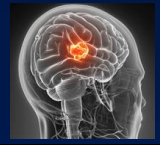
Friday, June 8th , 2018



ADVANCED NEUROIMAGING OF BRAIN TUMORS

RADIOGENOMICS, BIOMARKERS & RESPONSE ASSESSMENT

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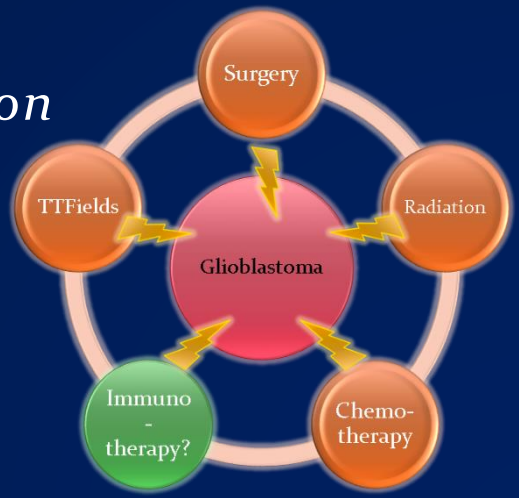


Penn Medicine's Abramson Cancer Center
and The Penn Brain Tumor Center PRESENT

NEURO-ONCOLOGY SYMPOSIUM
BRAIN TUMORS 2018

Master Class In Brain Tumor Treatment – Best Practices

A CME/CNE-Certified Conference

Disclosures

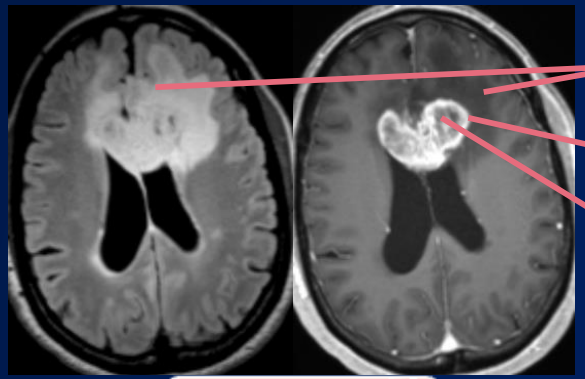
- Consultant: ACR Imaging Network (ACRIN) & ACR Image Metrix
  - GBM multi-institutional trial ABTC 0901
  - RANO Reader Eisai TM610-002 Study
  - Phase III RTOG 0825(4508)/ACRIN 6686
- Grant Support
  - PI - High Resolution MRI/MRS to Evaluate Therapeutic Response to Optune
  - PI: Galileo CDS Inc. – Clinical Diagnostic Decision Support in Radiology
  - Co-I: RSNA Education Scholar Grant: Development of a Novel Radiology Teaching Interface Using Bayesian Networks
  - Co-I: Guerbet 03277 Dose Finding Study in CNS MRI
- NovoCure Advisory board

Glioblastoma: *the miserable truth*

- Most common (70%) primary brain tumor in adults (14,000 new cases in 2017)
  - Incidence highest in patients 45-55 yrs, *"prime of life"*
  - *Rapidly progressive*
  - Neurological symptoms - depending on location
    - Seizure: most common presenting symptom
  - Most lethal form of brain cancer

52 Y/M 11/24/2017

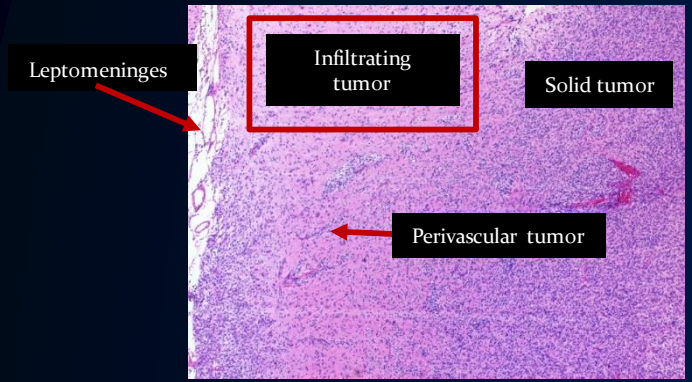
4 months later

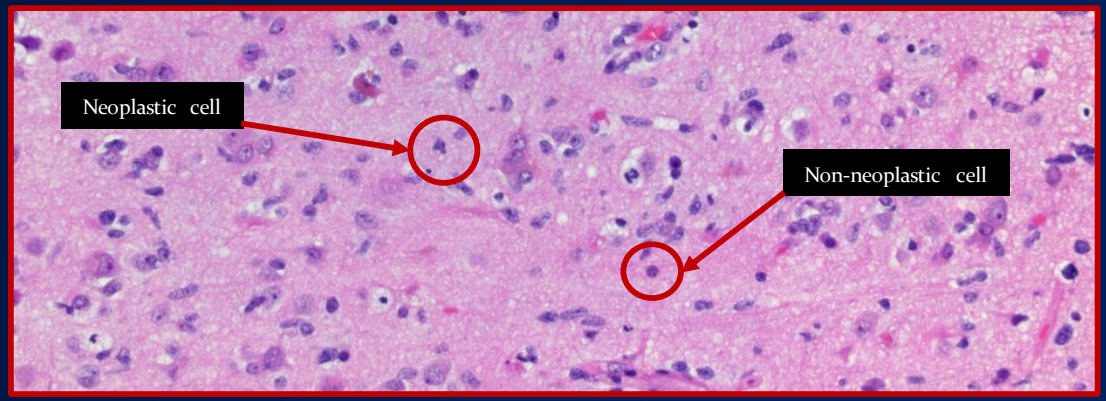


04/27/2018

Glioblastoma: *the miserable truth*

- Extremely aggressive, absence of discrete boundaries, one of the major determinants for the poor prognosis
  - Significant vasogenic edema
  - Malignant cells in normal appearing peri-tumoral WM as well in the contralateral cerebral hemisphere, ***invisible on conventional imaging***
  - "Like mixing black & white sand together" – makes differentiation from normal brain extremely difficult

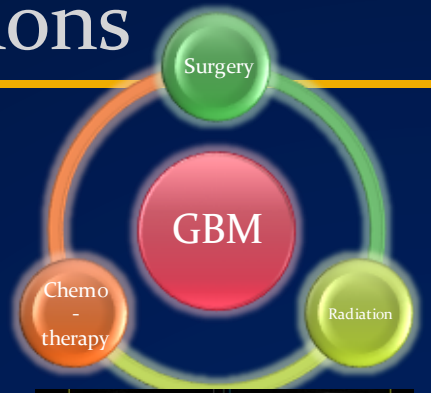


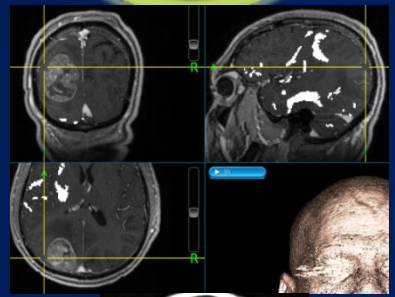


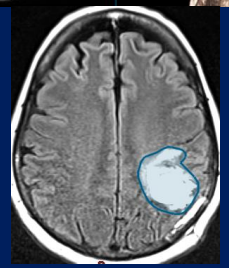
Infiltrating glioma (GBM): Courtesy - MacLean Nasrallah

Standard of care treatment & its limitations

- Visible tumor: What we see is what we treat!
  - Relieving symptoms & cytoreduction
- Maximal Safe Resection
  - Guided by the enhancement on T1-w MRI
  - Non-enhancing infiltrating & invisible tumor
    - Very difficult to completely remove, particularly true for tumors near eloquent areas
- Followed by radiation (RT) & chemotherapy (CT).





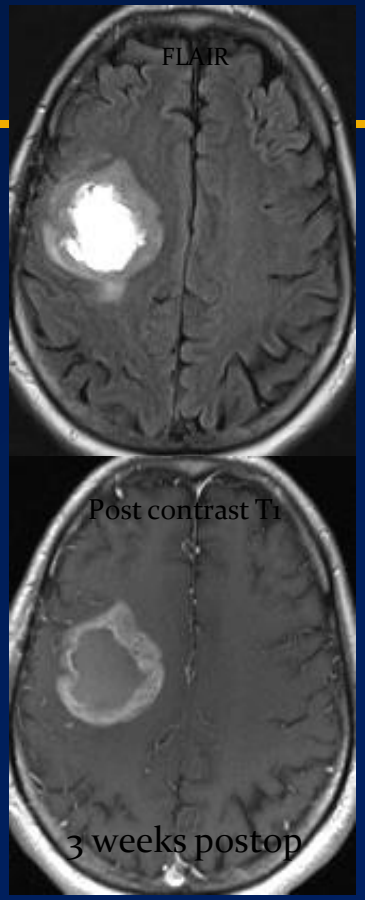


GBM: Courtesy – Donald O'Rourke & Robert Lustig

Standard of care treatment & its limitations

- Occult infiltration (invisible tumor), is most commonly seen in the immediate peri-tumoral region.
- More than 80% of patients experience recurrence, which is almost always seen in the peri-tumoral region.
- Median survival ~ 15 months with Sx + CCRT (5 year survival < 1%)

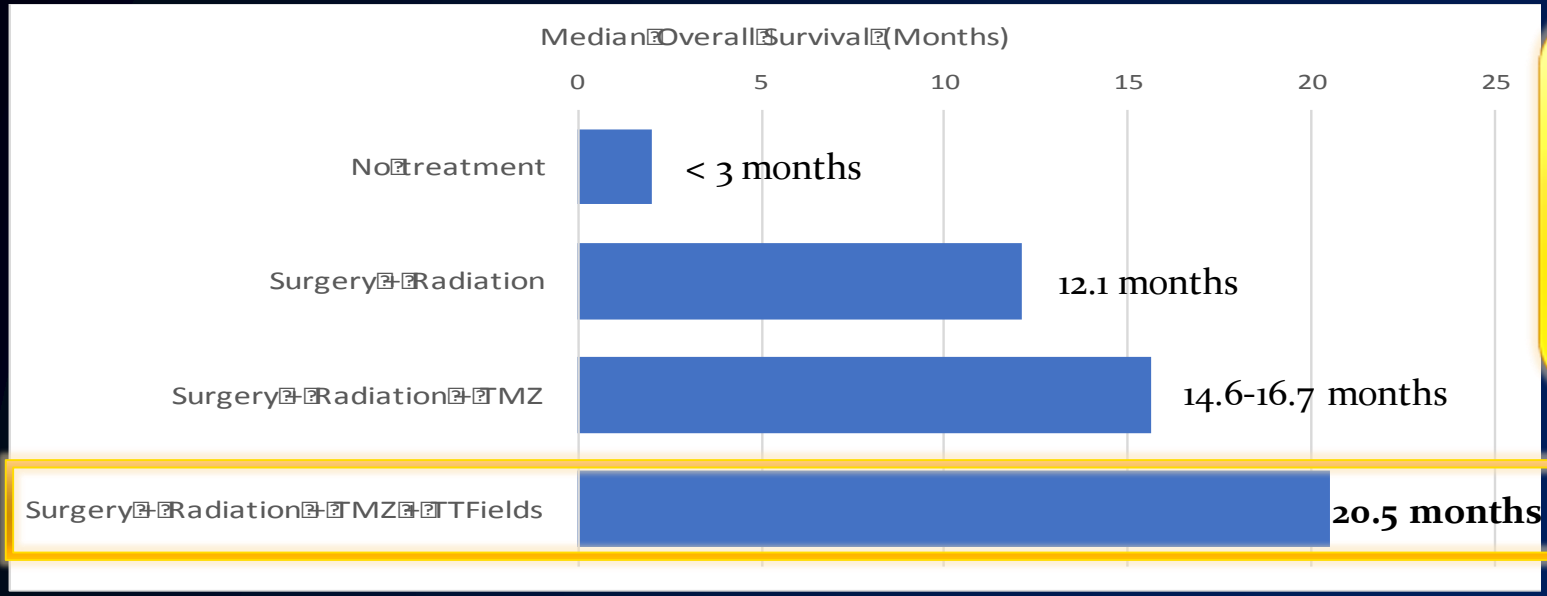
Novel approaches to diagnosis & treatment are desperately needed



... Like Edison, it is important to learn from the hundreds of failures to achieve Stupp's unprecedented track record of two paradigm-changing trials that have moved the survival curve to the right, whereas countless others have failed.

... Dr. Steven Brem MD, Penn, 2017.

Natural History of GBM & Impact of Available Therapies



TMZ: Temozolomide

Stupp R et al. Radiotherapy plus concomitant & adjuvant TMZ for glioblastoma. N Engl J Med. 2005;352(10):987-96.

Stupp R et al. Maintenance Therapy With Tumor-Treating Fields Plus TMZ vs TMZ Alone for Glioblastoma: A Randomized Clinical Trial. JAMA. 2015;314(23):2535-43.

