

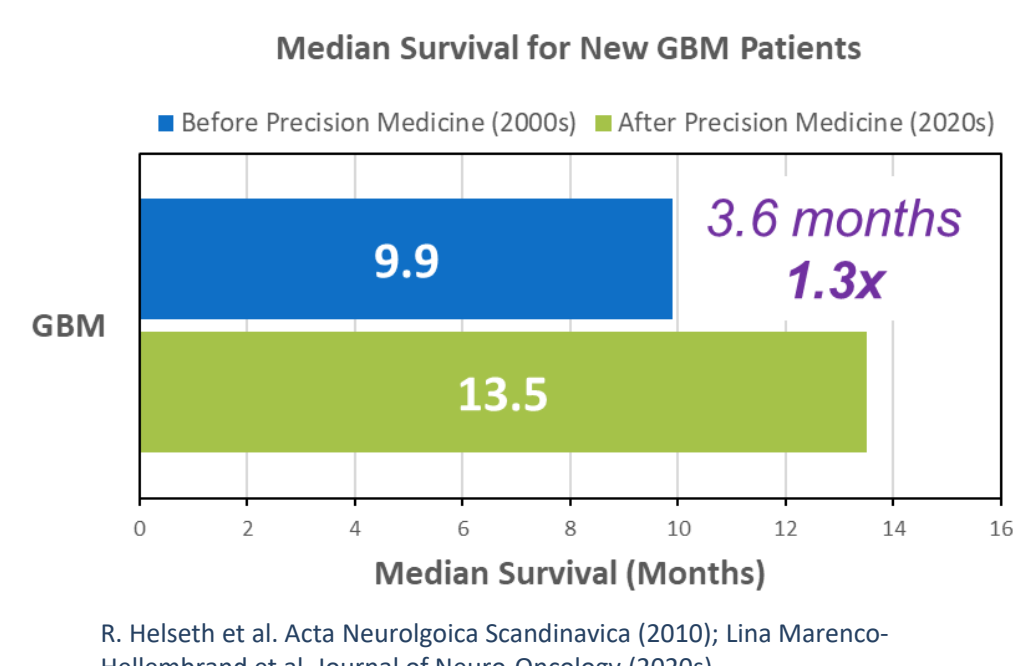
Objectives

- 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.

