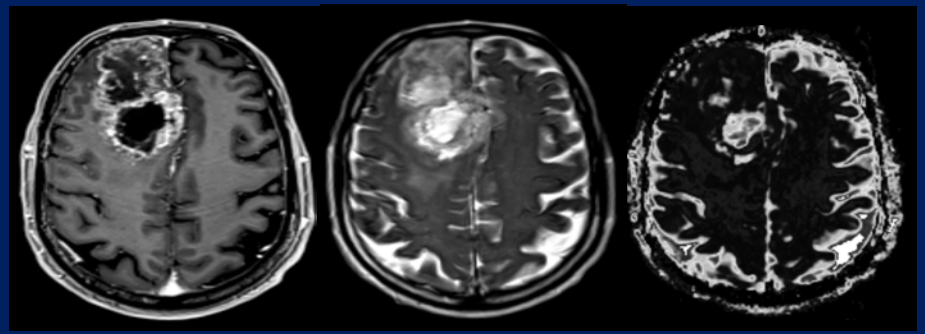
Advances in whole brain sMRI to improve glioma imaging

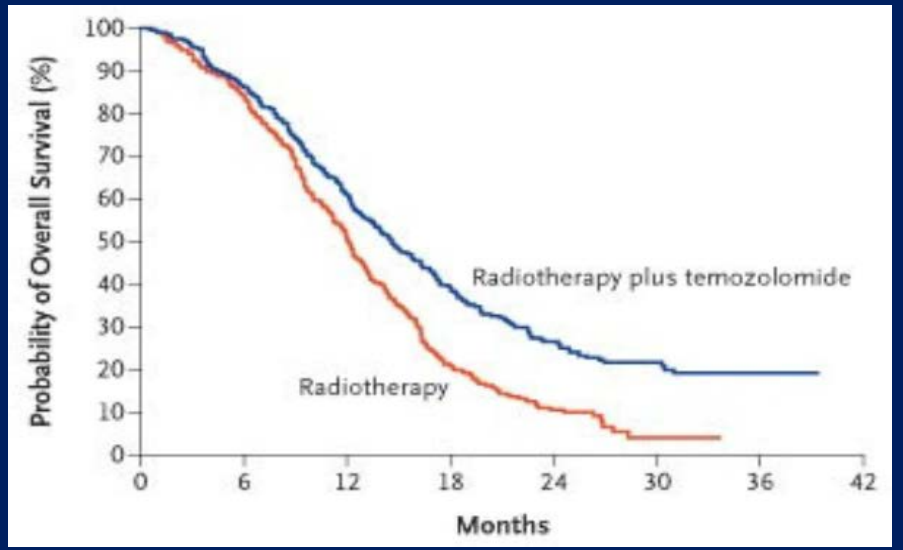
https://brainimaging.emory.edu/

Glioblastoma (GBM)

- Most common malignant primary brain tumor in adults
  - Highly infiltrative
  - Treated w/max resection + RT/TMZ
  - Median survival is 14-16 months



T1 T2 DWI

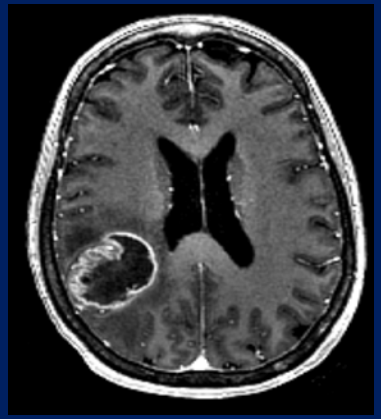


Stupp et al., NEJM 352:1987-92 (2005)

Limitations of Anatomical MRI for Gliomas

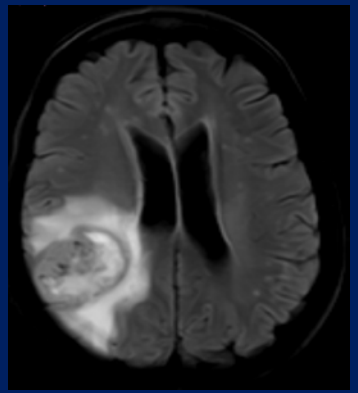
- Overlap in appearance between neoplastic and non-neoplastic lesions
- Overlap in appearance between different grades
- Infiltration beyond regions of contrast enhancement
- Difficult to distinguish edema from infiltrating tumor
- Not reliable to determine tumor progression
- Qualitative → limitations for treatment monitoring.

CE-T1



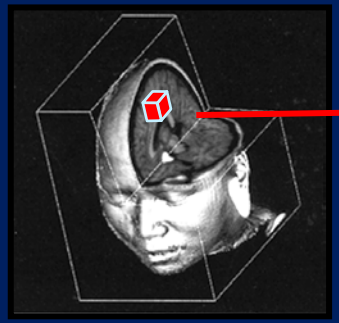
T1 Enhancement ≈ Leaky BBB & neovasculature

T2/FLAIR

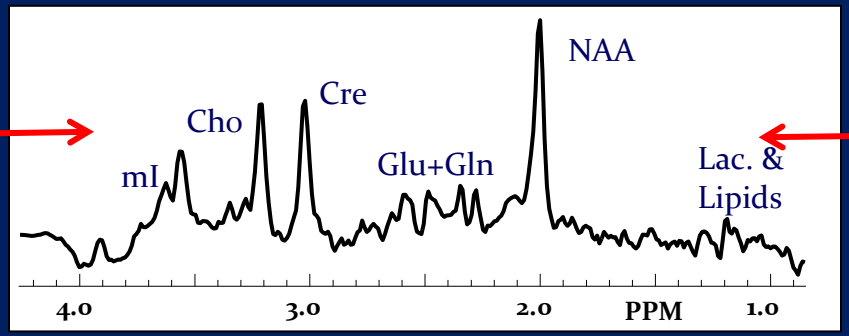


T2 Hyperintensity ≈ tumor, edema, ischemia, etc.

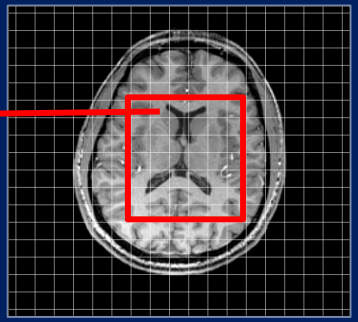
^{1}H MR Spectroscopy of the Brain



Single Voxel Spectroscopy



Non-invasive chemical analysis of tissue

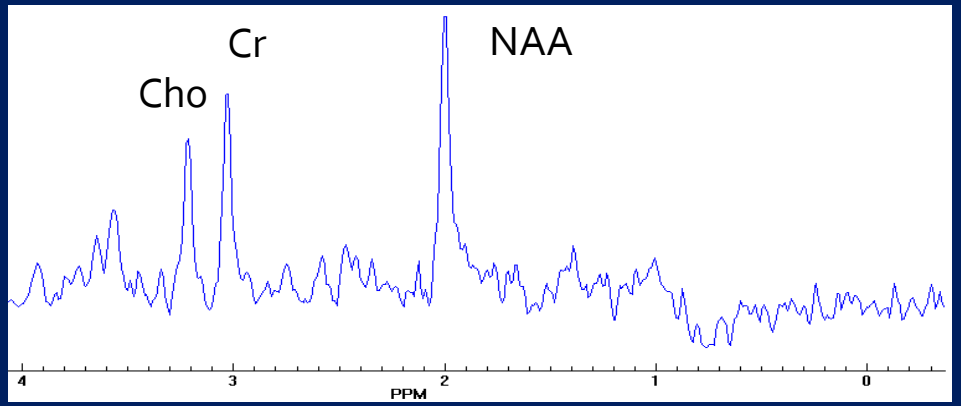


2D Spectroscopic Imaging (MRSI)

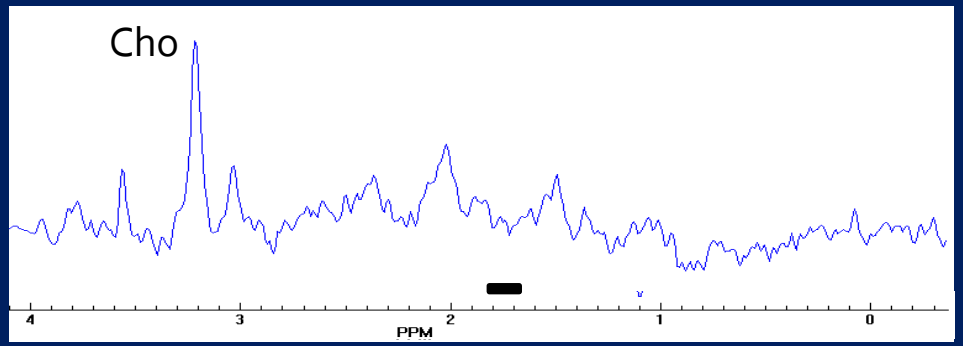
- **N-Acetylaspartate: (NAA) N**euronal Integrity
- **Creatines: (Cre)** Cellular Energetics
- **Cholines: (Cho)** membrane synthesis & degradation
- **Glutamate/ Glutamine (Glu/Gln):** Neurotransmitters
- **Lactate (Lac):** hypoxia
- **Mobile lipids:** Necrosis
- **GABA, Alanine, Aspartate, 2HG, glycine**
- **myo-Inositol: (mI)** Glial marker