Timeline of FDA Approved Therapies for Malignant Gliomas

June 14, 1996: Carmustine wafer for recurrent glioblastoma

January 12, 1999: Temozolomide for anaplastic astrocytoma

February 25, 2003: Carmustine wafer for newly diagnosed glioblastoma

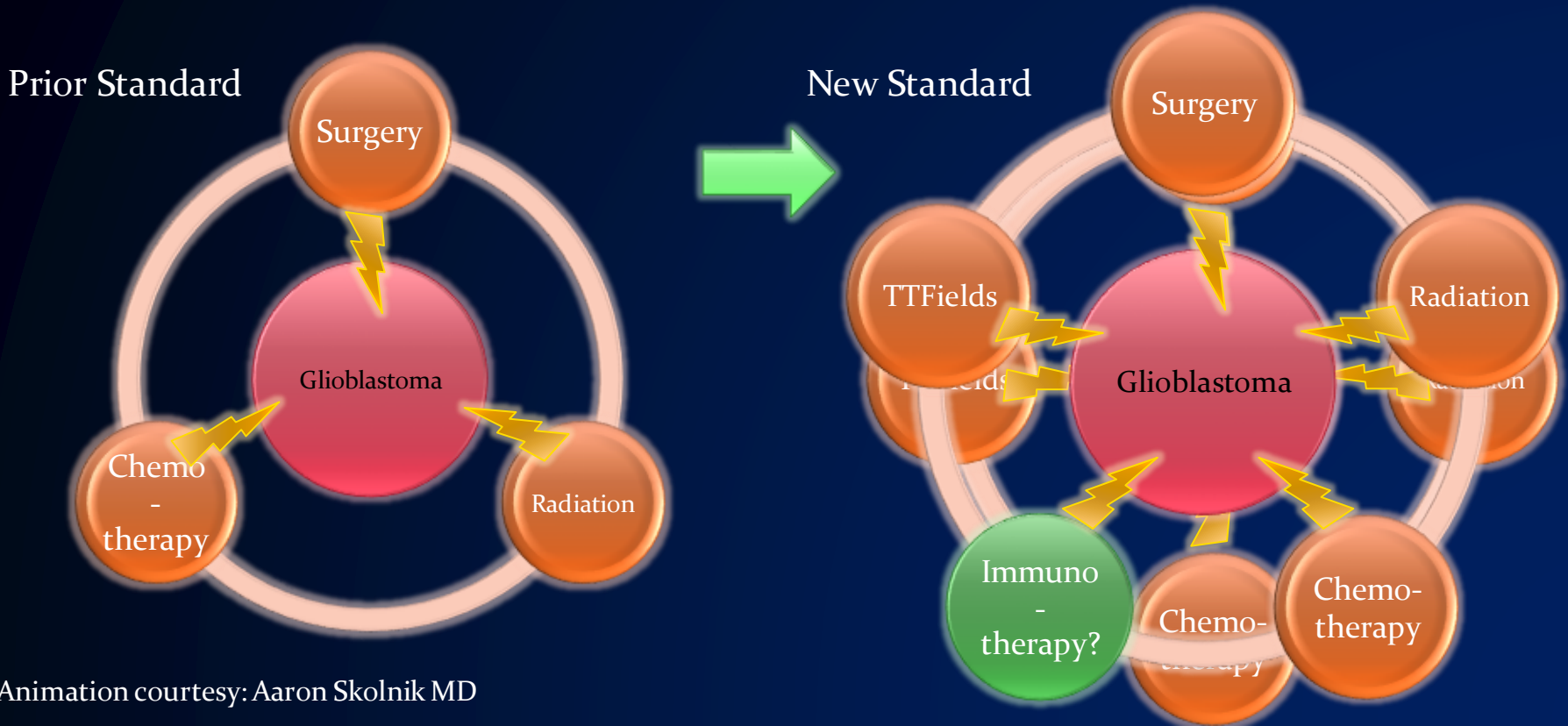
March 15, 2005: Temozolomide for newly diagnosed glioblastoma

May 5, 2009: Bevacizumab for progressive glioblastoma

April 15, 2011: TTFields for recurrent glioblastoma

October 5, 2015: TTFields for newly diagnosed glioblastoma

New Treatment Paradigm: Combination Therapy

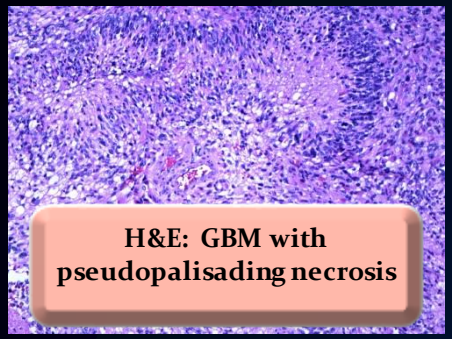


Animation courtesy: Aaron Skolnik MD

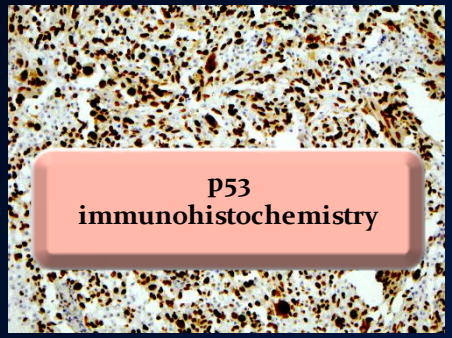
Combination Therapy: GBMs are heterogeneous!

1. In their genetic & epigenetic makeup
2. Levels of protein expression
3. Metabolic & bioenergetic behavior
4. Microenvironment
5. Biochemistry
6. Structural composition

The amalgamation of these various changes is manifested as abnormalities observed on Neuropathology & Neuroimaging

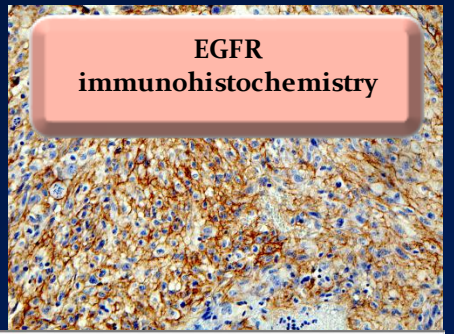


H&E: GBM with pseudopalisading necrosis

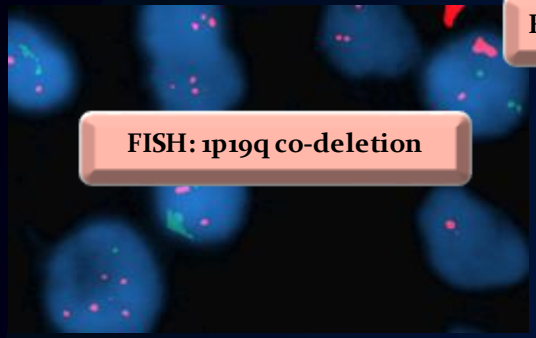


P53 immunohistochemistry

IDH1-R132H immunohistochemistry

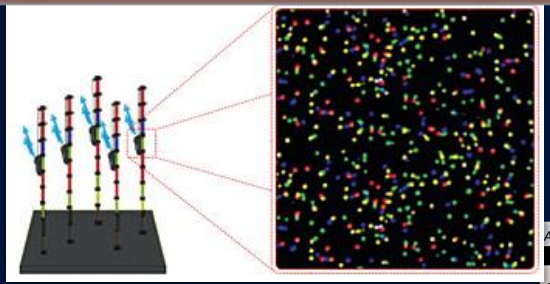


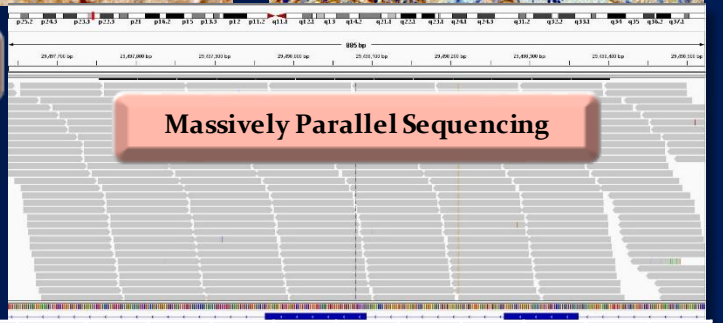
EGFR immunohistochemistry



FISH: 1p19q co-deletion

Fusion Transcript Panel Anchored Multiplex PCR



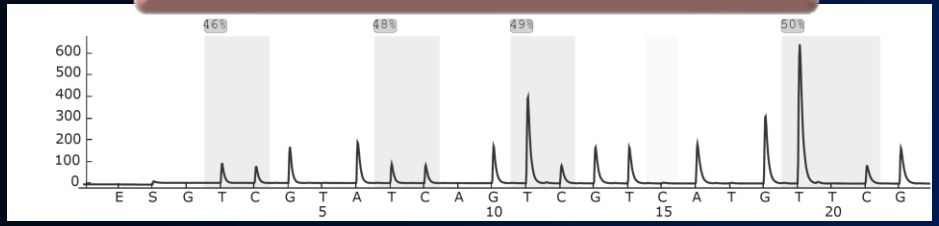


Massively Parallel Sequencing

ABL1	**AKT1**	AKT2	AKT3	**ALK**	APC	AR	ARAF	ARID1A	ARID2	ATM	ATRX
CDK4	CDK6	CDKN2A	CHEK2	CIC	CREBBP	CRKL	**CSF1R**	CTNNB1	DAXX	DDR2	DNMT3A
FBXW7	FGF3	FGFR1	FGFR2	FGFR3	FGFR4	FLT3	FUBP1	GATA3	GNA11	GNAQ	GNAS
KDR	**KIT**									MCL1	MDM2
NBN	NF1	NF2	NKX2-1	**NOTCH1**	NOTCH2	NOTCH3	**NRAS**	NTRK1	NTRK2	NTRK3	PAK1
RAD51	RAD51B	RAD51C	RAD51D	RAF1	RB1	**RET**	RHOA	RNF43	SETD2	SF3B1	SLIT2
TP53	TRAF7	TSC1	TSC2	TSHR	U2AF1	VHL	WT1	XRCC2			

NGS Solid Tumor Panel v2

Pyrosequencing for MGMT Promoter Methylation

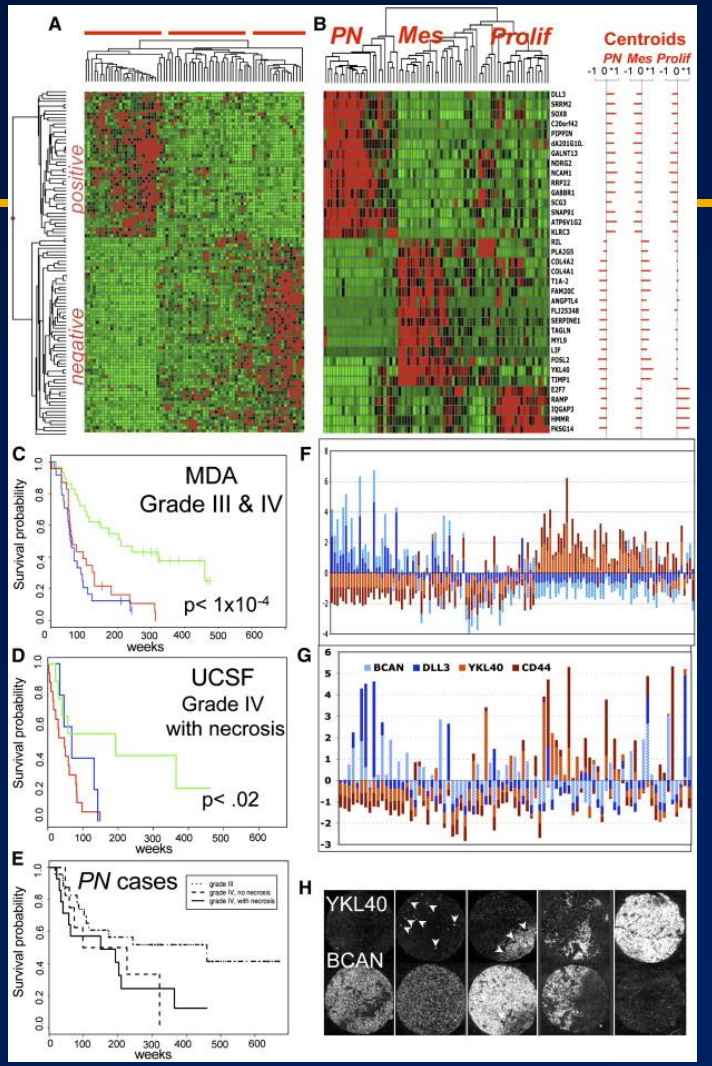


Courtesy: MacLean Nasrallah MD, PhD, April Schrank-Hacker, Qiagen, Jason Rosenbaum, Penn

Why do we need these?