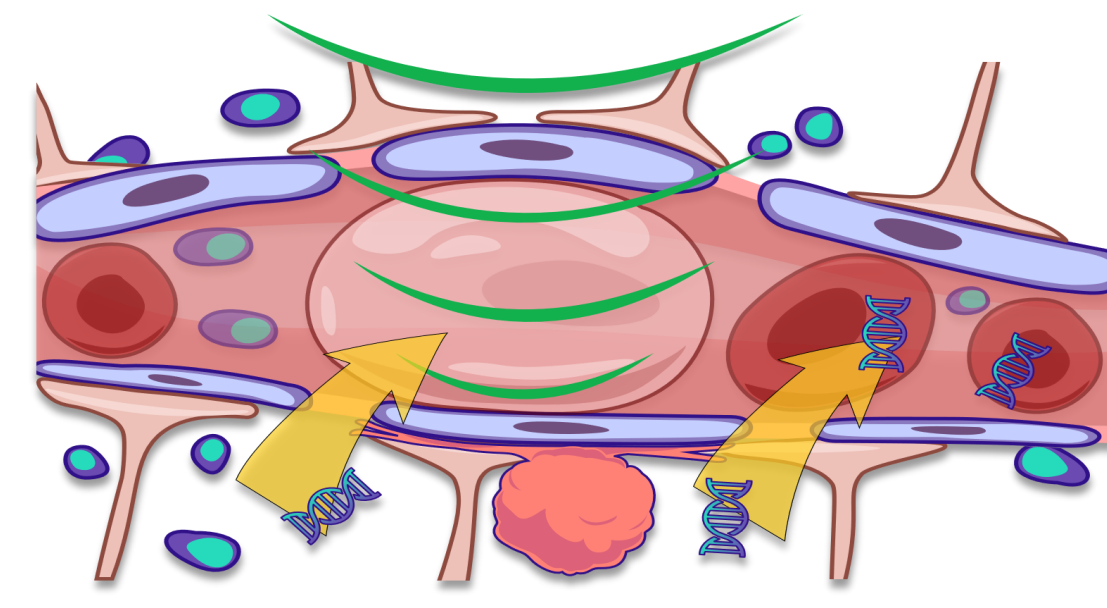
Background

The BBB Stops Our Most Effective Cancer Tools for GBM Patients

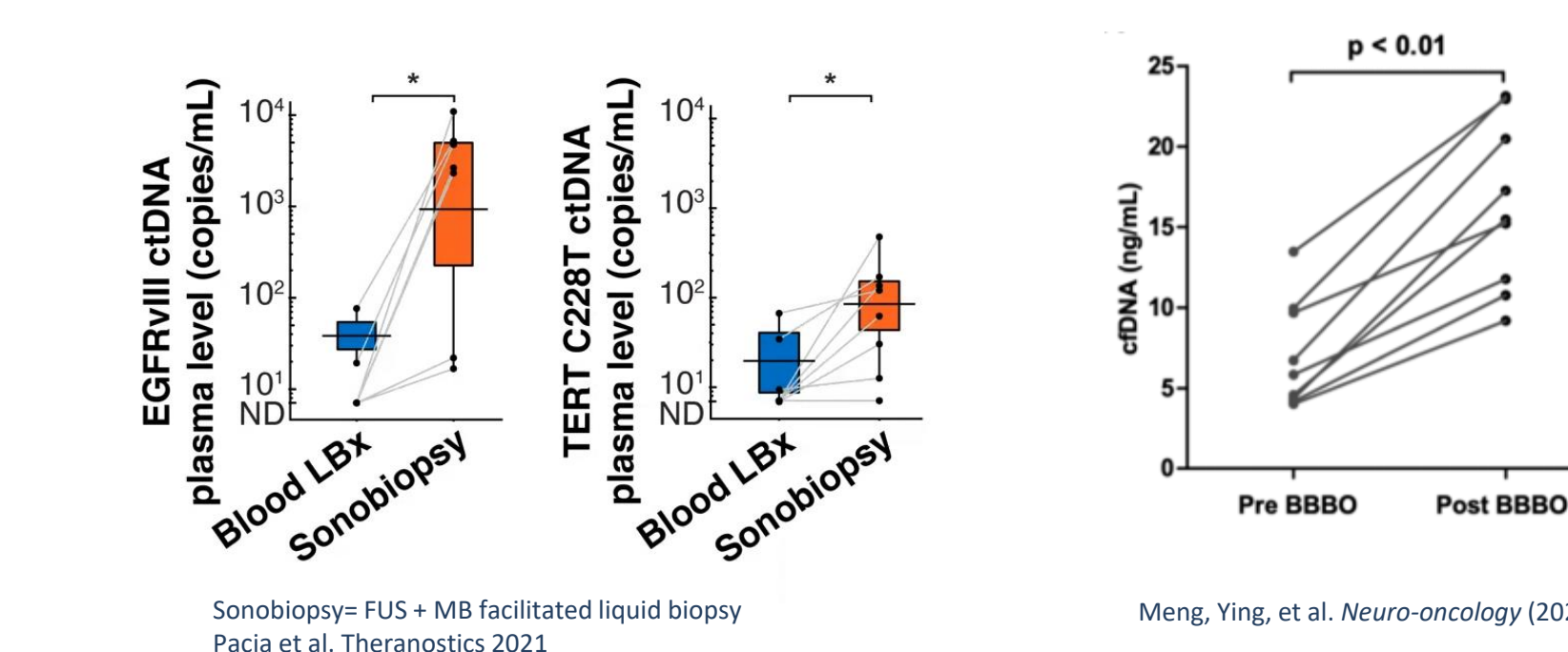
- Liquid Biopsy**
Not Used:
Too little DNA in peripheral blood
- Tissue Biopsy**
Rarely Used & Highly Variable:
High side-effect profile limits utility & access
- Systemic Therapies**
Limited Benefit:
Drugs have limited clinical benefit