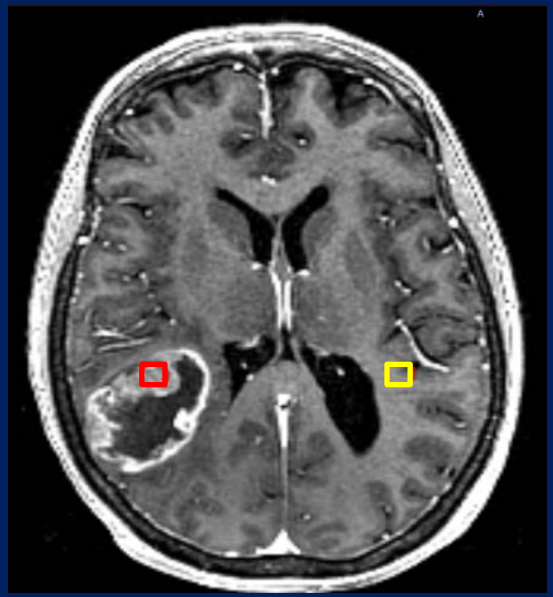
MR Spectroscopy of Brain Tumor

Normal



Tumor





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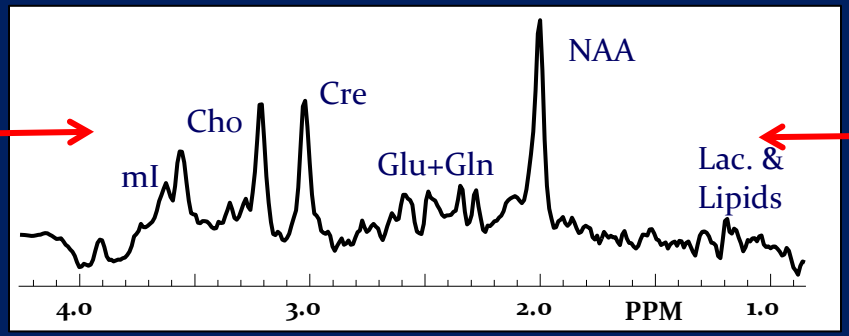

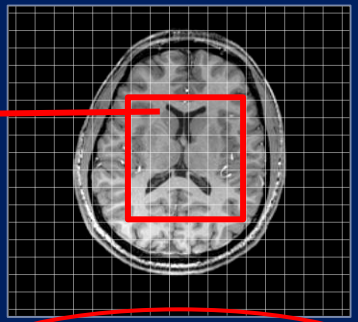

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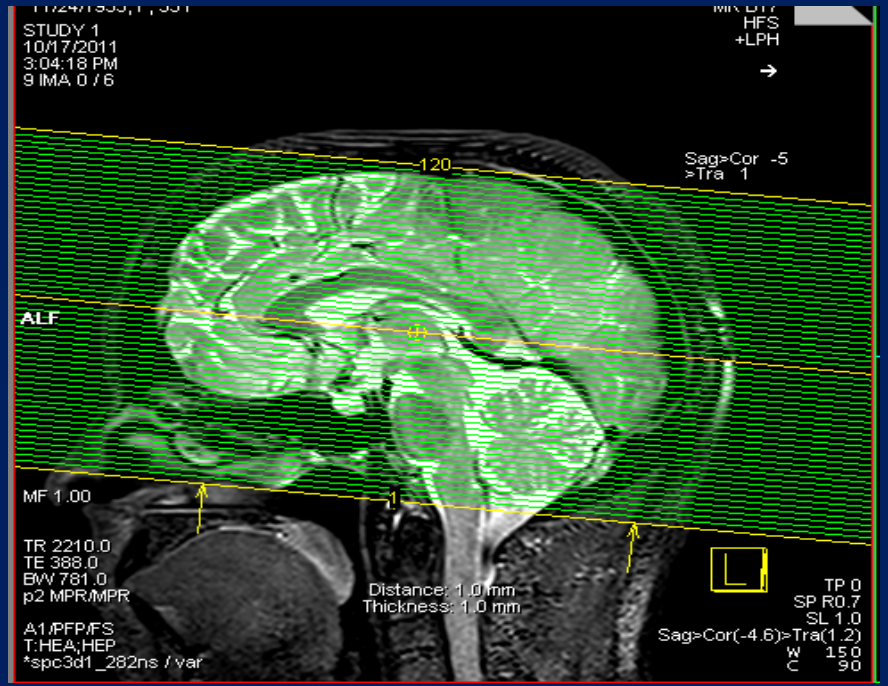
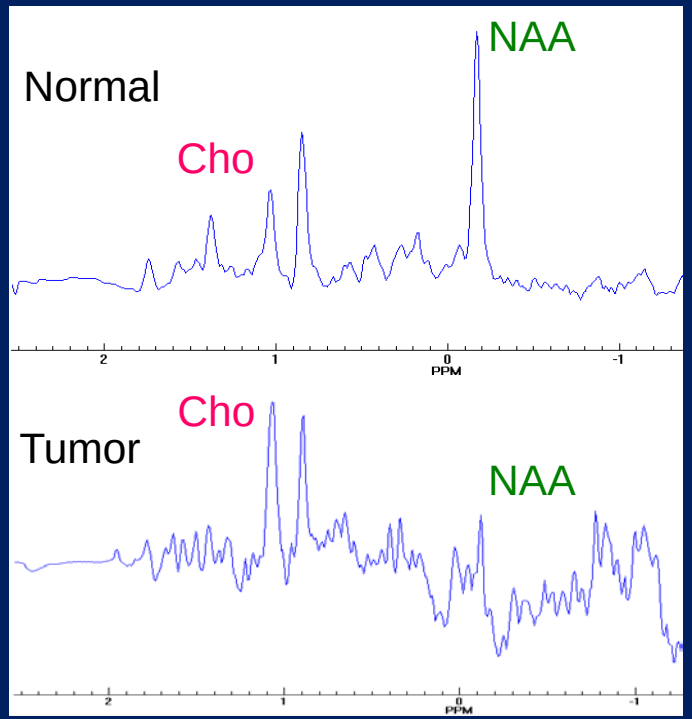
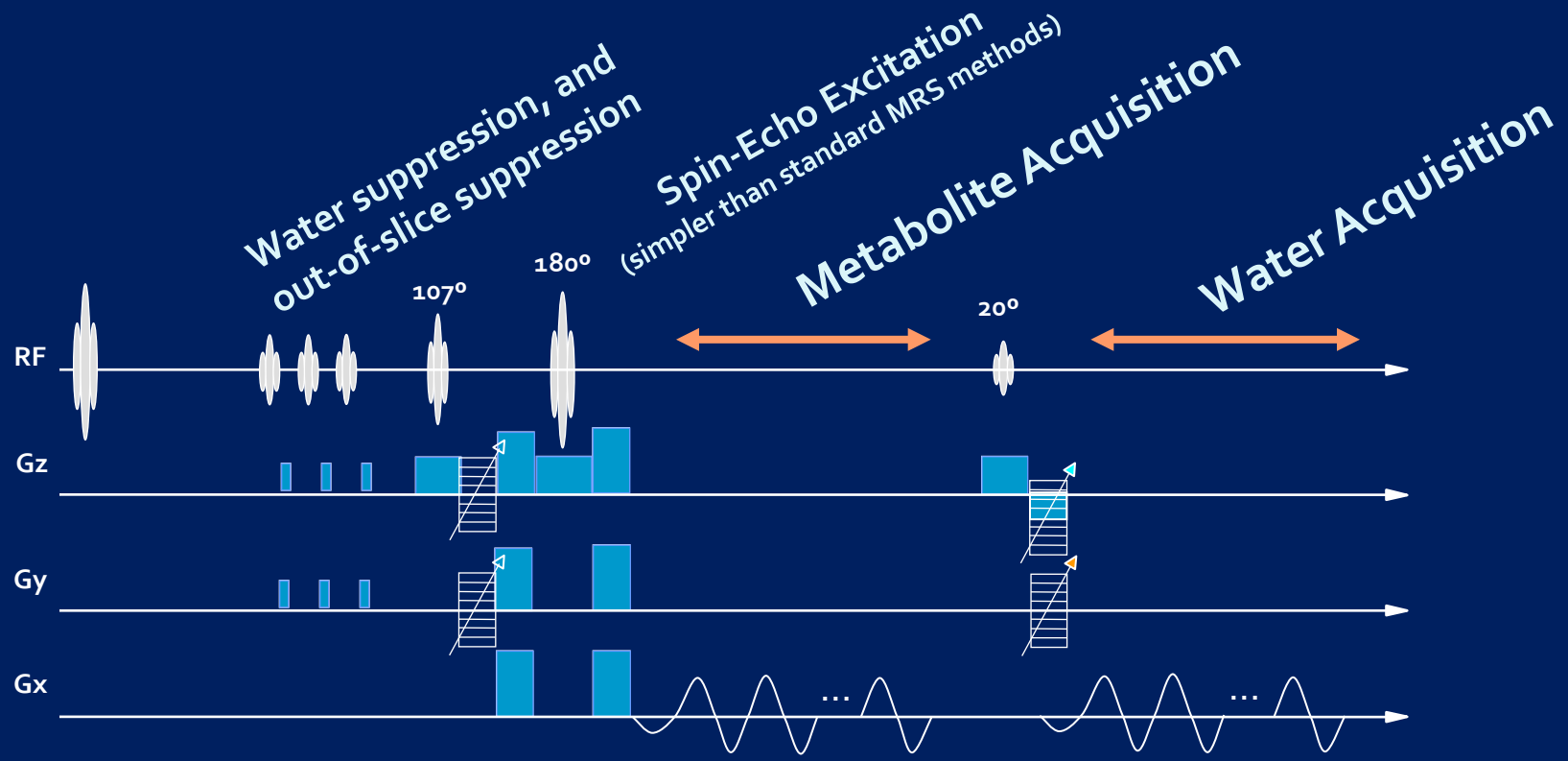
Current clinical implementations