- Tumor heterogeneity has been observed at the histological & genetic levels

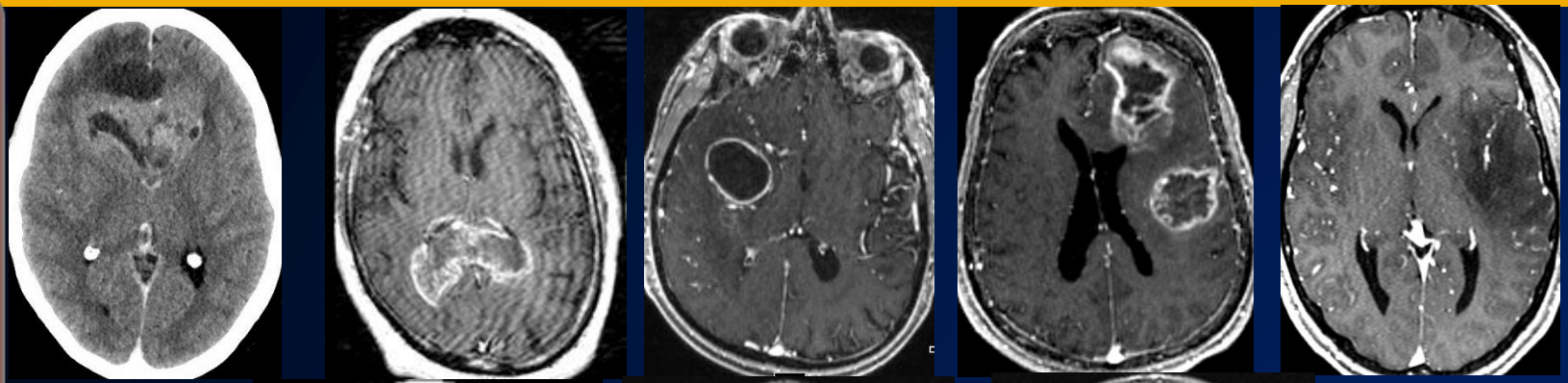
Increased levels of heterogeneity associated with adverse clinical outcomes



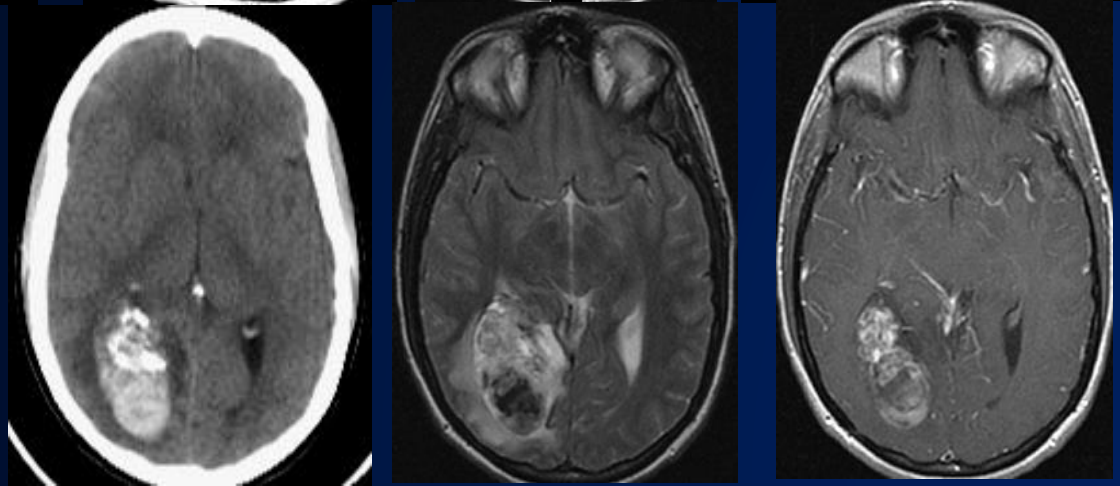
Phillips HS et al. Molecular subclasses of high-grade glioma predict prognosis, delineate a pattern of disease progression, and resemble stages in neurogenesis. Cancer Cell. 2006; 9(3): 157-73.

Glioma heterogeneity: Neuroimaging

5 different patients
GBM: WHO Grade IV



Oligodendroglioma:
WHO Grade II



Role of Neuroimaging

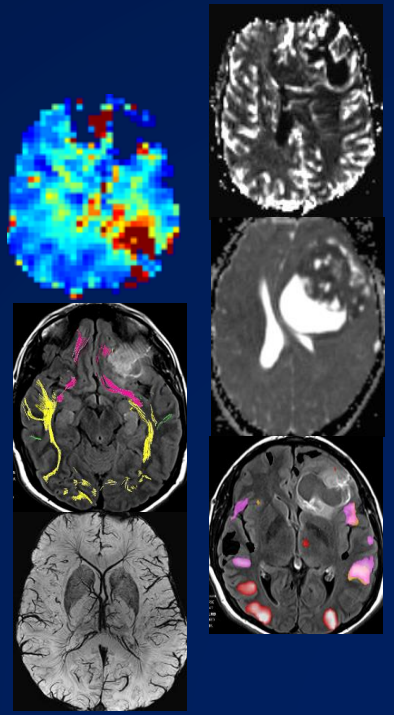
No longer limited to merely providing "anatomic details"

1. *Location & Size:* Where is it & how big is it?
   - On most basic level, *intra- vs. extra-axial?*
   - D/Dx, based on *location* & imaging findings
2. *Number:* One or more than one?
3. *Complications?*
   1. *H*ydrocephalus, *H*emorrhage or *H*erniation?
4. *Mimic:* Is it really neoplastic, could it be something ?

Role of Neuroimaging

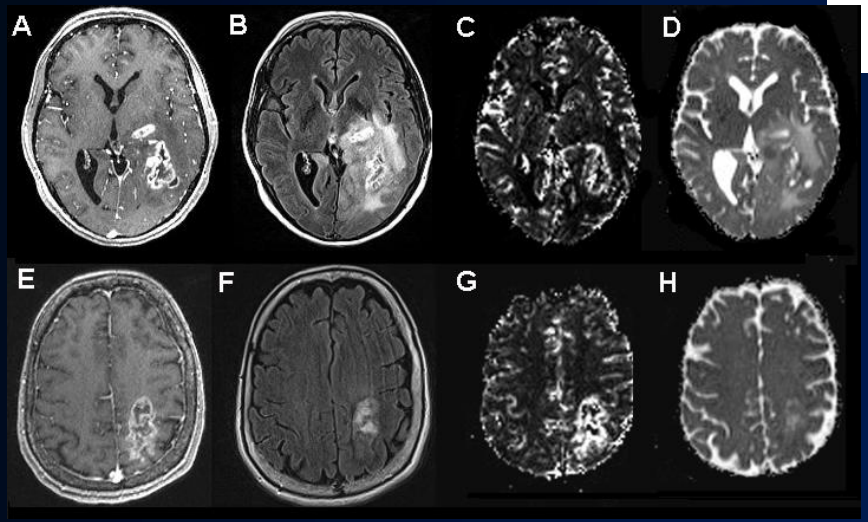
Functional, Physiologic, Metabolic & Genomic information

- Angiogenesis → Perfusion imaging
  - Vascularity → CBV
  - Vascular integrity → Permeability
- Cellularity → Diffusion imaging
- Metabolism → MR Spectroscopy
- Functional anatomy, eloquent mapping → f-MRI, DTI
- Oxygenation status → SWI



Role of advanced neuroimaging techniques: MR perfusion

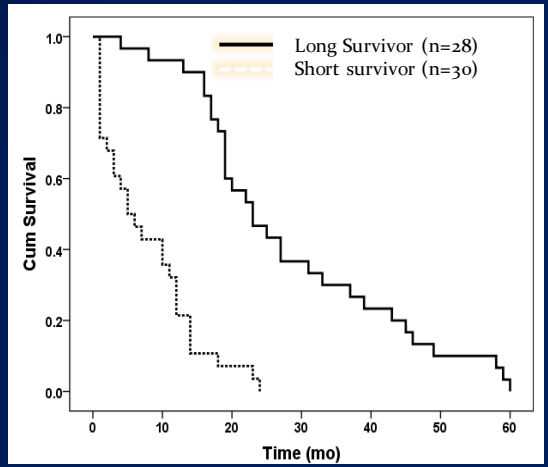
- Prognostic imaging based biomarker



ORIGINAL RESEARCH
ADULT BRAIN

Prognostic Value of Dynamic Susceptibility Contrast-Enhanced and Diffusion-Weighted MR Imaging in Patients with Glioblastomas

G. Çoban, S. Mohan, F. Kural, S. Wang, D.M. O'Rourke, and H. Poptani



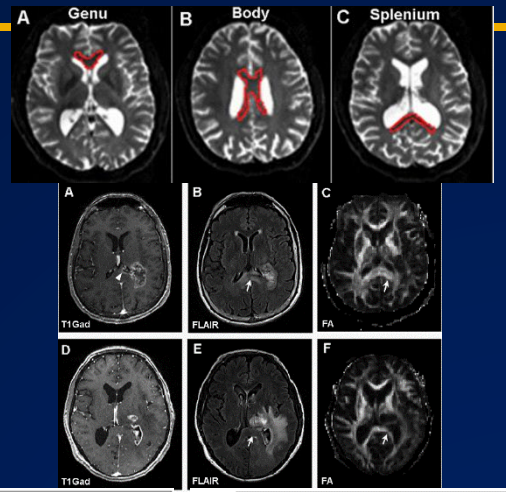
AJNR. 2015 Jul;36(7):1247-52.

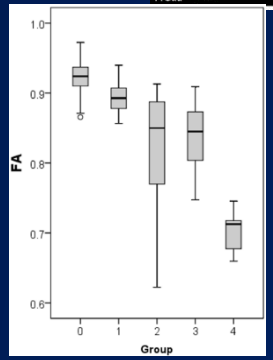
Diffusion Tensor Imaging & detection of invisible tumor

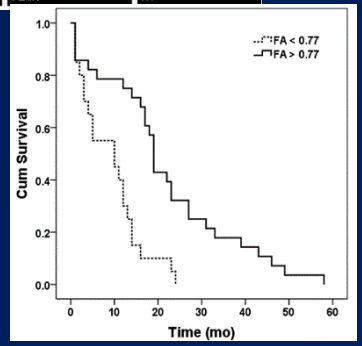
- 48 GBM patients & 17 normal subjects.
- Divided into 4 groups based on CC invasion & OS
  - Long survival without CC invasion; short survival without CC invasion; long survival with CC invasion; short survival with CC invasion.

- Patients with short survival & CC invasion had lowest FA values (0.64± 0.05) from the CC compared with other groups ($p < 0.05$).
  - Kaplan-Meier survival curves demonstrated that the mean survival time was significantly longer for patients with high FA (>0.77) compared with those with low FA (<0.77) ($p < 0.001$).

DTI can quantify tumor infiltration & predict OS in GBM patients.







Mohan S et al. AJR. (Under Review)

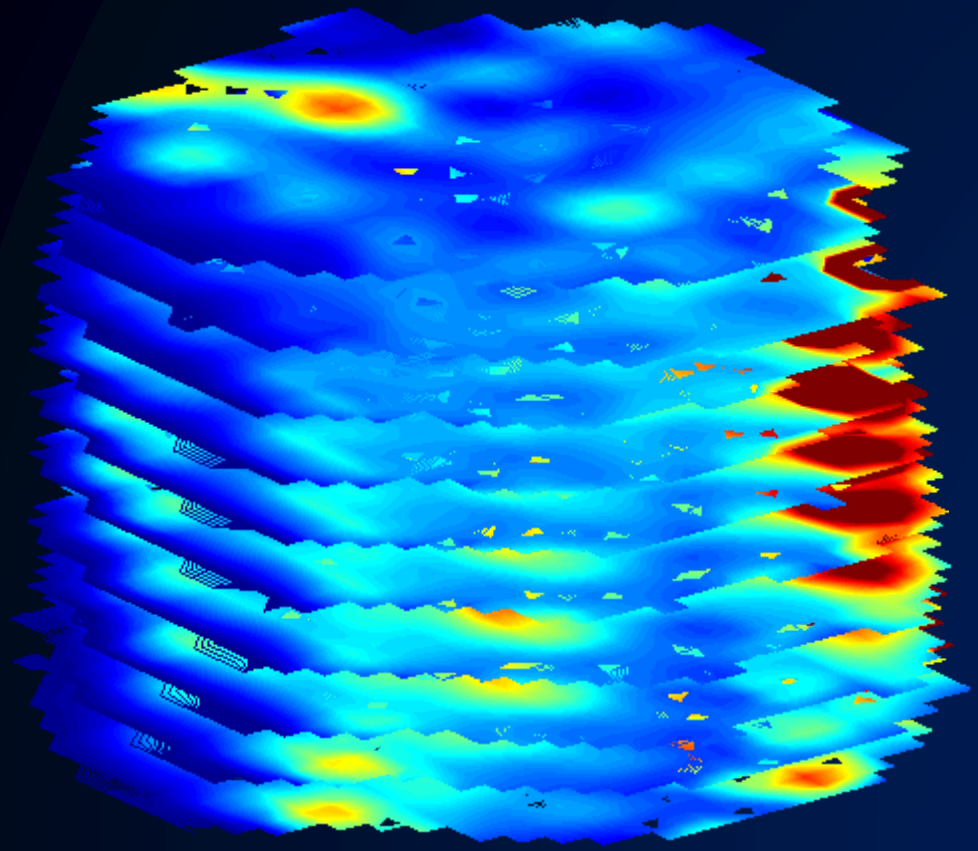
Next generation (neuro-oncologic) imaging

- EPSI
  - Echo-planar Spectroscopic imaging
- CEST
  - Chemical Exchange Saturation Transfer
- MR fingerprinting
- Slip interface imaging/MR Elastography
- Multi-shell HARDI
- NODDI
- DSI
- RSI
- DKI