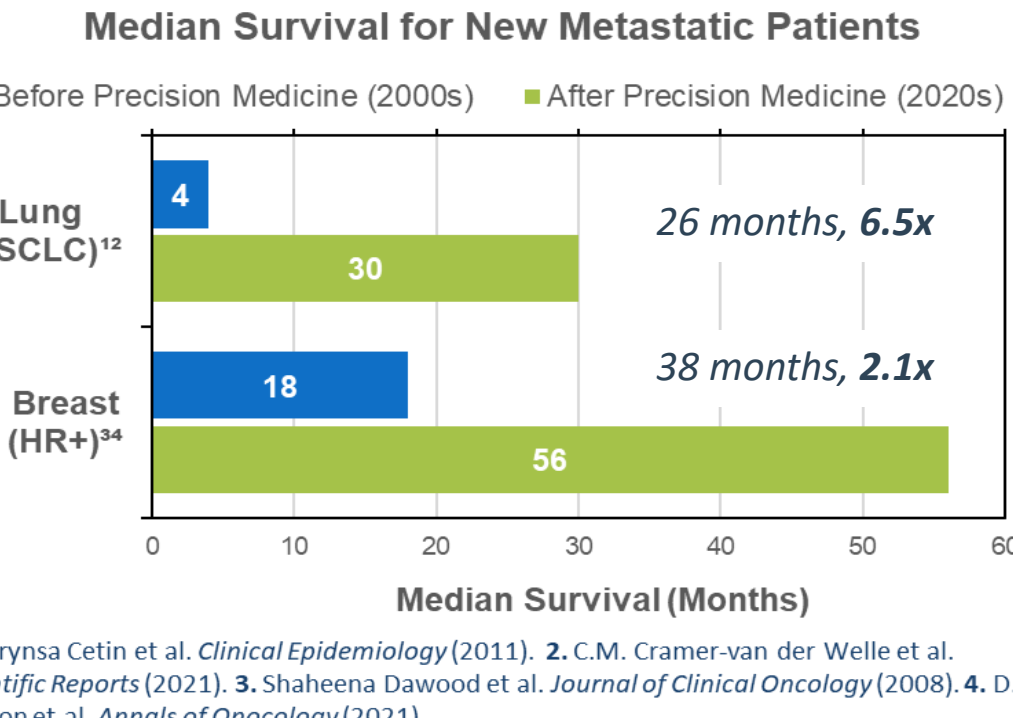
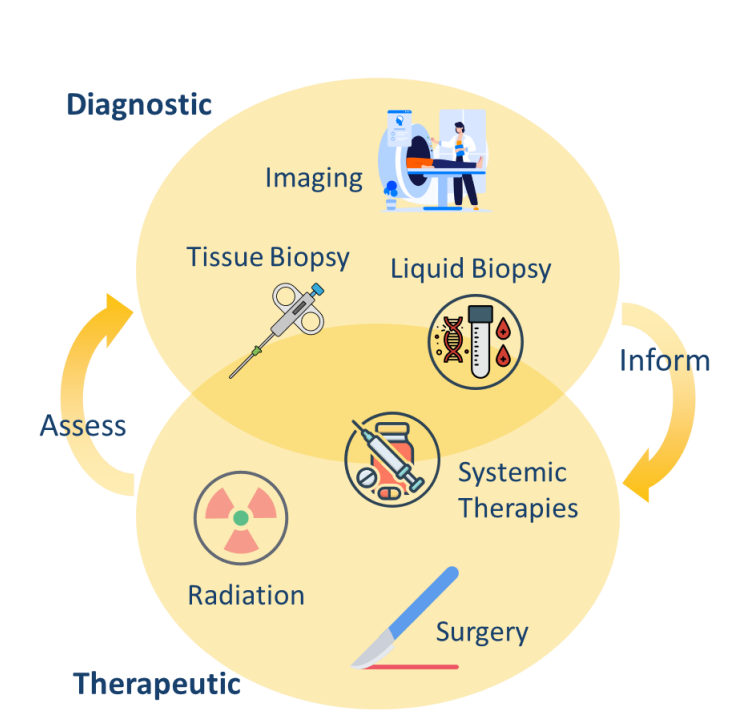
BBB Opening with FUS + MB may enable Liquid Biopsy in GBM