Whole Brain 3D MRSI @ 0.1cc (spectroscopic MRI, sMRI)

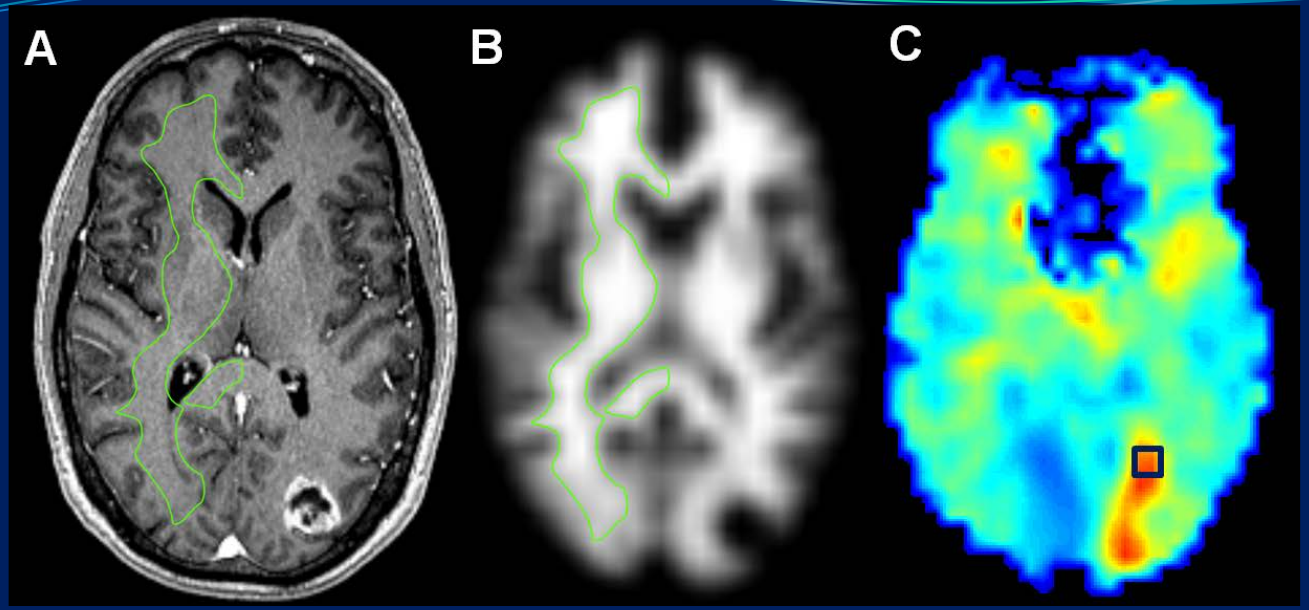




Echo-Planar SI (EPSI) with Interleaved Water Reference



A. Ebel, A.A. Maudsley. Magn. Reson. Med. 53:465, 2005



T1w-CE with NAWM Contour

White Matter Map with NAWM Contour

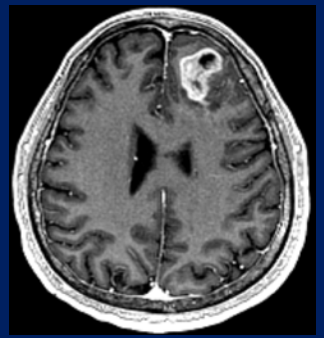
AI_{CHO} Map with ROI

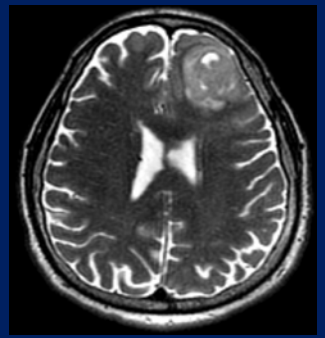
$$AI_{metab}^{linear} = \frac{S_{metab}^{voxel}}{mean_{metab}^{NAWM}}$$