7 Tesla MAGNETOM Terra

Habitat Imaging & From Macro-Micro

Multi-Slice EPSI: Cho/Cr Maps

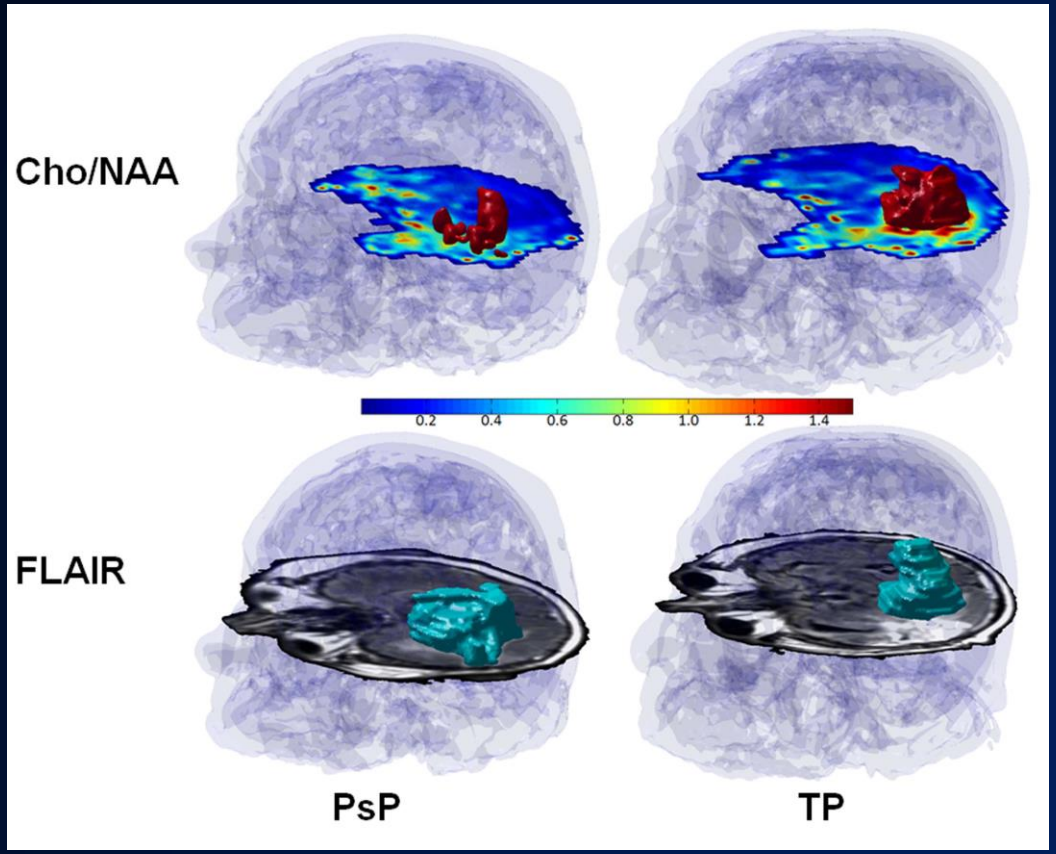


- Whole-Brain
- High Resolution
- Single Scan

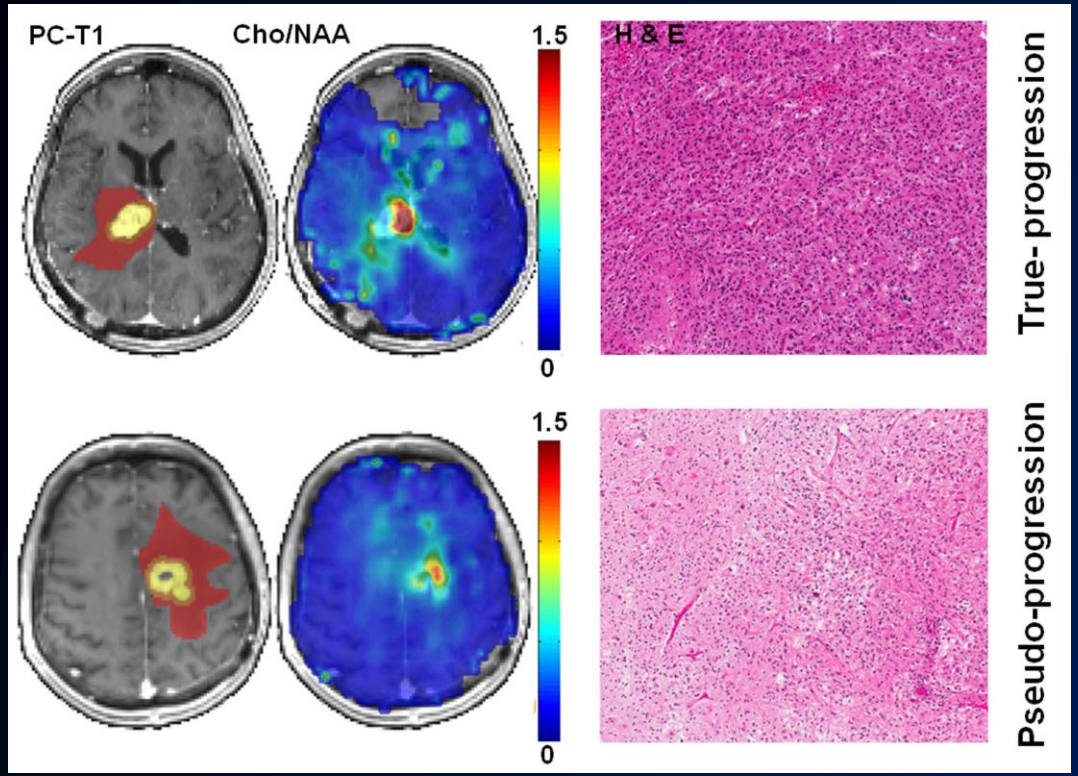
Cho/Cr Map

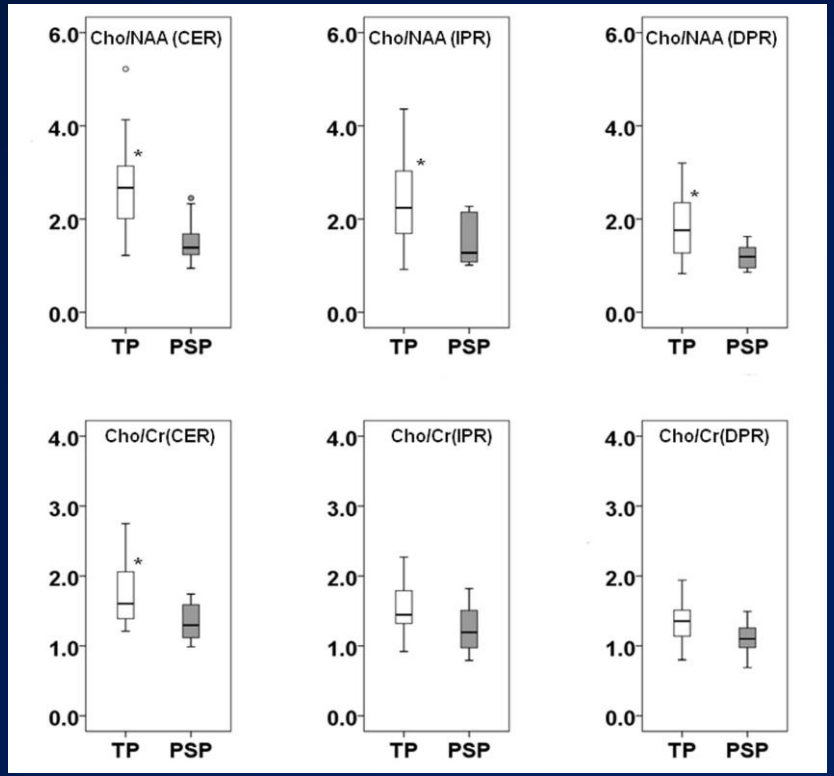
True Progression

EPSI: True Vs. Pseudoprogression



EPSI: True Vs. Pseudoprogression





Verma G/Chawla S et al. NMR in Biomed (Accepted)

Immunotherapy: Response Assessment

frontiers in Neurology

GENERAL COMMENTARY
published: 05 February 2018
doi: 10.3389/fneur.2018.00051

Commentary: Pitfalls in the Neuroimaging of Glioblastoma in the Era of Antiangiogenic and Immuno/Targeted Therapy

Aaron D. Skolnik[1], Sumei Wang[2], Pallavi P. Gopal[3] and Suyash Mohan[2]*

[1]Radiology, Penn Medicine Princeton Health, Plainsboro, NJ, United States, [2] Neuroradiology, Hospital of the University of Pennsylvania, Philadelphia, PA, United States, [3] Pathology, Yale School of Medicine, New Haven, CT, United States

Keywords: glioblastoma multiforme (GBM), MRI, diffusion magnetic resonance imaging, antiangiogenic therapy, targeted therapy, tumor-treating fields

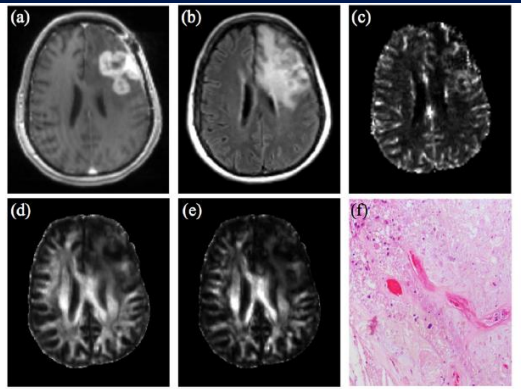
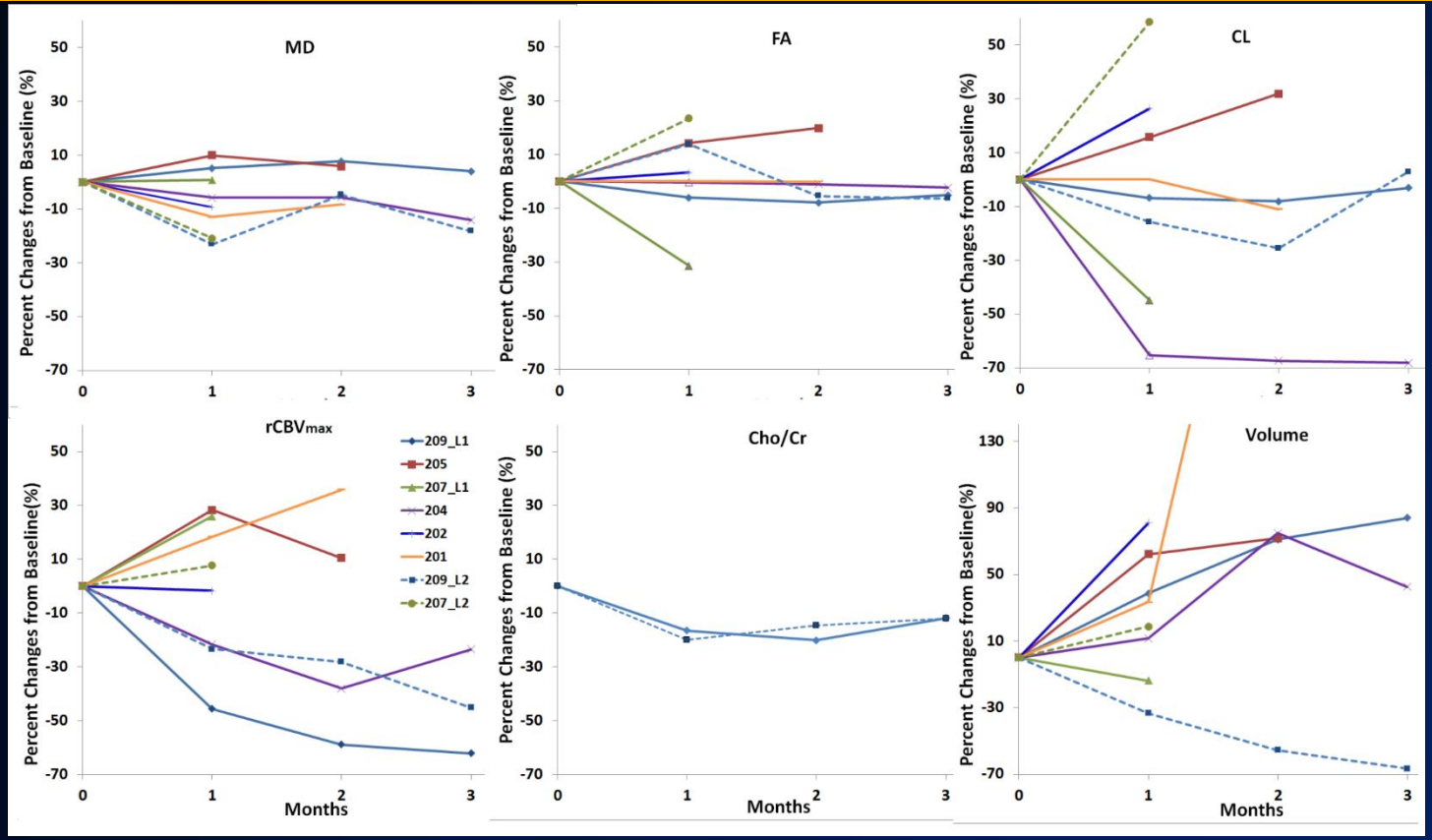


FIGURE 1 | 47-year-old woman with GBM, status post gross total resection and chemoradiation, treated with dendritic cell vaccine immunotherapy (ICT-107) (four vaccine treatments over 2 months prior to this imaging.) **(A)** Contrast-enhanced T1-weighted image shows large lobulated nodular enhancing lesion measuring 4.5 cm × 2.8 cm at site of previously resected GBM which had increased from prior scans. **(B)** FLAIR images demonstrate a large area of associated T2/FLAIR signal abnormality in the left hemisphere. **(C)** DSC shows elevated rCBV from the enhancing region of the tumor. Overall constellation of these conventional and advanced imaging findings were concerning for true progression. Logistic regression model combining rCBVmax with FA **(D)** and CL **(E)** according to analysis used in Wang et al. AJNR 2016 did not meet criteria for true progression (rCBVmax 4.396, FA 0.112, CL 0.0418) (12), suggesting a significant component of treatment-related changes. However immunotherapy was discontinued due to concern for progression. **(F)** Pathology from surgical resection performed 2 weeks later demonstrates predominant treatment effect (~80%) with hyalinization of vessels and tissues, geographic necrosis, and macrophage infiltration. Recurrent infiltrating glial tumor cells with marked nuclear pleomorphism were also present, comprising approximately 20% of the specimen. Abbreviations: GBM, glioblastoma multiforme; FLAIR, fluid attenuation inversion recovery; DSC, dynamic susceptibility contrast; rCBV, relative cerebral blood volume; rCBVmax, maximum relative cerebral blood volume; FA, fractional anisotropy; CL, linear anisotropy coefficient.