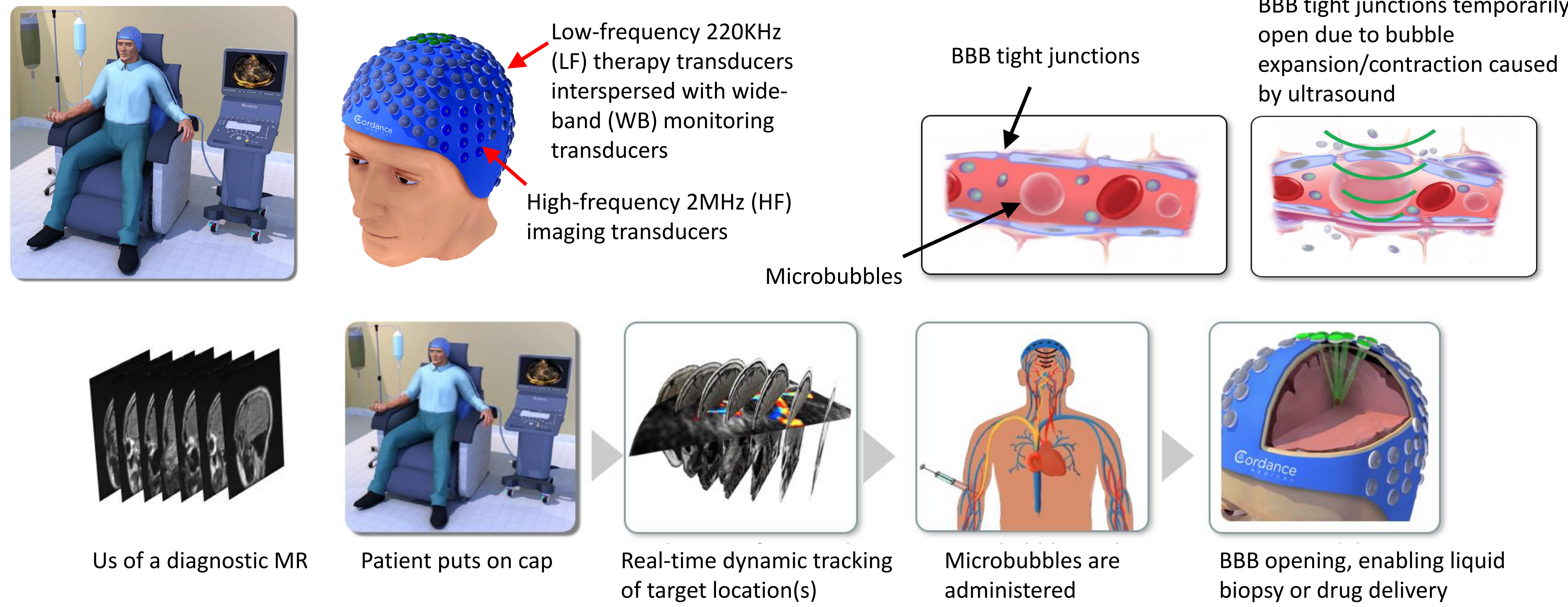
FUS increases cfDNA & ctDNA in GBM models & human patients



