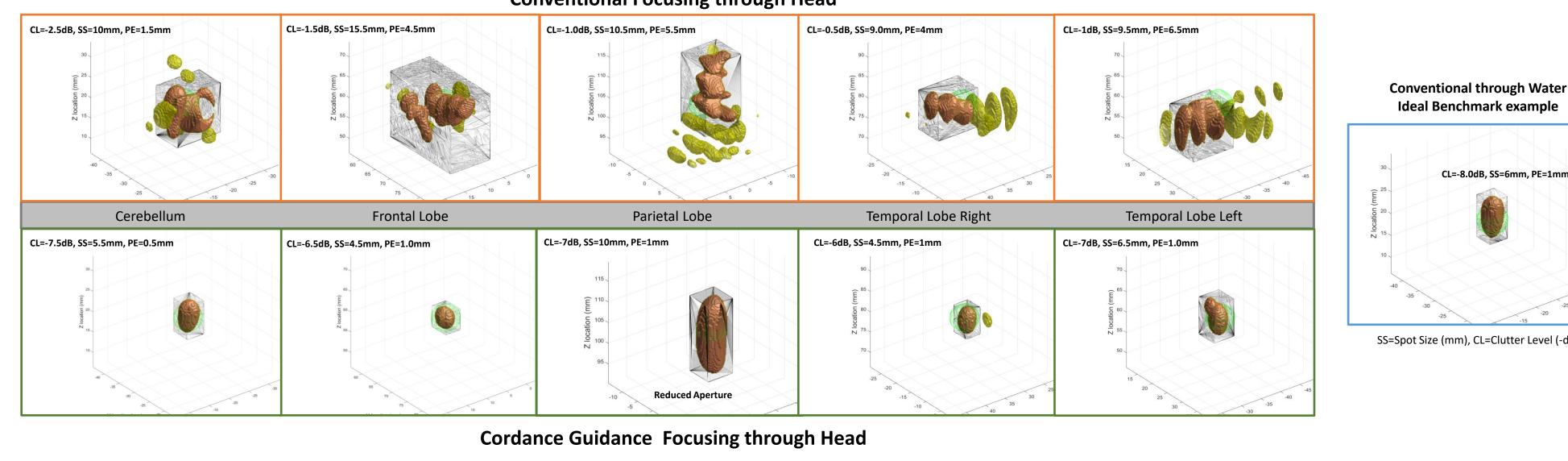


C Whole Transcriptome NGS

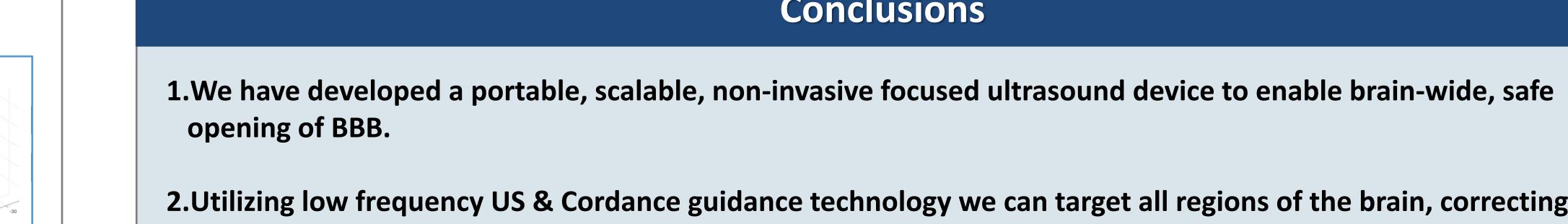
Evans Blue

open BBB

diffusion through



Conventional Focusing through Head



SS=Spot Size (mm), CL=Clutter Level (-dB)

2.Utilizing low frequency US & Cordance guidance technology we can target all regions of the brain, correcting for variance in physical and acoustic properties.

Conclusions

3.Designed a clinical trial schema to evaluate the safety and efficacy of the Cordance Device for improving liquid biopsy results in primary brain and brain metastatic cancer patients.