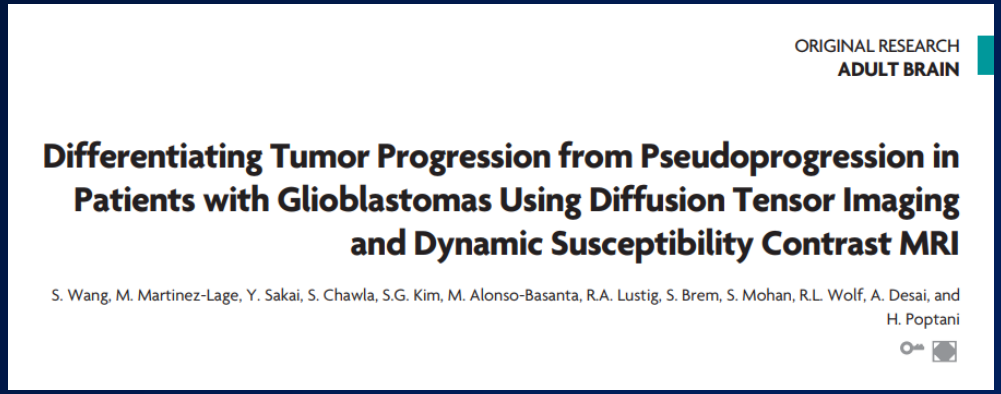
Anti EGFRvIII CAR-T cell therapy



Progression Probabilities (PP)

- Three parameters (FA, CL & $rCBV_{max}$) from the enhancing part of the tumor

β_0 = -16.17, β_1 = 194.01, β_2 = -285.65, & β_3 = 1.21.

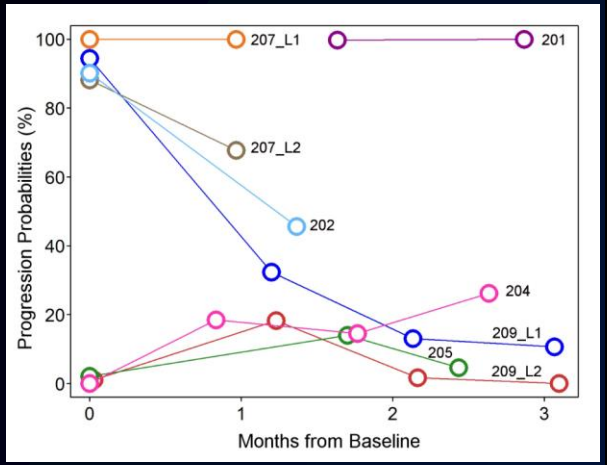

ORIGINAL RESEARCH
ADULT BRAIN

Differentiating Tumor Progression from Pseudoprogression in Patients with Glioblastomas Using Diffusion Tensor Imaging and Dynamic Susceptibility Contrast MRI

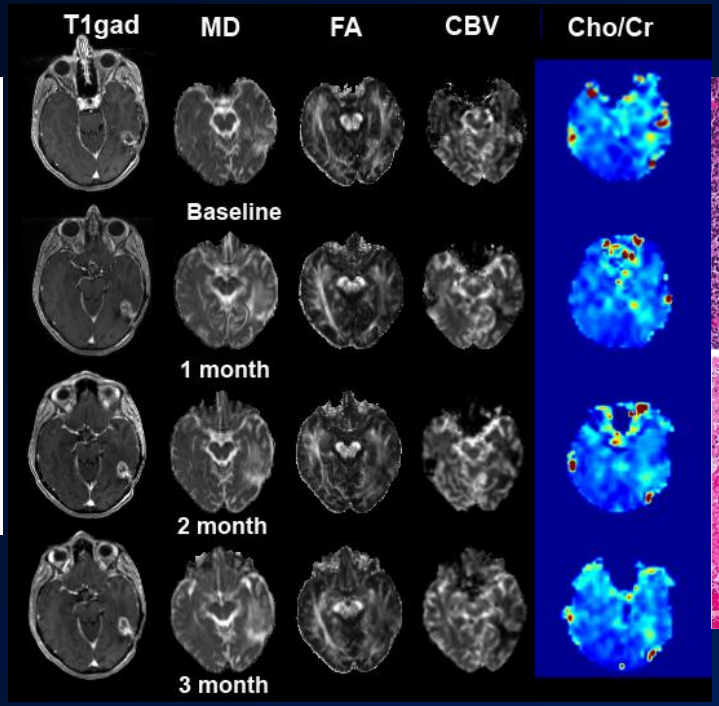
S. Wang, M. Martinez-Lage, Y. Sakai, S. Chawla, S.G. Kim, M. Alonso-Basanta, R.A. Lustig, S. Brem, S. Mohan, R.L. Wolf, A. Desai, and H. Poptani

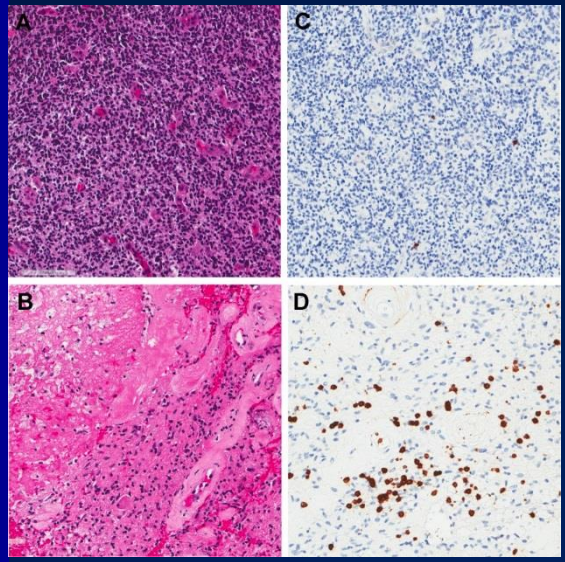
$$f(FA,CL,rCBV_{max}) = \frac{1}{1+\exp(\beta_0 + \beta_1 FA + \beta_2 CL + \beta_3 rCBV_{max})}$$

American Journal of Neuroradiology. January 2016, 37 (1) 28-36.



Changes of progression probabilities (PP) using the predictive model for 8 lesions in 6 patients. Probability of TP is 50-100%; PsP is 0-50%.

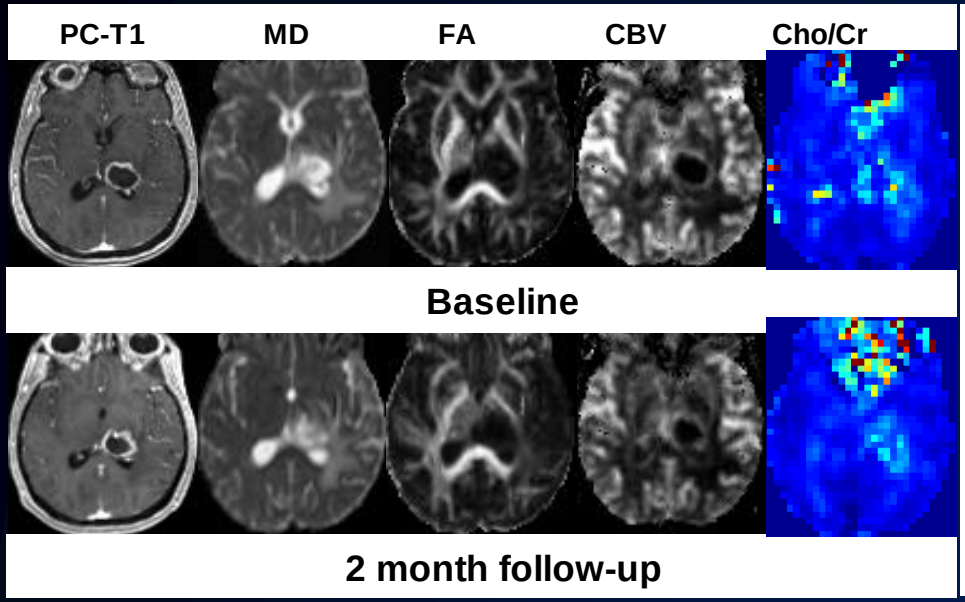




Case 209. Our model predicted it as PsP (PP =0.10 - 0.32) at 3 follow-up studies. HPE demonstrated predominant treatment-related changes including extensive geographic necrosis and hyalinized vessels (B) and increased T cells (D) 104 days after CAR-T cell infusion.

British Journal of Cancer: Special Issue on Immunotherapy (Under Review)

TTFields: Multi-parametric Approach



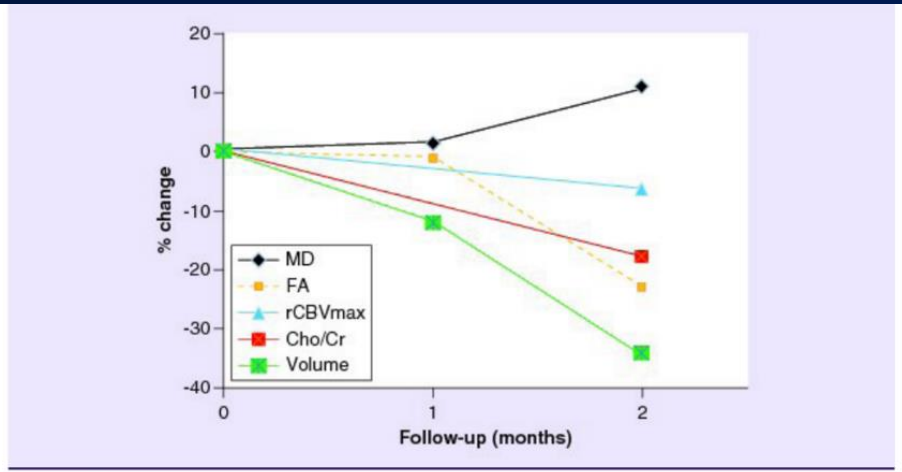


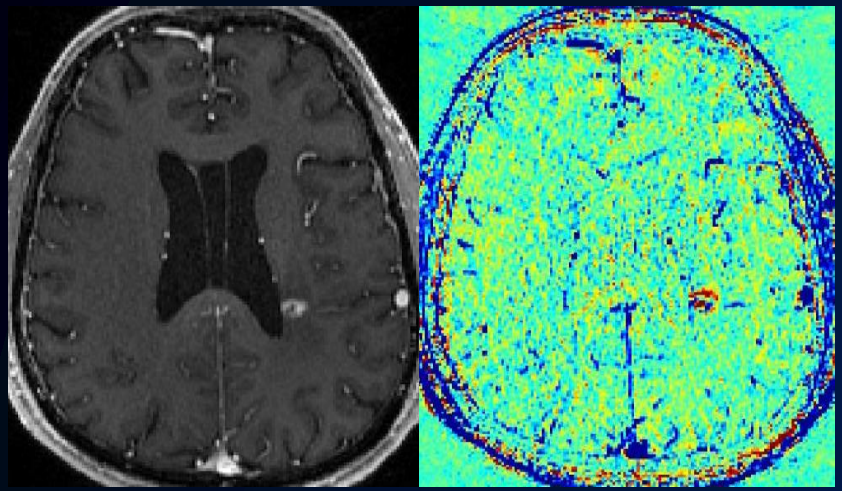
Figure 4. Percentage changes in parameters from baseline to 1- and 2-month follow-up periods from a patient with GBM treated with TTFields plus temozolamide. Trends toward decreased tumor volume, $rCBV_{max}$, Cho/Cr and FA along with an increased MD were observed at follow-up relative to baseline indicating tumor growth arrest.