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

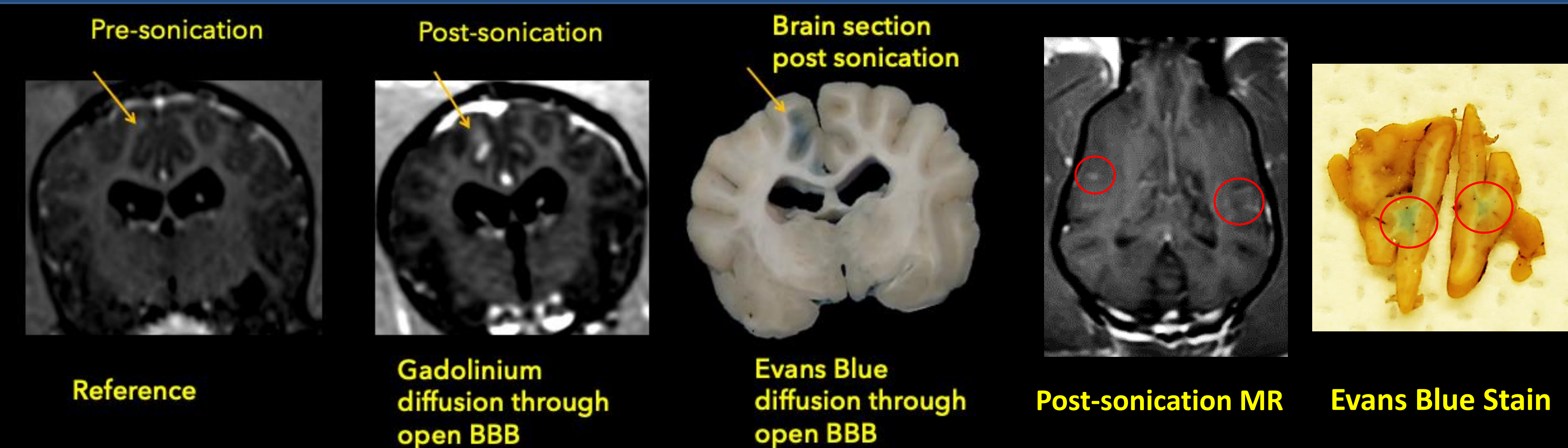


The Cordance NeuroAccess™ Device: Non-invasive, Painless BBB-Opening

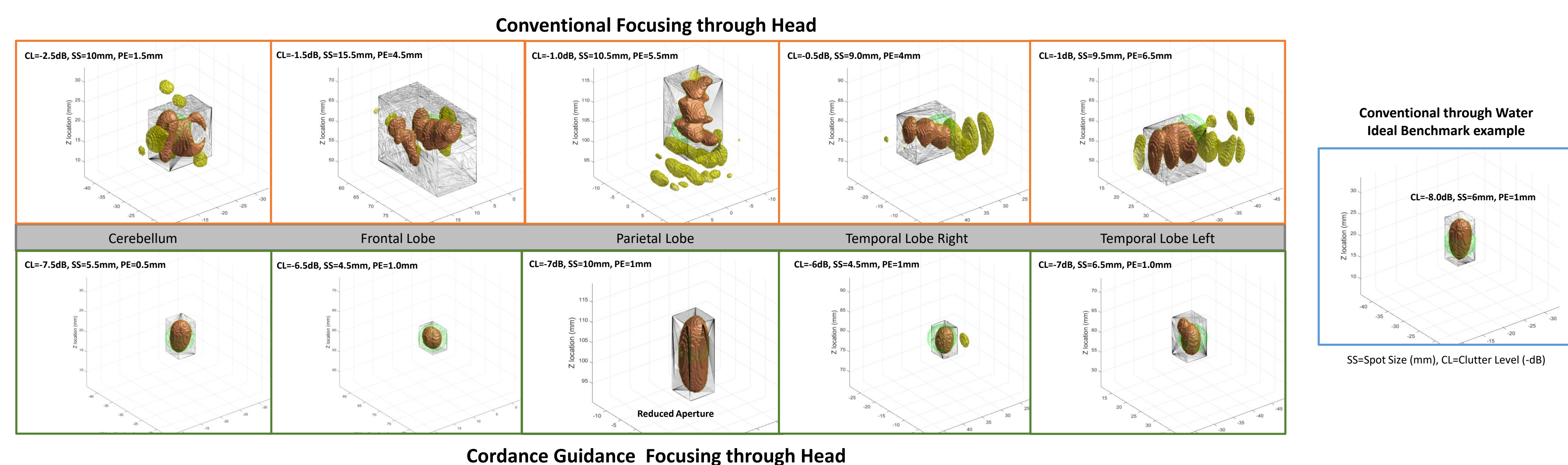


- The Cordance cap contains three types of transducers:
 - Low-frequency (220KHz) for providing therapy (i.e., opening the BBB).
 - High-frequency (2MHz) for imaging through the temporal lobe (used for non-invasive alignment with diagnostic MRI).
 - Wide-band monitoring transducers.
- Acoustic coupling and conformability to physical shape are provided by a fillable, disposable jacket between the cap and head.