Cordova et al. 2016

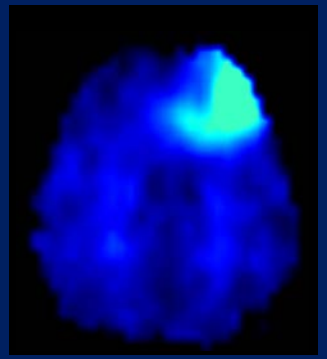
sMRI: Tracerless Metabolic Imaging

T1w-CE

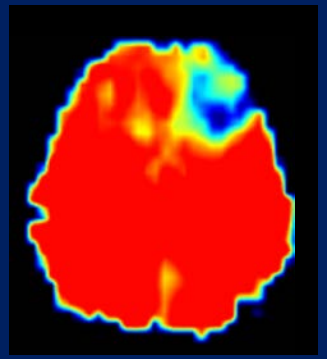




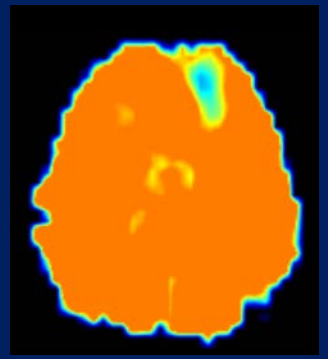
T2w



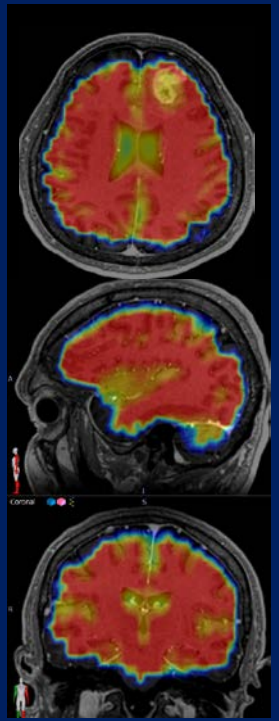
Choline



NAA

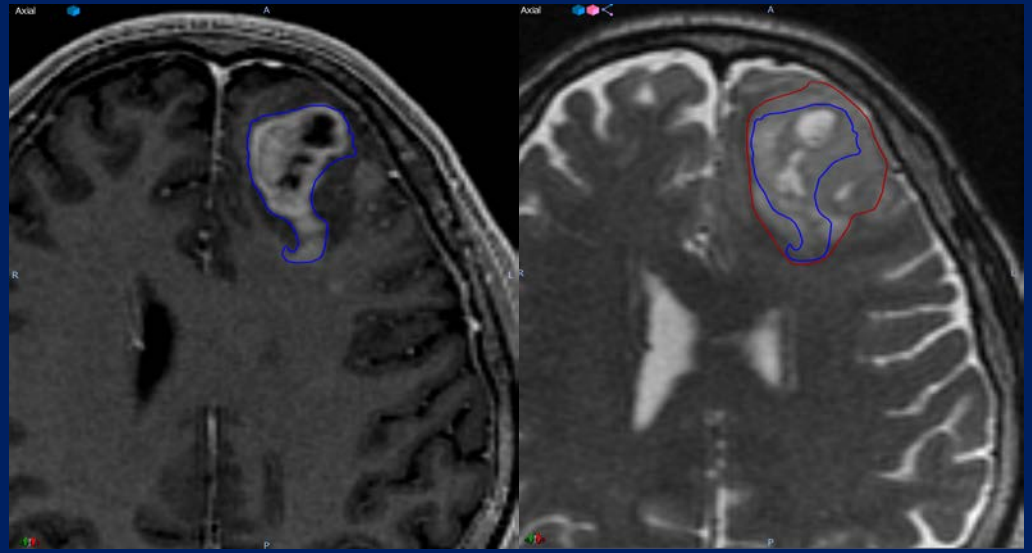


Creatine



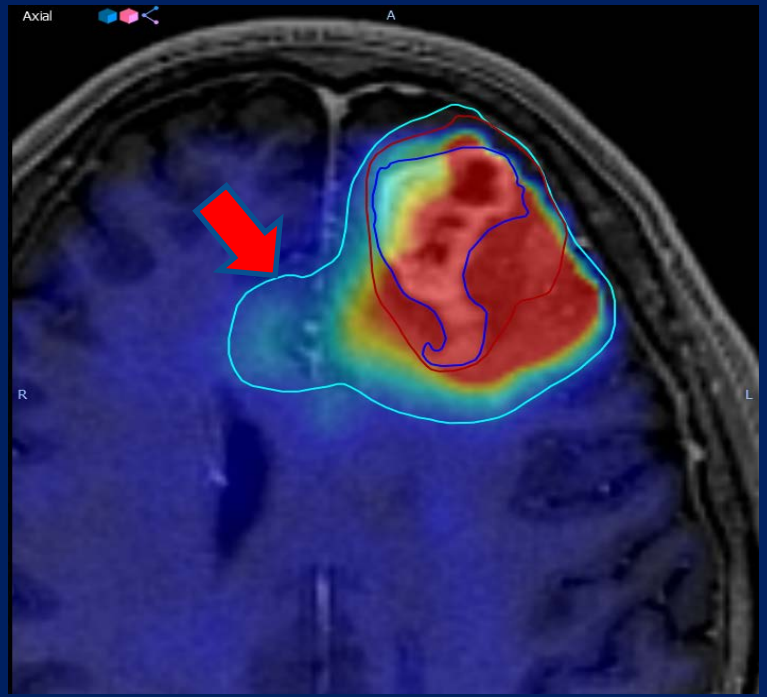
Internal Water

Whole Brain sMRI



Contrast-enhanced T1w-MRI

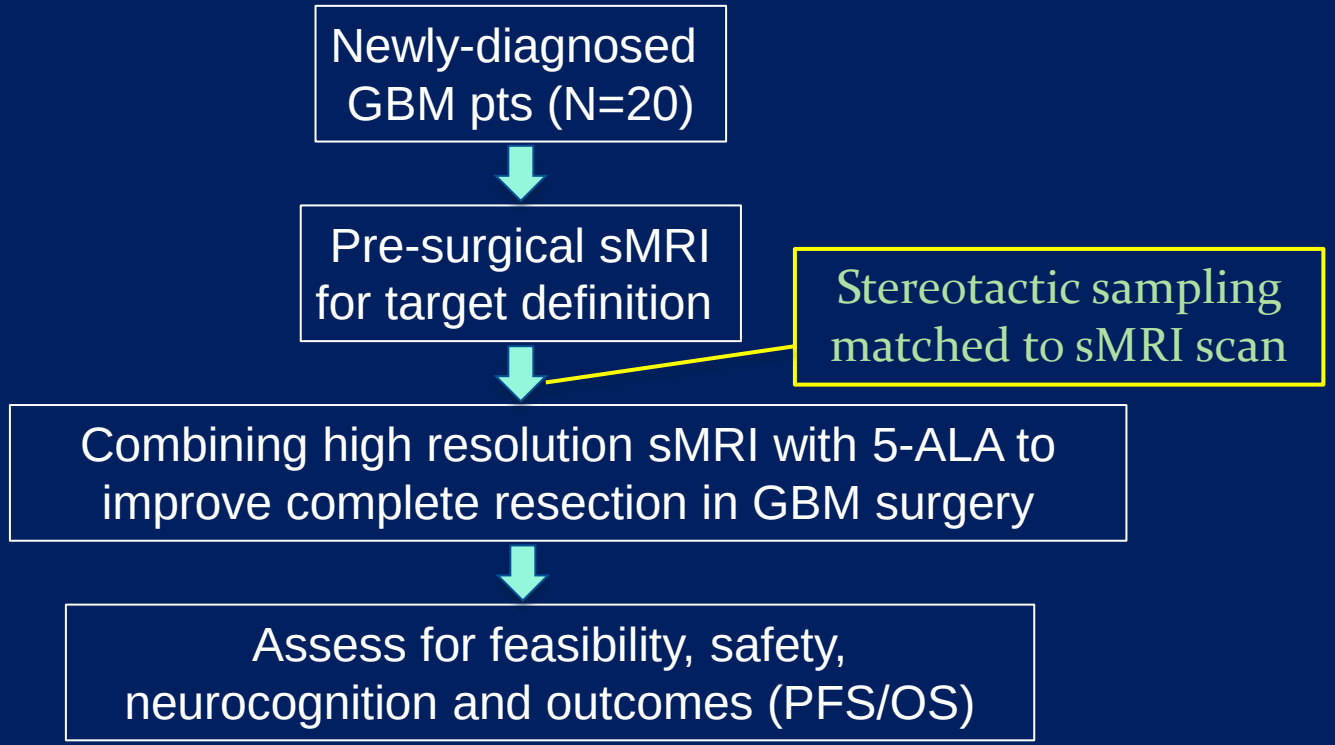
T2w



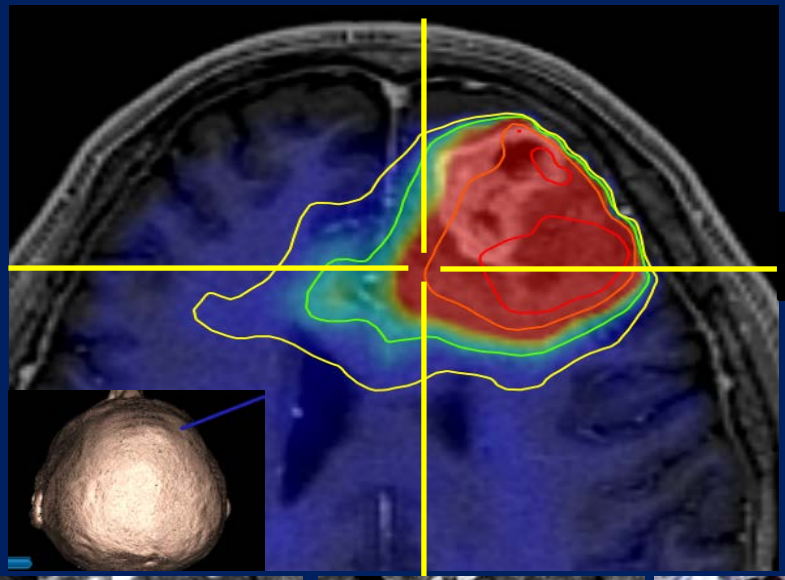
Cho/NAA

Pilot Study for GBM surgery

(R21CA186169: sMRI to guide tumor resection)

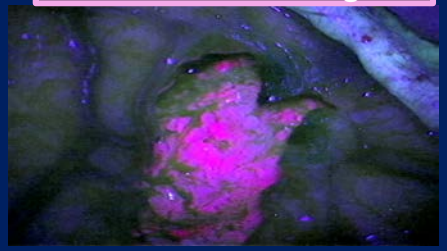


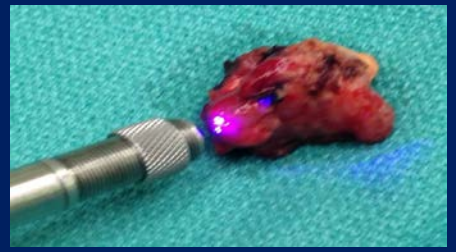
Fluorescence and Histological Validation of sMRI Tumor Infiltration