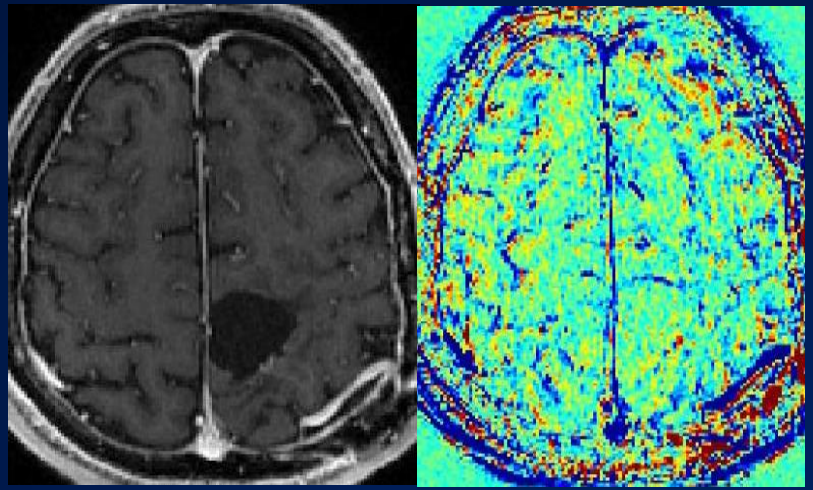
- PC-T1: Post-Contrast T1-weighted, MD: Mean Diffusivity, FA: Fractional Anisotropy, CBV: Cerebral Blood Volume, Choline to Creatine ratio

- Early response to TTFields showed trends toward
  - Increasing MD
  - Decreasing tumor volume, FA, rCBV and Cho/Cr

Mohan S, et al. Assessment of early response to tumor-treating fields in newly diagnosed glioblastoma using physiologic and metabolic MRI: initial experience. CNS Oncol. 2016 Jul;5(3):137-44.

Treatment Response Assessment Maps (TRAMs)





rCBVmax =2.12

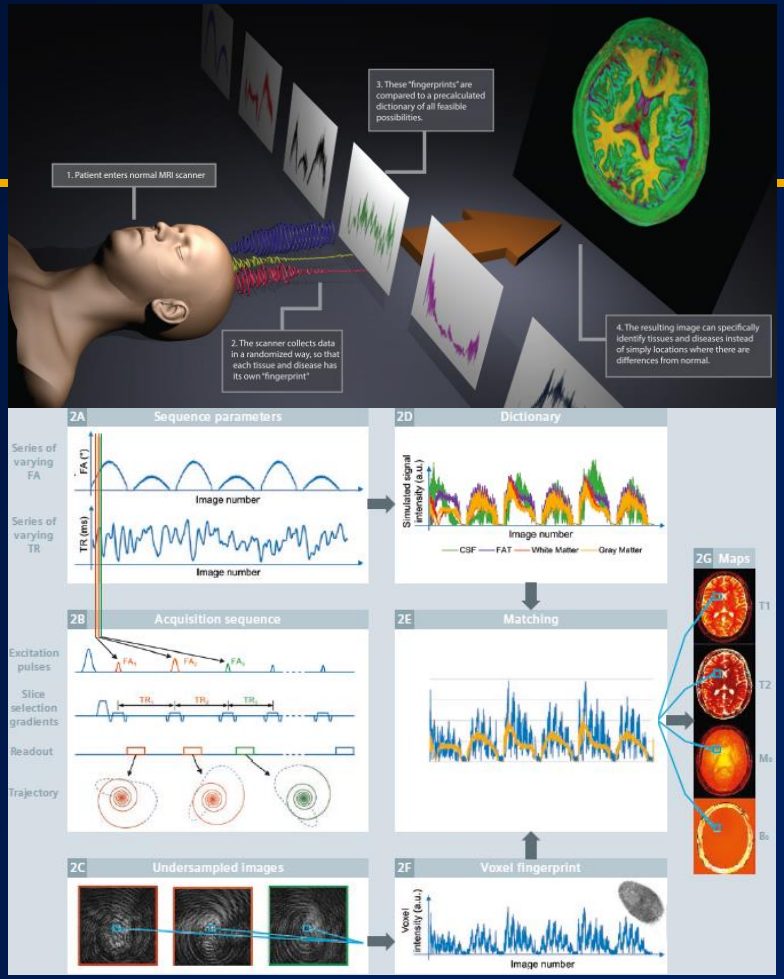
FA=0.17

MD =0.98*10^{-3}mm^2/s

Case # 1 @ Penn: New tool for response assessment!

MR fingerprinting

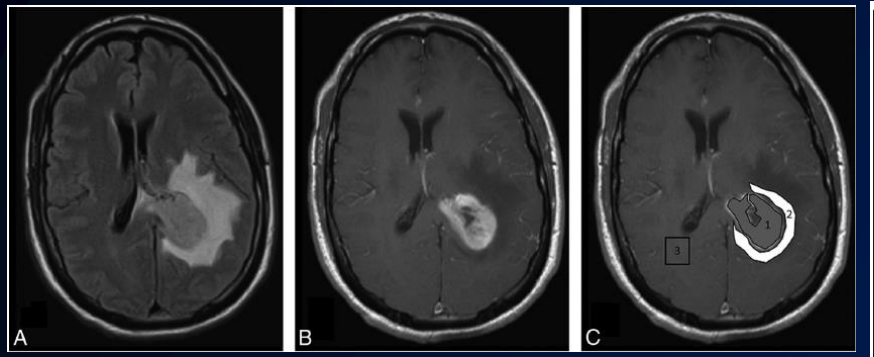
- Novel framework, where the pulse sequence is designed to measure tissue properties.
- Generates unique signals, or ‘fingerprints’, for each tissue within a single acquisition.
- Provides information to improve diagnosis, prognosis &/or therapeutic assessment.

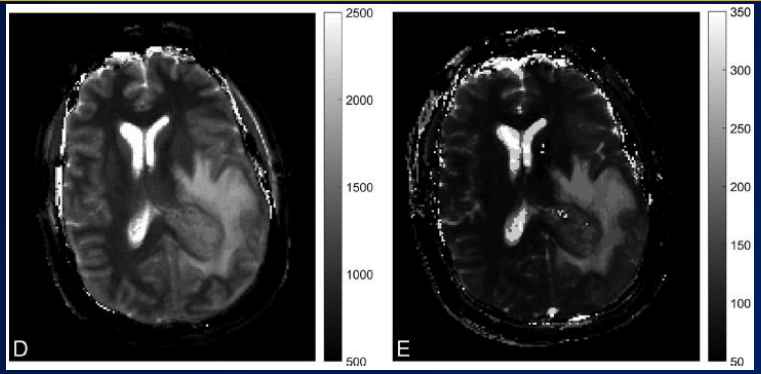


Ma D, et al. MR fingerprinting. Nature 2013; 495:187-192;

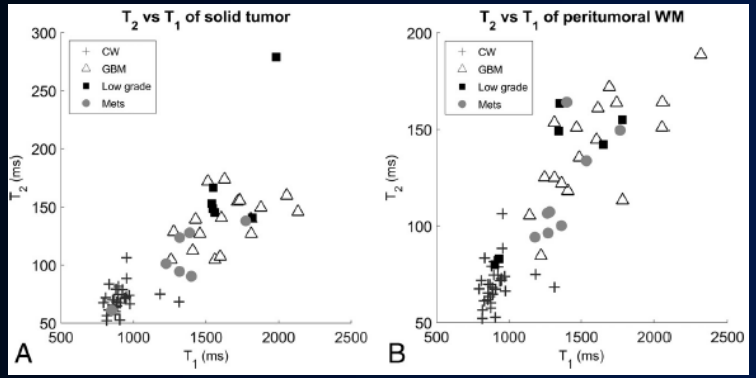
Courtesy: Chaitra Badve, MD, Case Western Reserve University

MRF: Applications - Differentiates LGG & Mets; GBM & LGG.





(A) FLAIR **(B)** Post-gad T1w images, **(C)** Post-gad T1w image with ROI overlay (central gray ROI=solid tumor; white ROI=peritumoral white matter; blank ROI=contralateral WM. **(D)** MRF-derived quantitative T1 map; **(E)** MRF-derived quantitative T2 map (grayscale).



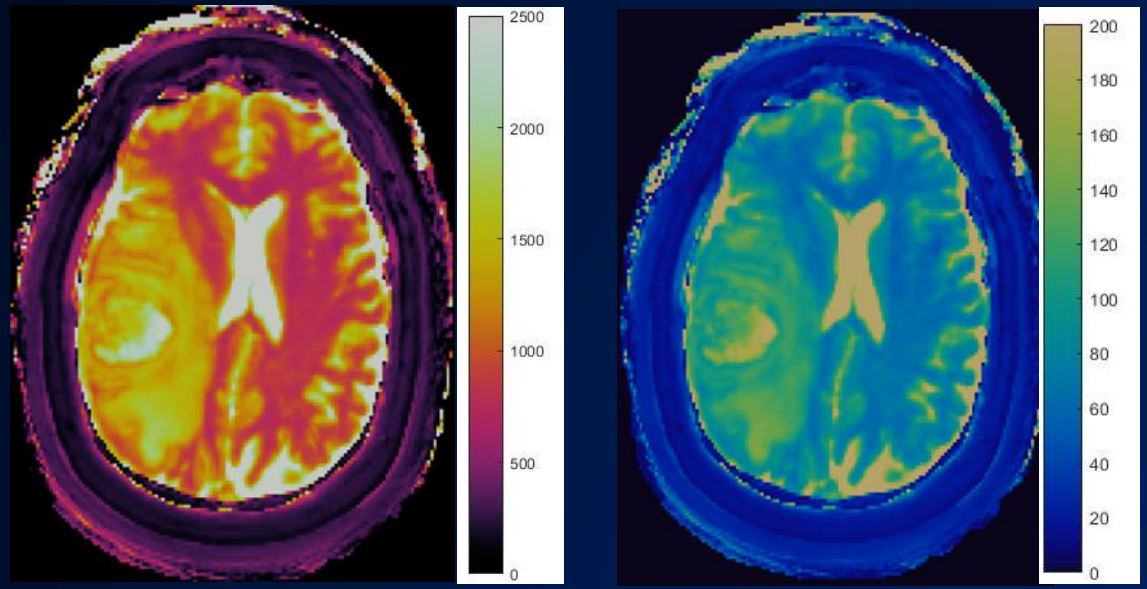
Scatterplot of T1 vs T2 values in all tumor types for different regions **(A)** Solid Tumor **(B)** Peritumoral WM

Badve C, et al. MR Fingerprinting of Adult Brain Tumors: Initial Experience Am J Neuroradiol 2017;38:492-499.

3D MRF in a GBM

Currently exploring MRF differentiation of brain tumors using 3D MRF.

Resolution: 1.2 x 1.2 x 3 mm^3



MRF-derived quantitative T1 & T2 maps. 3D acquisition allows whole brain coverage

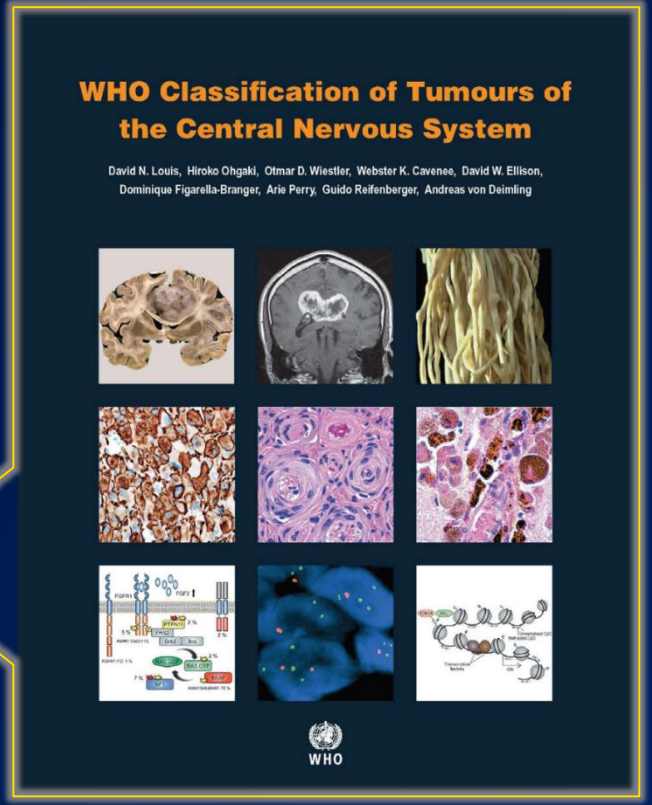
Badve C, et al. Volumetric 3D MR fingerprinting of adult brain tumors. Society for Neuro-Oncology Annual Meeting 2017; San Francisco, CA. *Oral (to be presented).*