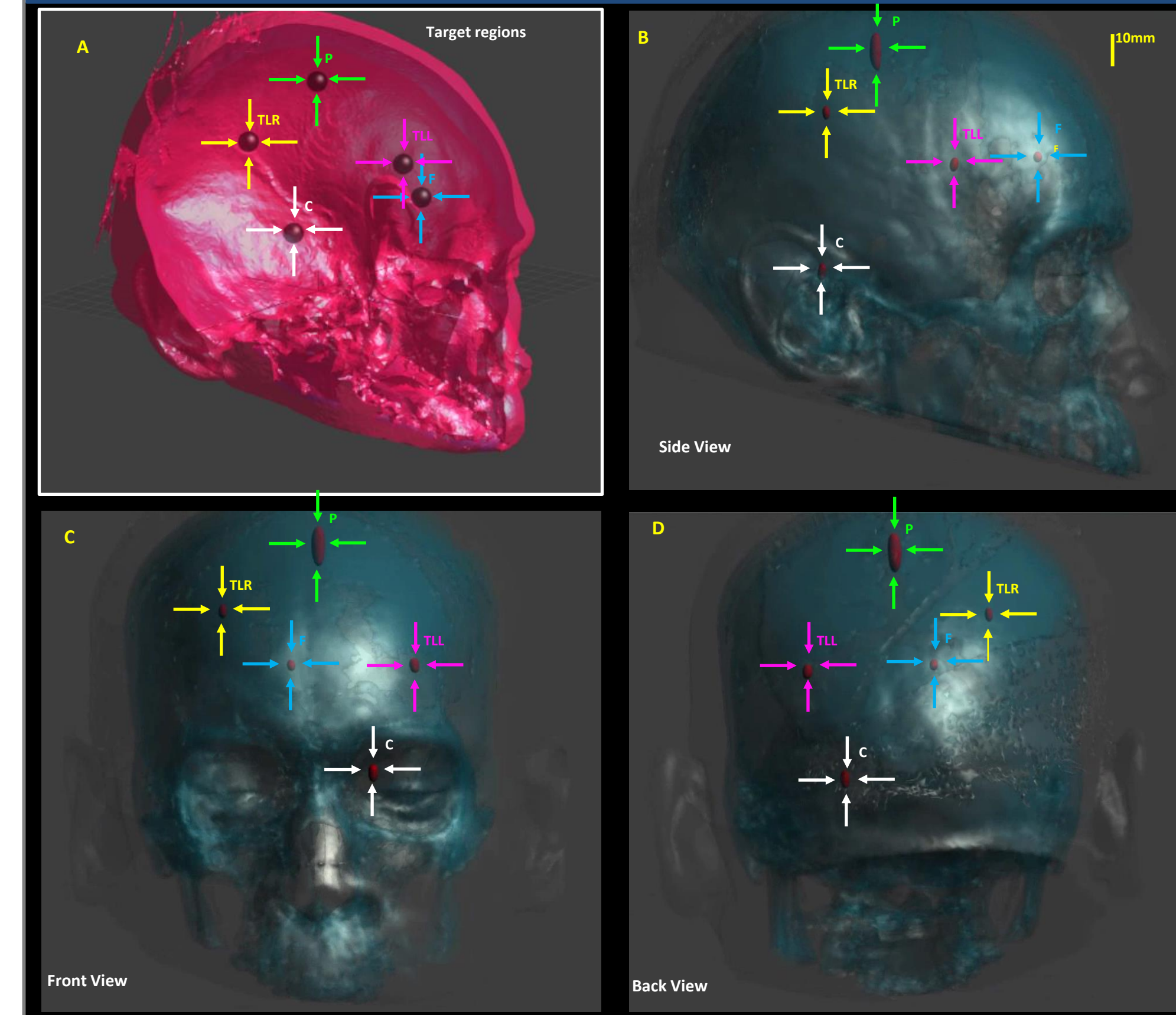
Pre-Clinical Opening of the BBB in a Large Animal