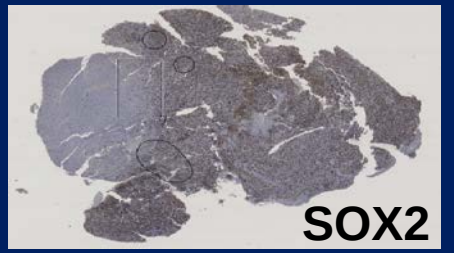


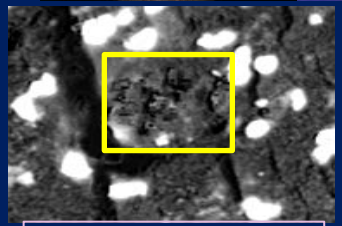
White Light

405 nm Blue Light

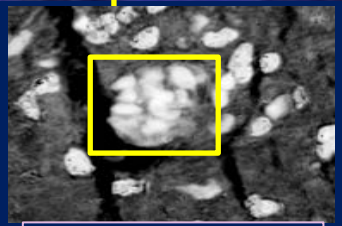




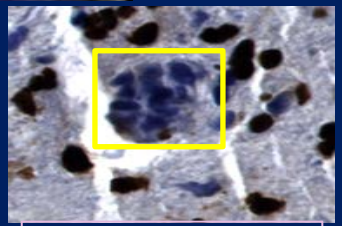




SOX2 Signal



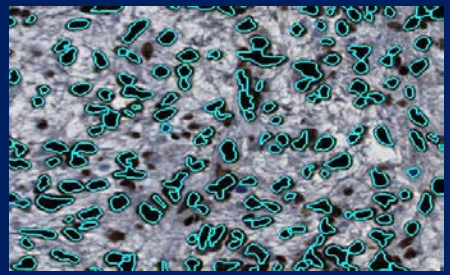
HXN Signal



Stained Slide

Segment Nuclei and Tissue Area

Automated Nuclear Classification



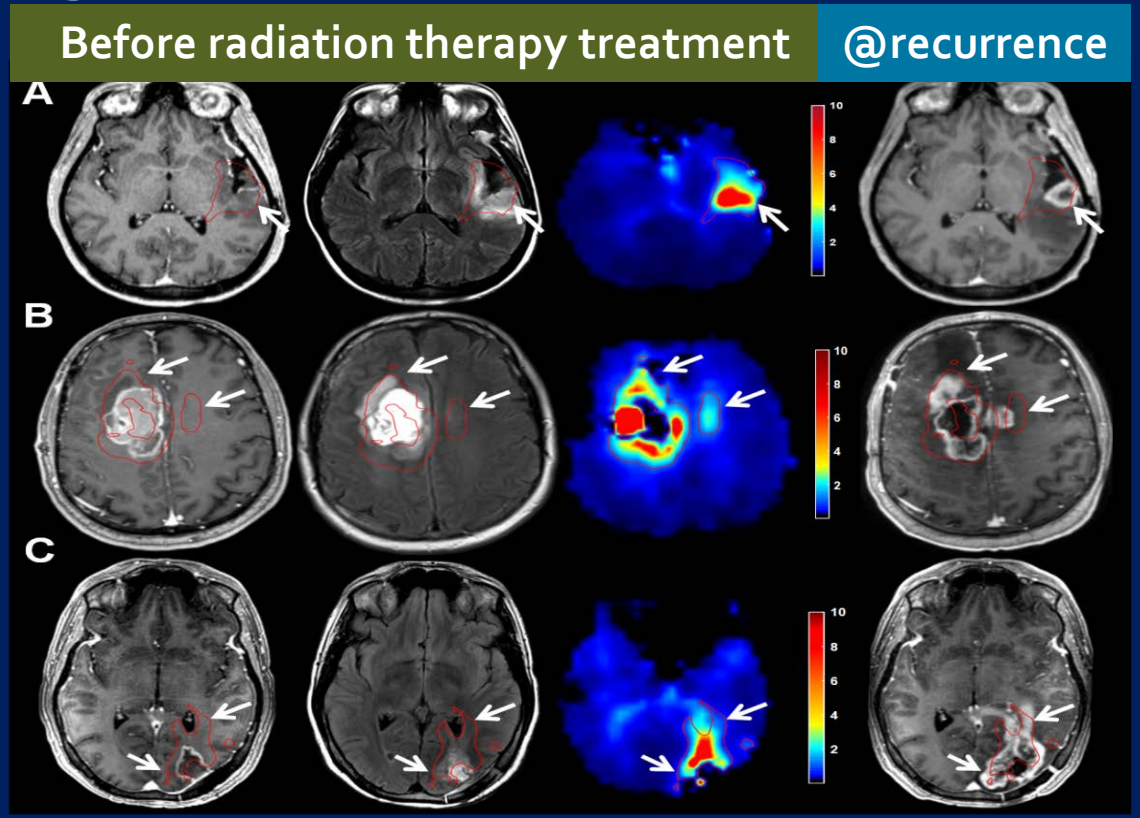
sMRI Identifies Infiltrating Tumor *in vivo*

sMRI biomarkers vs SOX2 Density

Biomarker	ρ	p-value
NAA	-0.50	0.01*
Cho	0.63	5E-4*
Cho/NAA	0.82	<1E-4*
DWI-ADC	0.17	0.40

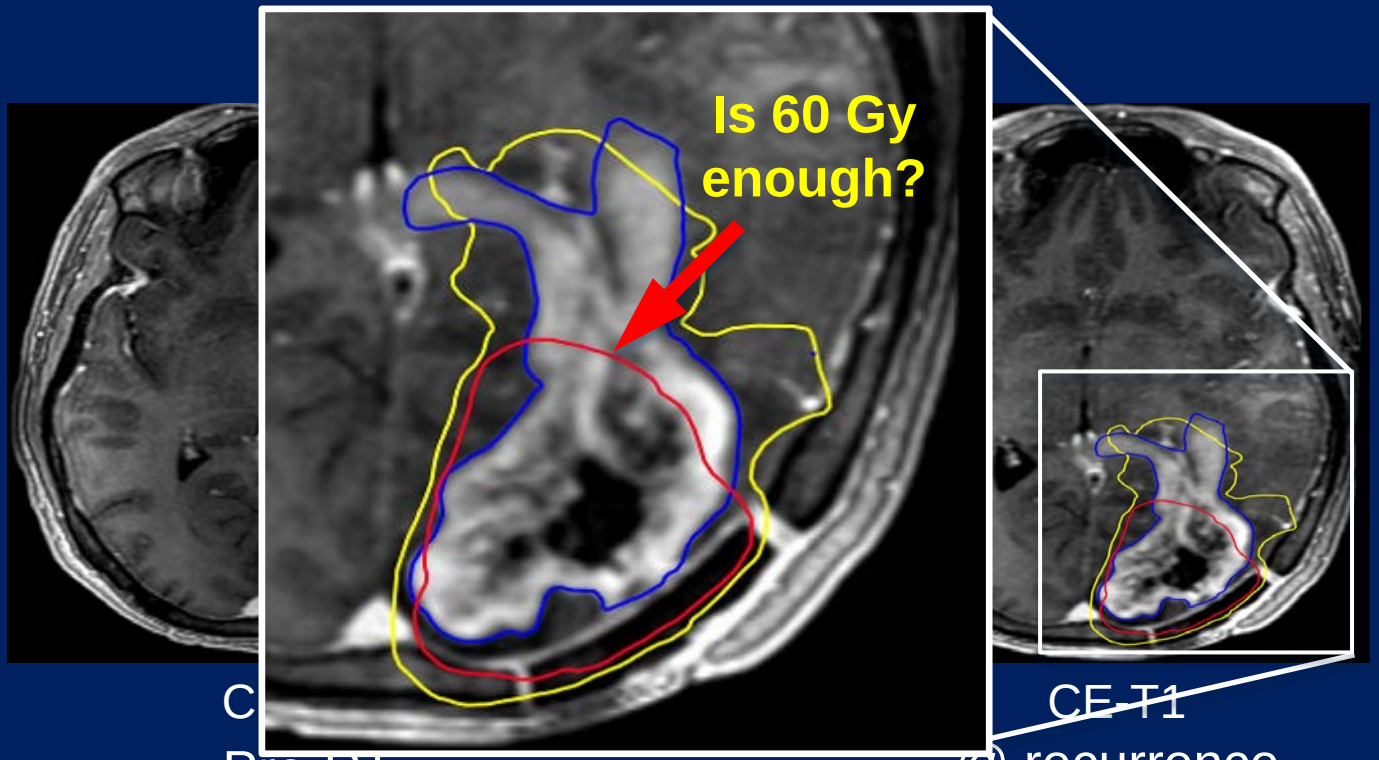
Cordova et al., Neuro Oncol 18:1180-9 (2016)

sMRI High-Risk Recurrence Regions



Cordova et al., Neuro Oncol 18:1180-9 (2016)