GBM: A new look in 2016

Molecular & genetic tumor definition

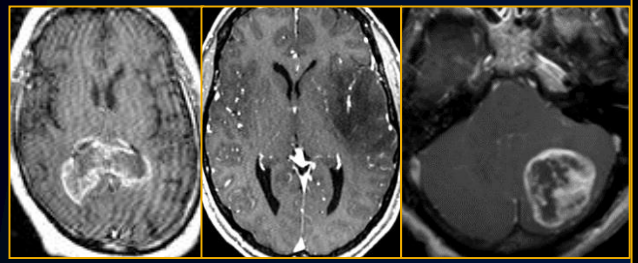
Advantages

- ✓ Greater correlation with tumor behavior
- ✓ Useful for clinical care & research
- ✓ More objective
- ✓ Provides insights into tumorigenesis



Key Update: Glioblastoma & IDH mutation

Only molecular marker included in the updated 2016 WHO classification



- Formally subdivided by *presence or absence of mutation in the isocitrate dehydrogenase (IDH) gene*
- Vast majority of mutations occur in codon 132 of IDH1, (IDH2 rare)

WHO Grade IV GBM IDH Mutation

YES

NO

GBM

IDH Mutant

GBM

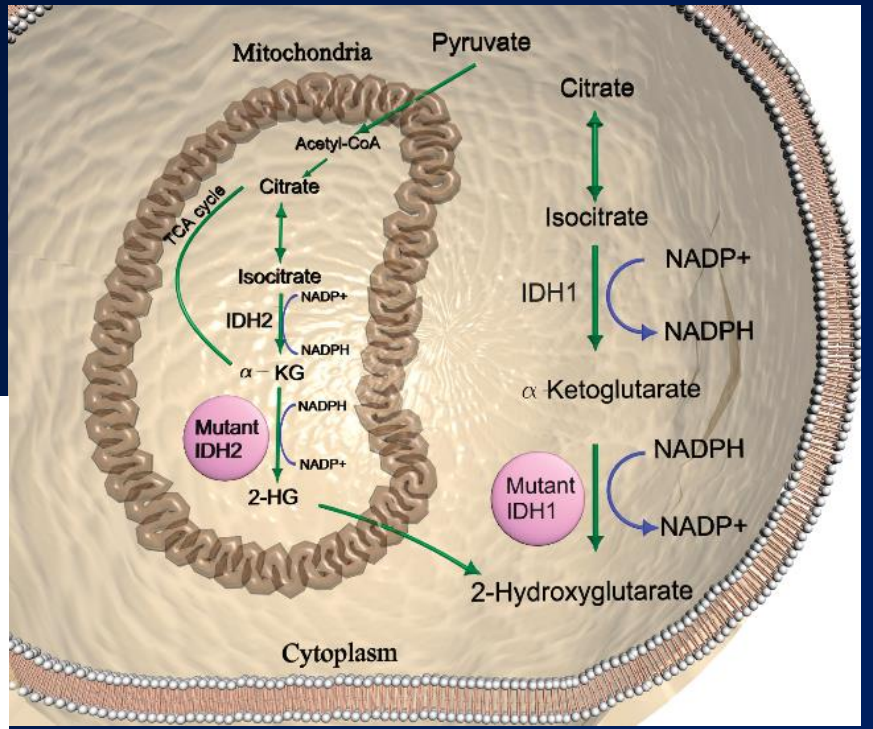
IDH Wild-type

WHO Grade IV Astrocytoma (GBM) in 2017

GBM, IDH Mutant	GBM, IDH wild-type
• ~10% of GBM	• ~90% of GBM
• Younger	• Older
• *Better prognosis*	• *Poorer prognosis*
• More likely MGMT methylated	• Most "primary" GBM
• Most "secondary" GBM	
• *Targeted therapies*	

Relevance to Radiology

- Mutant IDH causes accumulation of 2-HG (5-35 mM)
- *2HG can be detected by MRS*
- May influence surgical planning/therapy
- Response assessment



Verma *et al. J Transl Med* (2016) 14:274
DOI 10.1186/s12967-016-1035-1

Journal of Translational Medicine

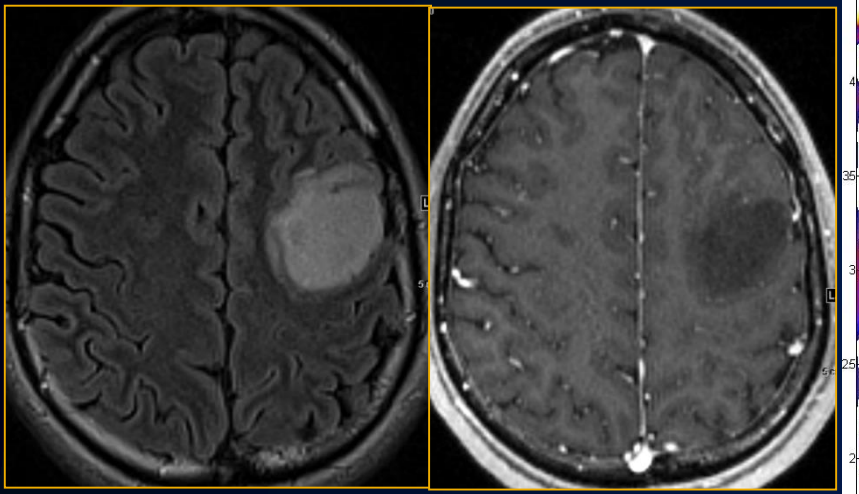
RESEARCH Open Access

Non-invasive detection of 2-hydroxyglutarate in IDH-mutated gliomas using two-dimensional localized correlation spectroscopy (2D L-COSY) at 7 Tesla

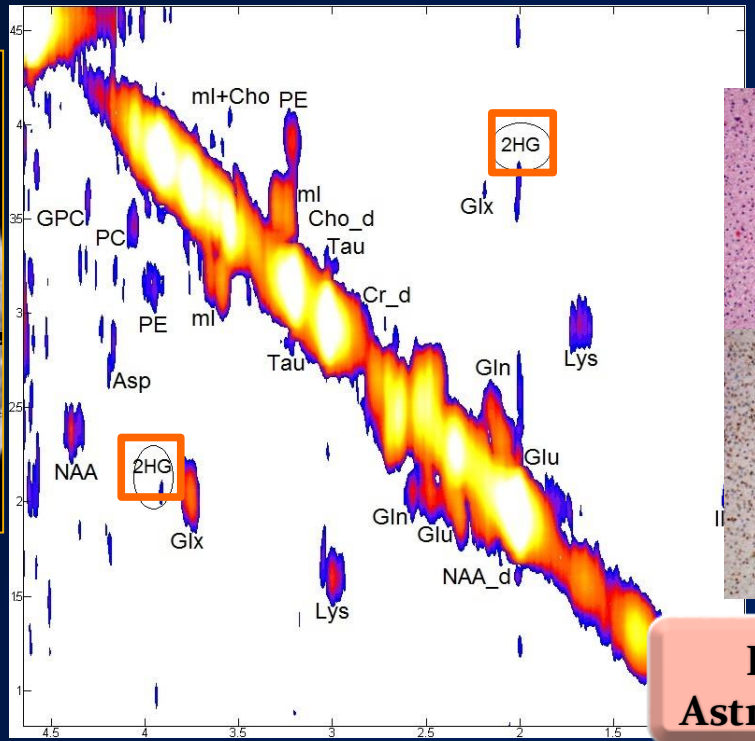
Gaurav Verma[1†], Suyash Mohan[1*†], MacLean P. Nasrallah[2], Steven Brem[3], John Y. K. Lee[3], Sanjeev Chawla[1], Sumei Wang[1], Rajakumar Nagarajan[4], M. Albert Thomas[4] and Harish Poptani[5]

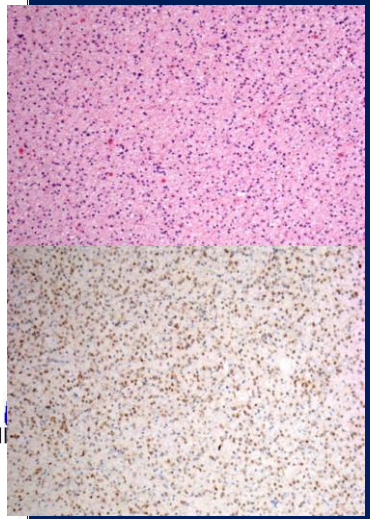
MR Spectroscopy at 7 Tesla

18 Y/M after a grand mal seizure



7T 2D L-COSY Spectrum

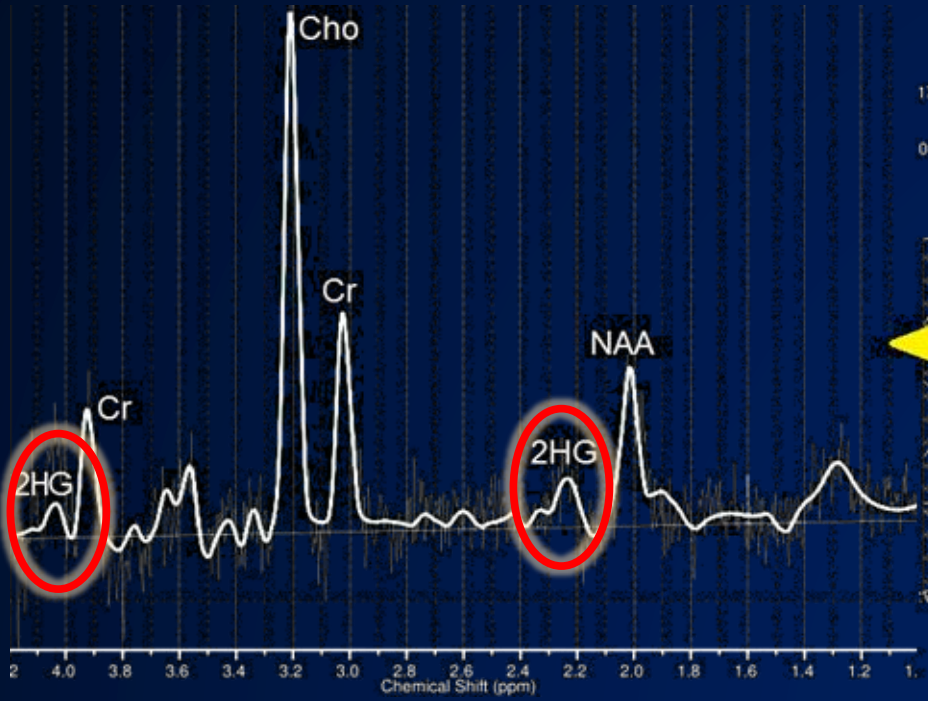


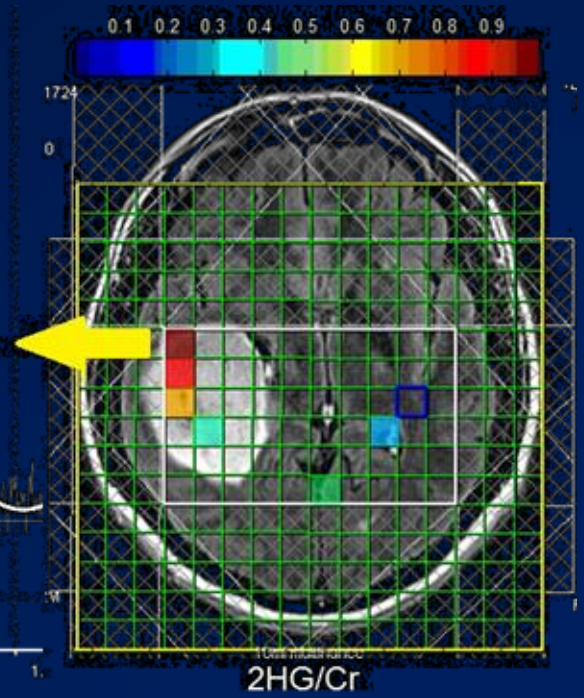


IDH Mutant Astrocytoma (G-II)

Chemical Shift Imaging (CSI) at 3.0 T

- 2D CSI
  - TE/TR = 97/1700 ms
  - 1.5 ml voxels
  - 6:53 min
  - *Optimized for 2HG*
- LCModel Fitting



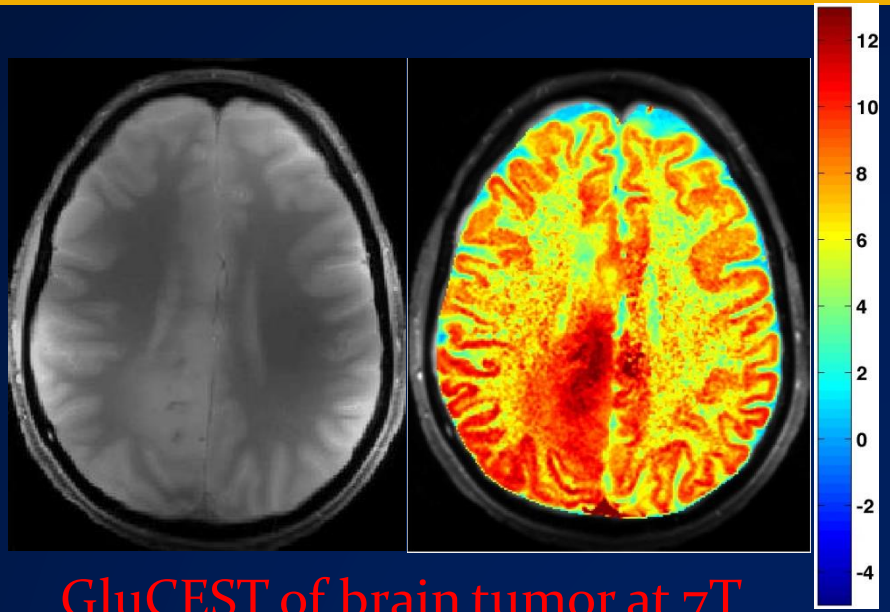


IDH Mutant Grade III AA

Verma G et al: ISMRM 2017

CEST imaging at 7.0 Tesla

- 3 open protocols
  - Glutamate CEST
  - Creatine CEST
  - Lactate CEST
- TP vs PsP
- Neuroinflammation after Immunotherapy