Impact of Cordance Guidance in Improving Accuracy



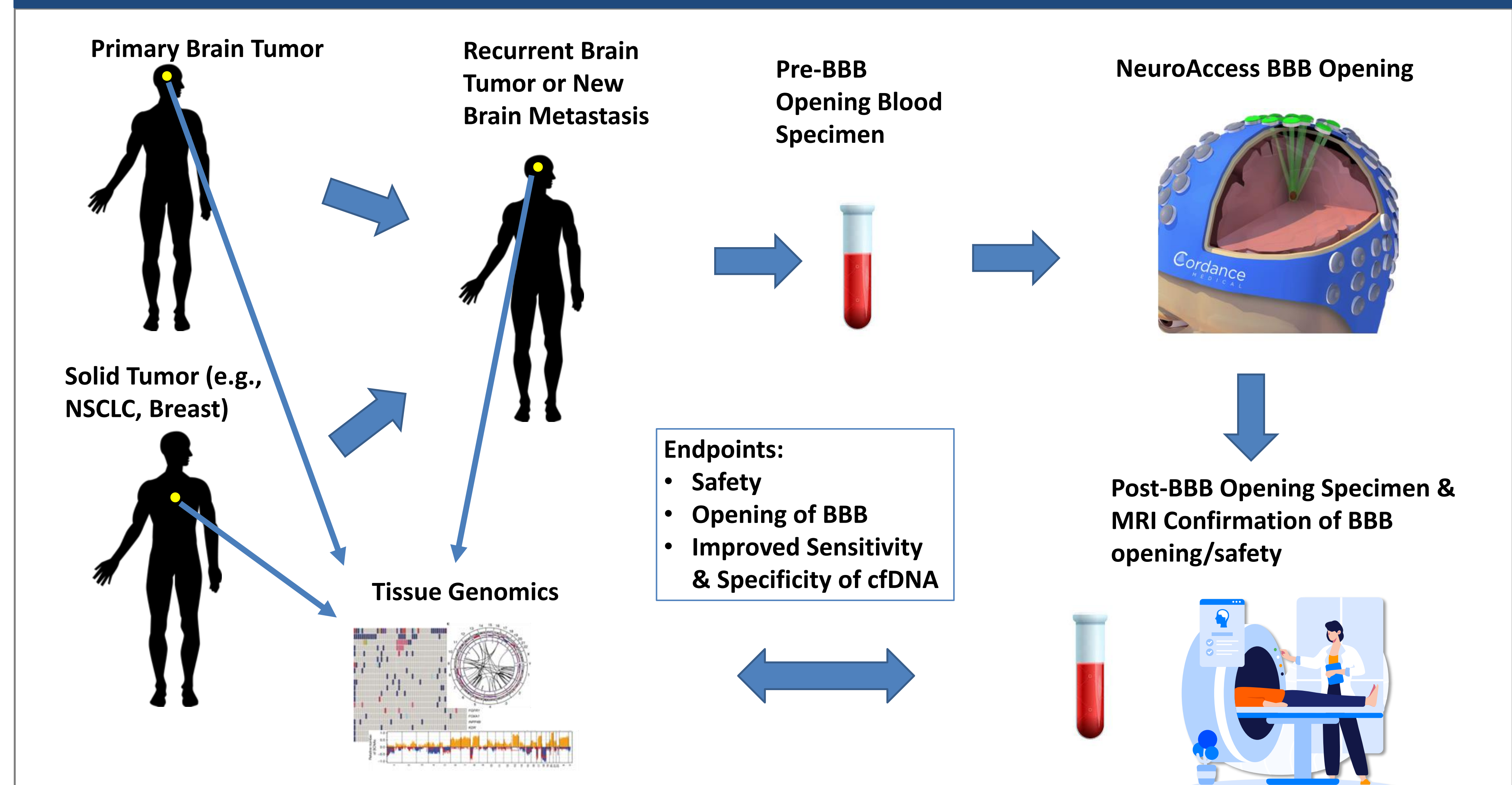
Cordance Guidance Accurately Targets All Regions of the Brain