Example of Dose Coverage w/sMRI Targets



2.0x Cho/NAA (pre-RT)

Recurrence

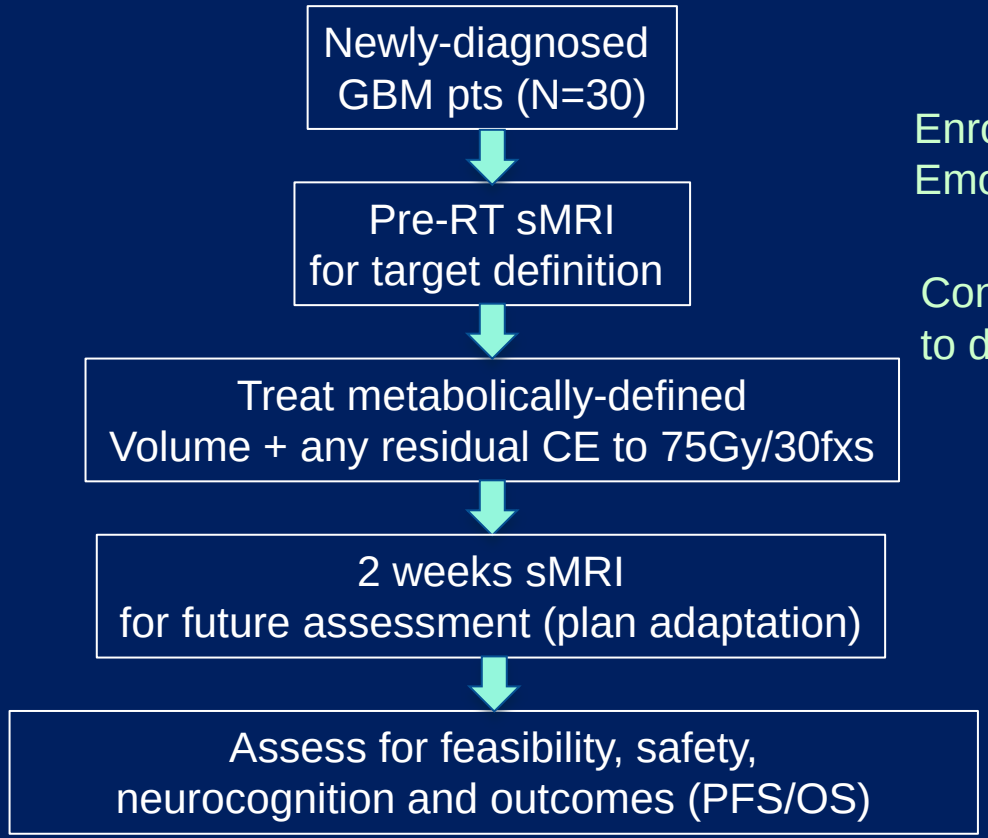
Current 60Gy

Cordova et al., Tomography 2:366-73 (2016)

Are current methods for defining RT targets good enough?

Pilot Study for GBM Dose Escalation

(R01CA214557: sMRI to guide dose escalation)

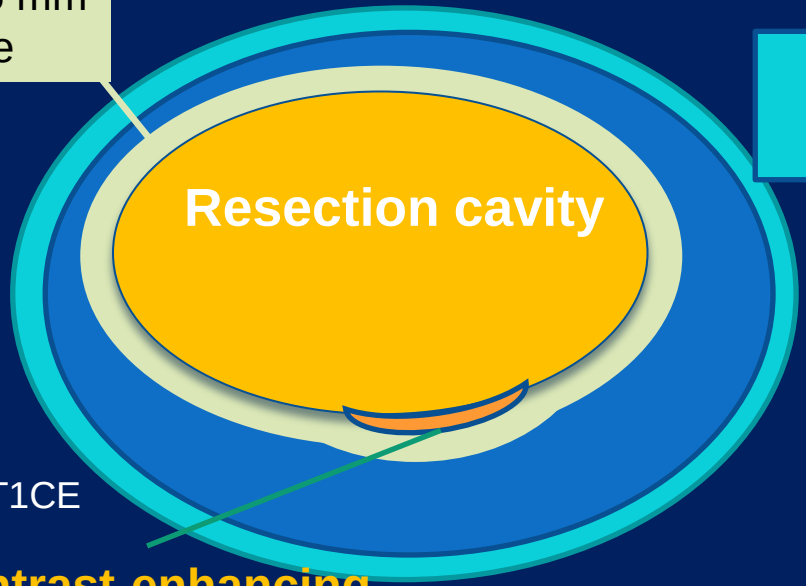


Enrollment at 3 institutions
Emory, Hopkins, Miami

Conventional MRI will be used
to define 60 and 50 Gy volumes

1-year PFS (30-35% -> 55-60%)

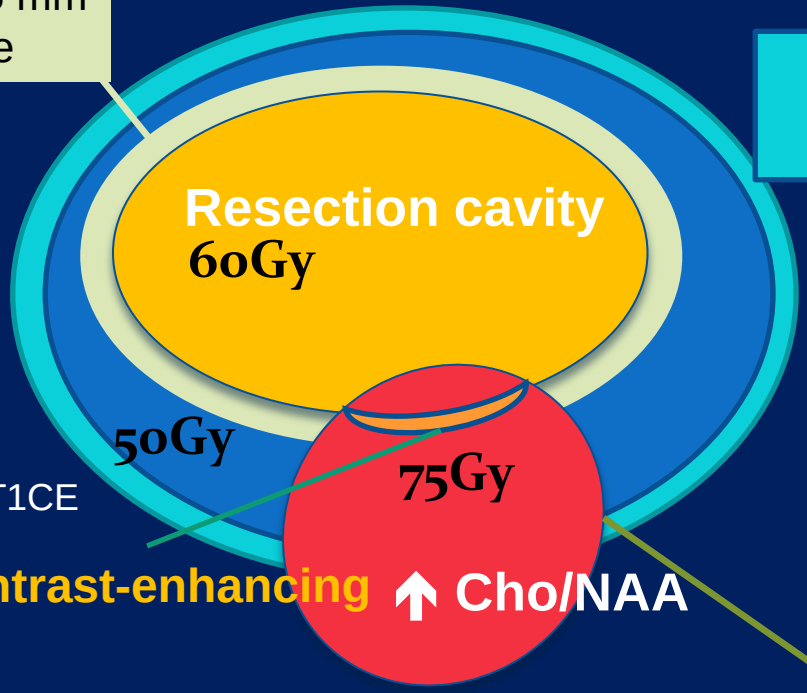
Current Standard RT Target Volume



GTV1: T2/FLAIR+ resection cavity+T1CE
GTV2: resection cavity+T1CE

PTV: adds additional 3 mm
PTV1: 46-54 Gy
PTV2: 60 Gy

RT Target Modification with sMRI



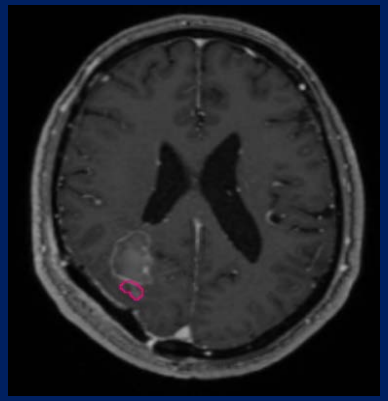
GTV1: T2/FLAIR+ resection cavity+T1CE
GTV2: resection cavity+T1CE
GTV3: sMRI+T1CE

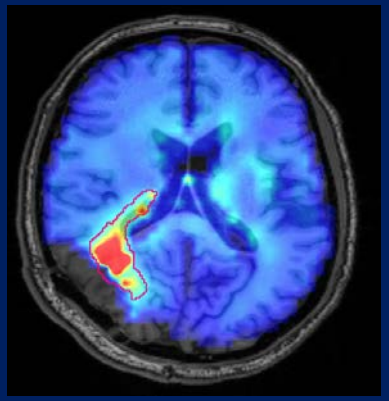
PTV: adds additional 3 mm
PTV1: 50 Gy
PTV2: 60 Gy
PTV3: 75 Gy

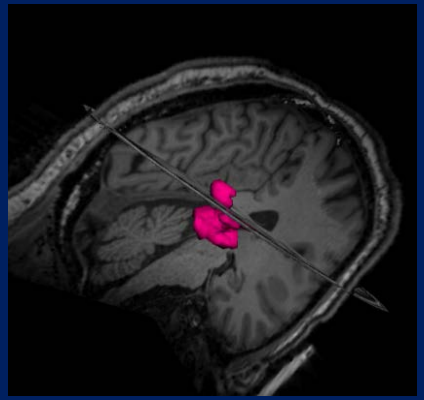
CTV3 Modification with sMRI (Emory #2)

CE-T1w

Cho/NAA=2x



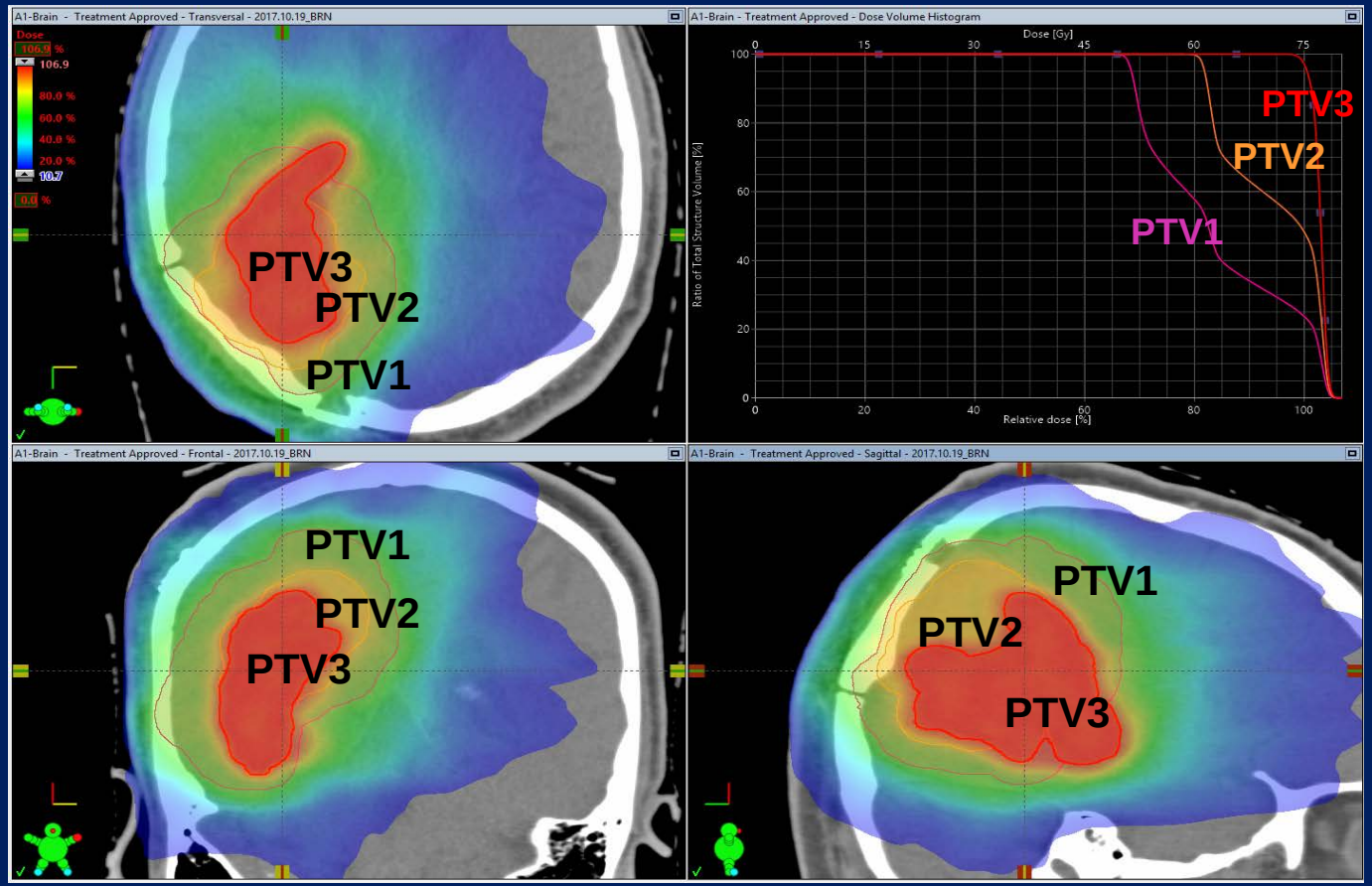




2.59cc

23.82cc

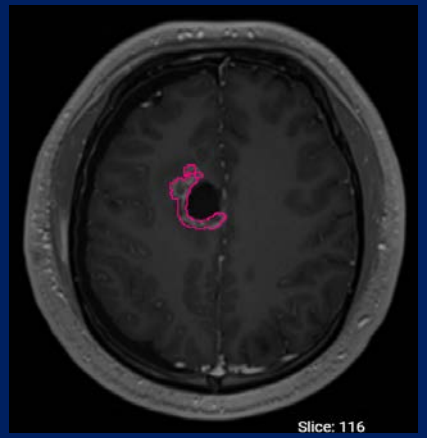
Isodose Lines (75, 60, 50 Gy) of IMRT Plan

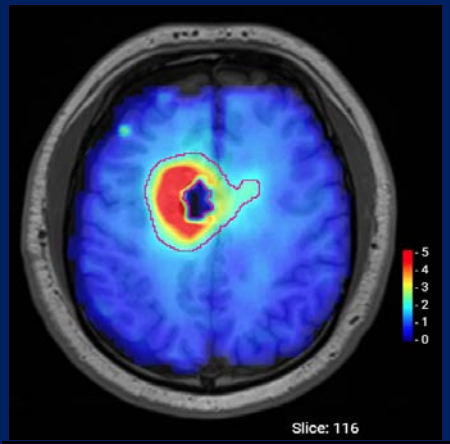


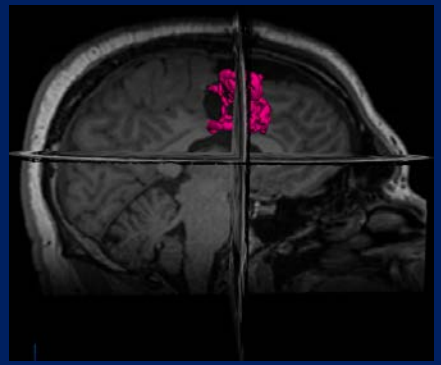
CTV3 Modification with sMRI (Miami #4)