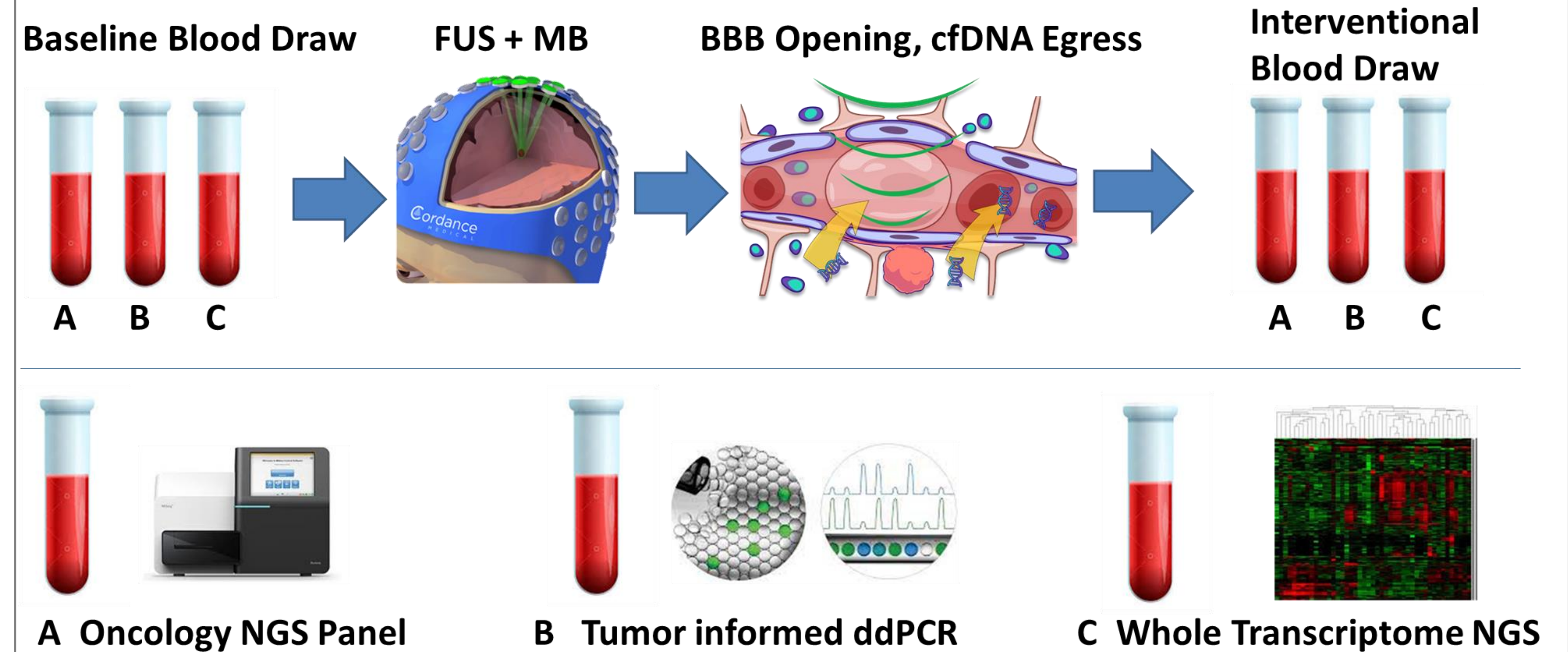
P: Parietal Lobe Target
TLR: Temporal Lobe Right Target
TLL: Temporal Lobe Left Target
F: Frontal Lobe Target
C: Cerebellum Target

- 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)
- 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



Process for Analysis of Blood Specimens



Conclusions

- We have developed a portable, scalable, non-invasive focused ultrasound device to enable brain-wide, safe opening of BBB.
- Utilizing low frequency US & Cordance guidance technology we can target all regions of the brain, correcting for variance in physical and acoustic properties.
- 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.