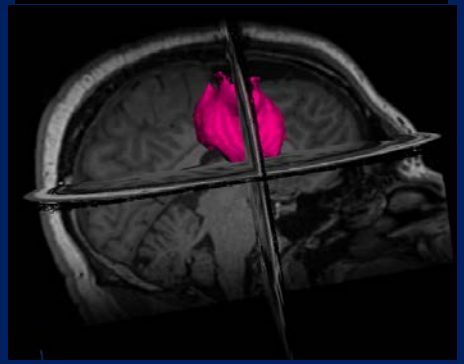
T1w-CE

Cho/NAA=2x









2.3cc

34.8cc

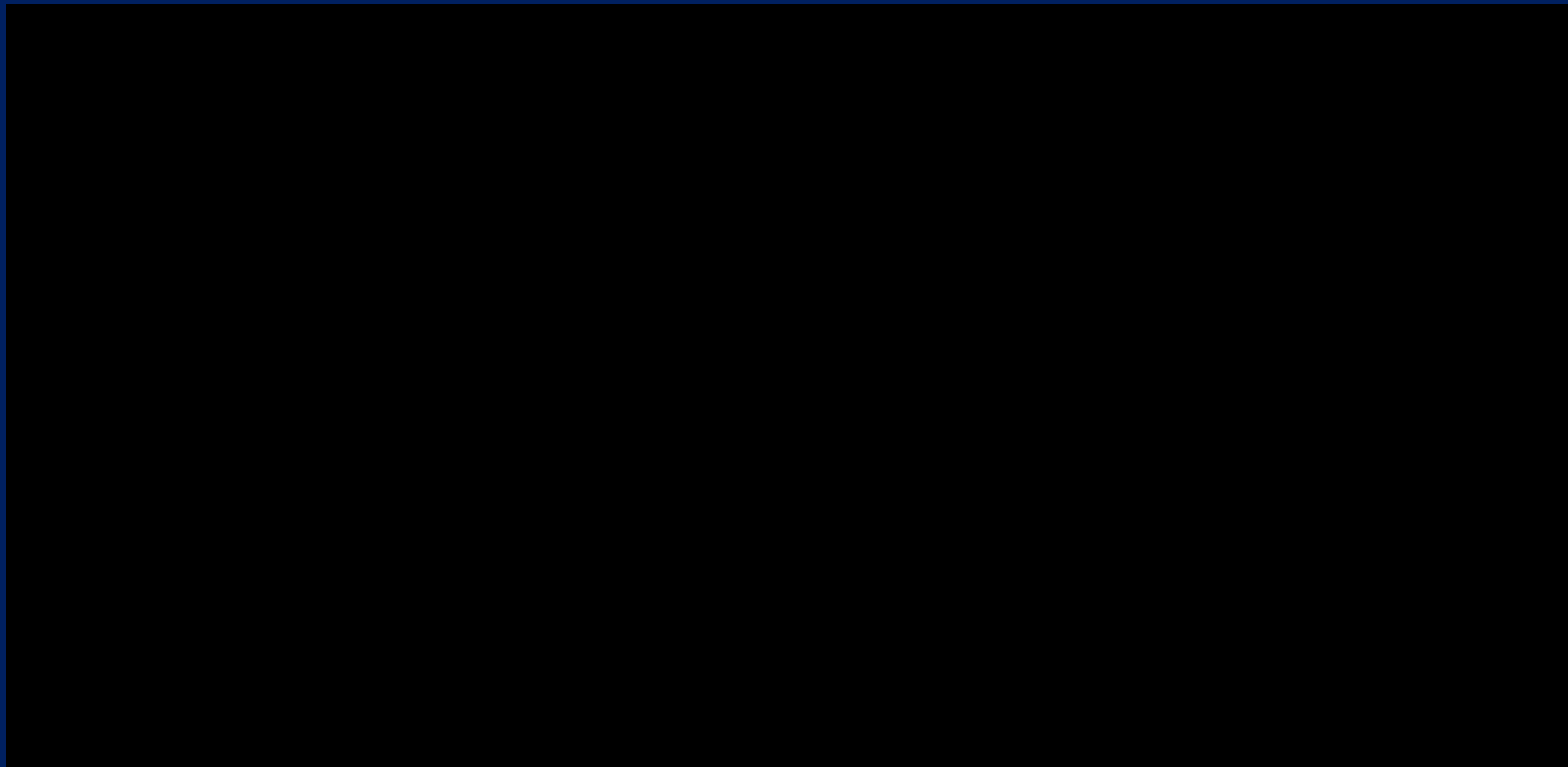
sMRI Cloud App

BrICS
Brain Imaging Collaboration Suite

- ✓ User-friendly, intuitive display
- ✓ Fit for busy clinicians, not for MR spectroscopists
- ✓ Web-based, no software installation needed
- ✓ Centralized Analysis for multisite trials
- ✓ Automated Quality control
- ✓ Auto-Segmentation for target volume definition
- ✓ Real-time collaborative editing capability
- ✓ Securely store anonymized sMRI data sets, including other clinical images, RT plans, and genomic/histological information

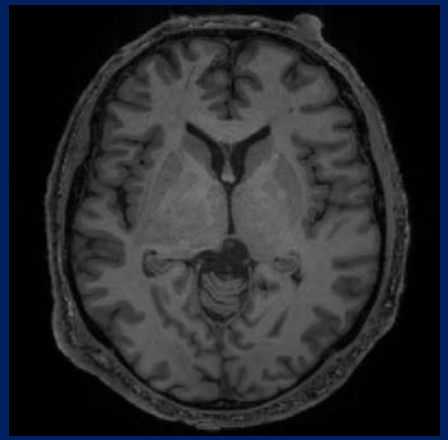
sMRI Cloud App

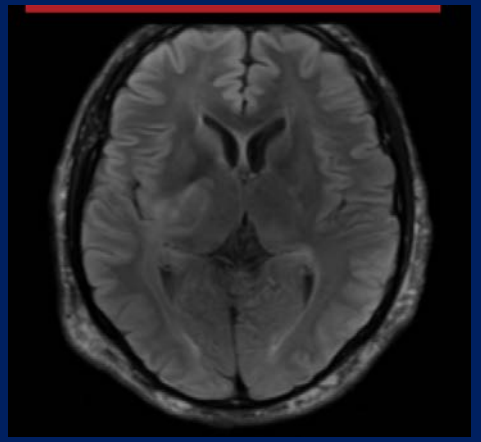
BrICS
Brain Imaging
Collaboration Suite



No Biopsy or RT targets on CE-T1w

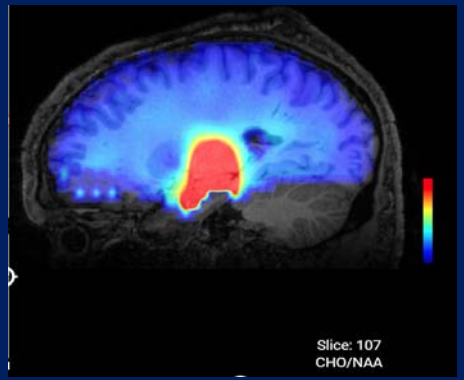
T1w

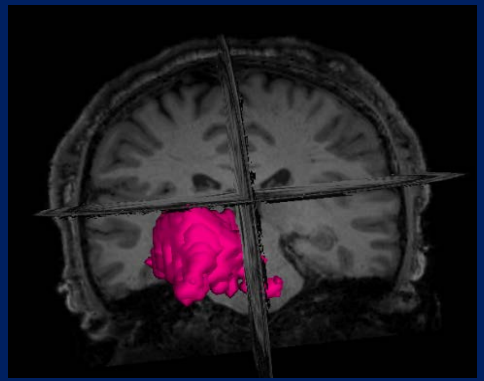




FLAIR

Cho/NAA
(Sagittal)





Cho/NAA
3x volume

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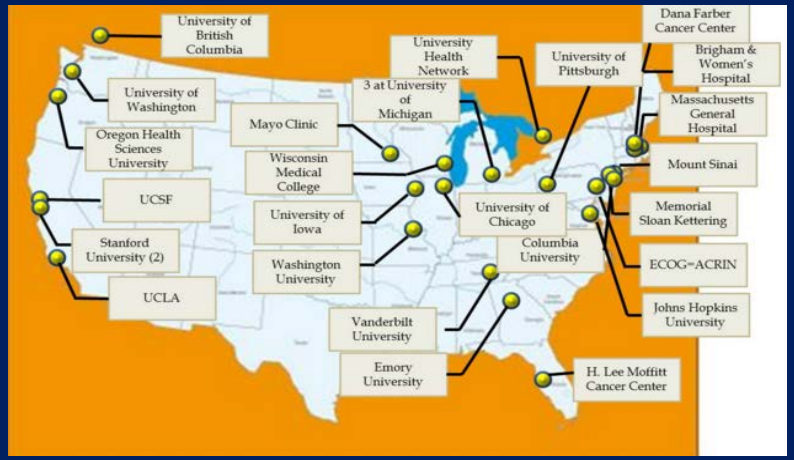

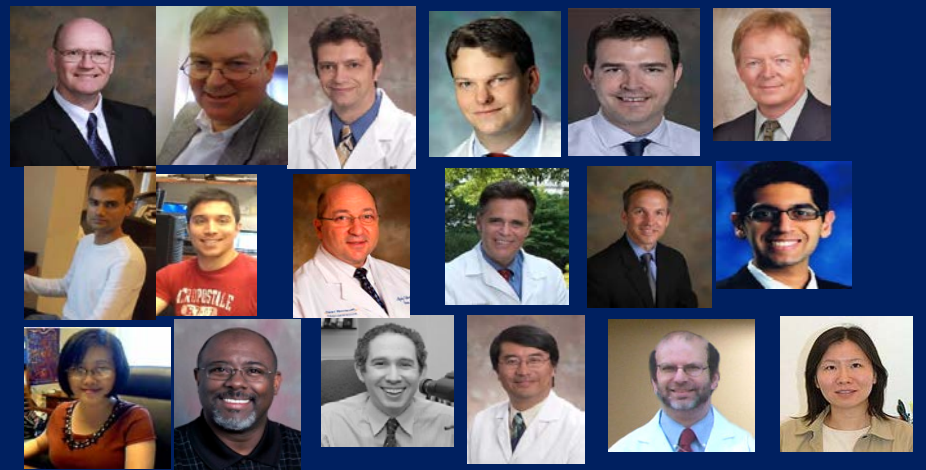


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