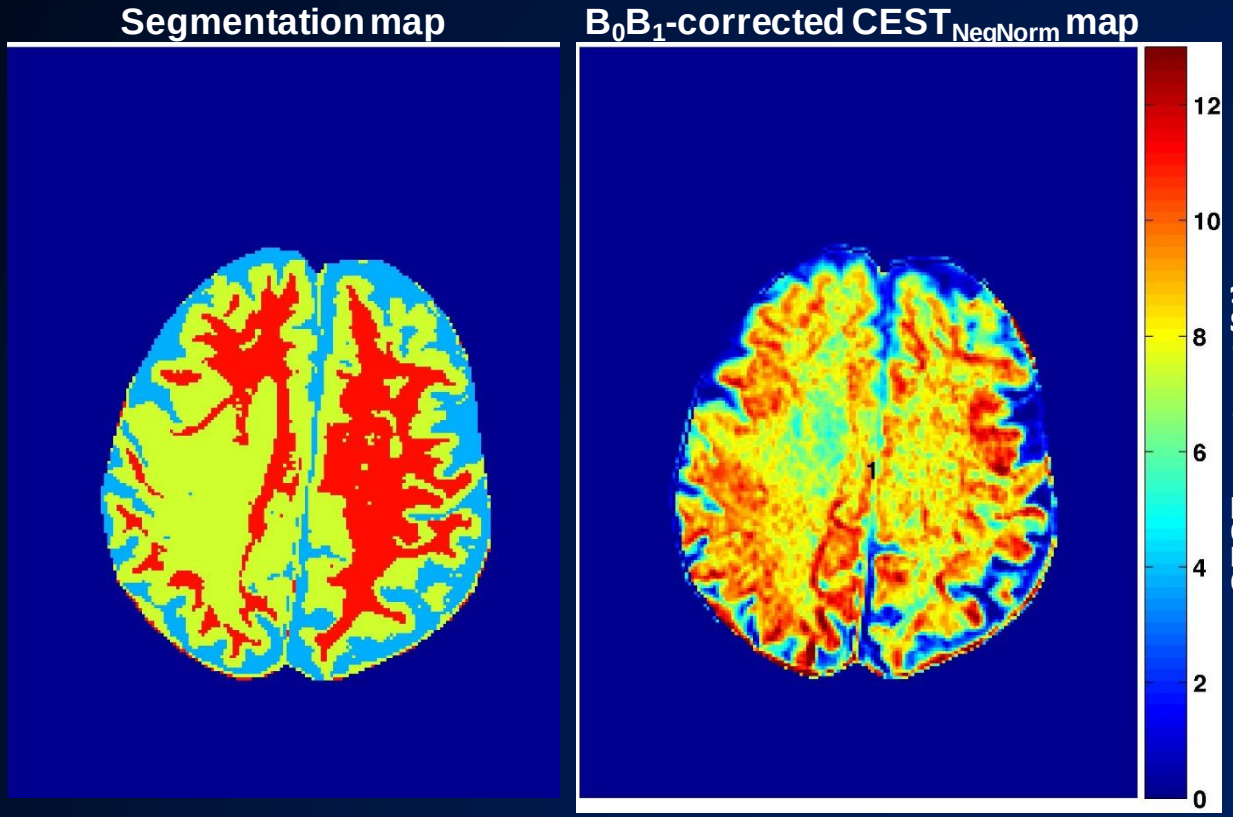


GluCEST of brain tumor at 7T

Collaboration between UPENN Neurology (Kate Davis) & Radiology (Ravi Reddy, Joel Stein, et al.) and Royal Melbourne Hospital: Andrew Neal, Prof Terence O'Brien, Prof Patrick Kwan

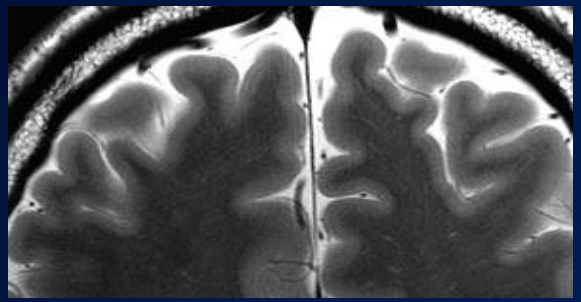
Glutamate CEST at 7Tesla: Low grade glioma

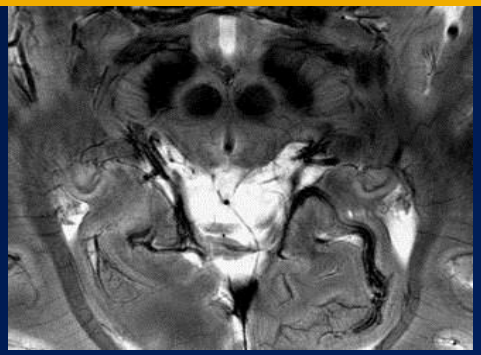
May 24, 2018

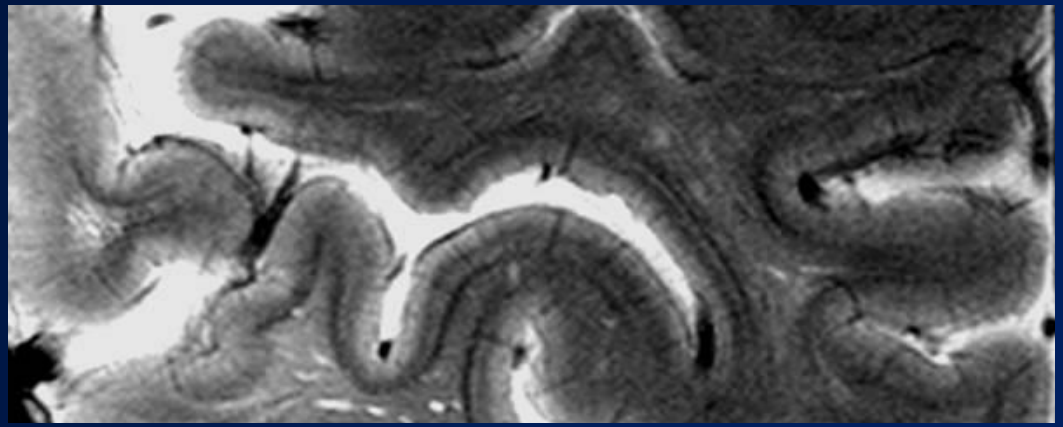


Ultra-high-field strength 7-Tesla MRI

- High signal
- High contrast
- High resolution
- ↑ iron and venous structures



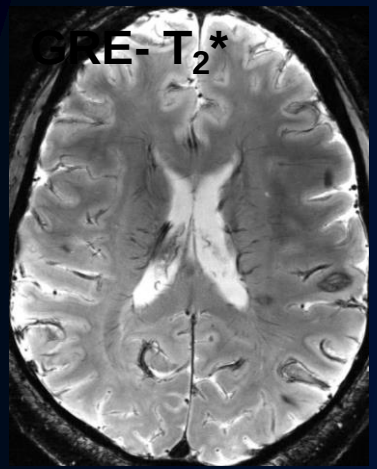


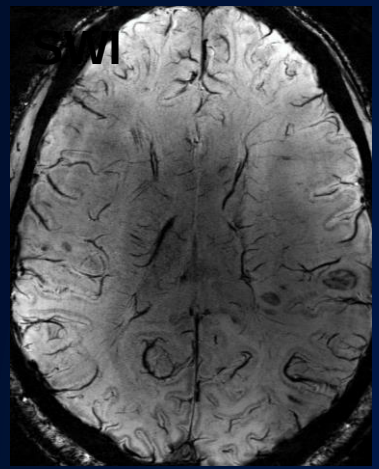


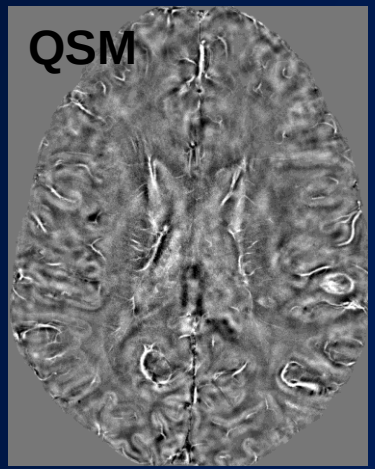
Courtesy – Sanjeev Chawla

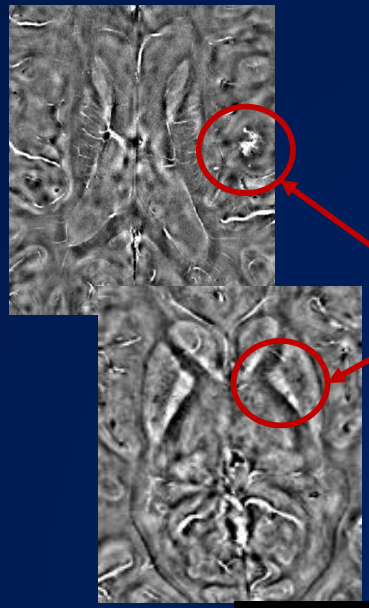
SWI & QSM on 7 Tesla

- Abnormal iron accumulation is associated with development of high-grade neoplasms.
  - Associated with profound iron mediated neuroinflammation & glutamatergic excitatory activities.
  - Over expression of transferrin receptors in tumors compared to normal brain/bland peri-tumoral edema.
- QSM: Newly developed technique offers a highly sensitive tool for iron detection & quantification









7T QSM maps demonstrate hyperintense signals in a glioma & globus pallidus indicating iron deposition

Courtesy – Sanjeev Chawla

Published OnlineFirst July 27, 2017; DOI: 10.1158/1078-0432.CCR-17-0560

Cancer Therapy: Clinical

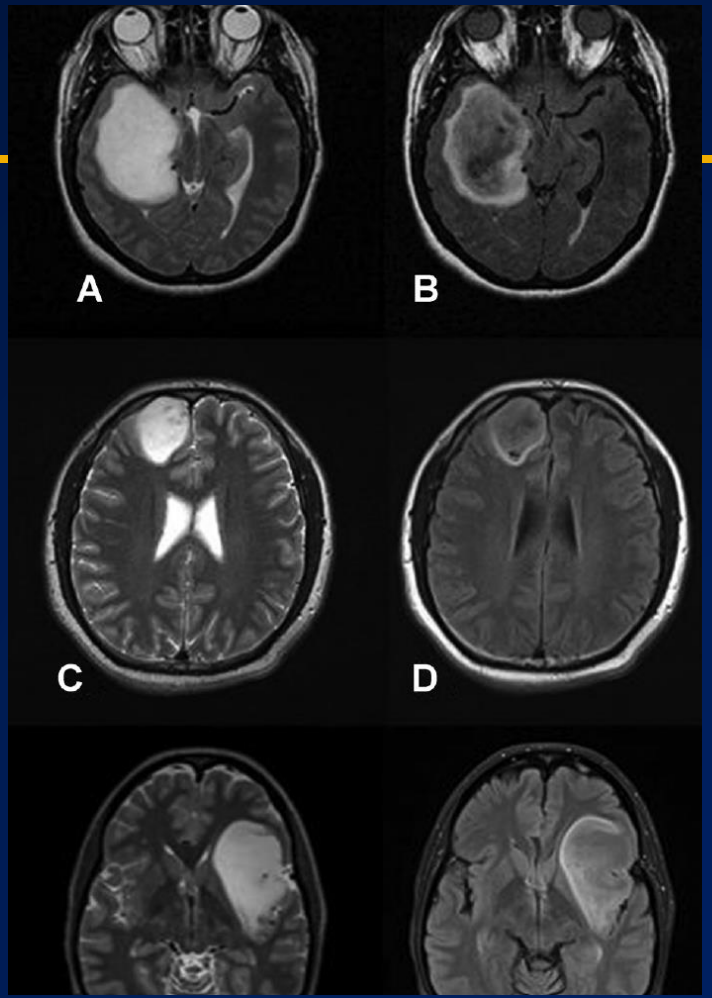
Clinical Cancer Research

T2–FLAIR Mismatch, an Imaging Biomarker for IDH and 1p/19q Status in Lower-grade Gliomas: A TCGA/TCIA Project

Sohil H. Patel[1], Laila M. Poisson[2], Daniel J. Brat[3], Yueren Zhou[2], Lee Cooper[4,5], Matija Snuderl[6], Cheddhi Thomas[6], Ana M. Franceschi[7], Brent Griffith[8], Adam E. Flanders[9], John G. Golfinos[10], Andrew S. Chi[10,11], and Rajan Jain[7,10]

Translational Relevance

Among lower-grade gliomas, the presence of the T2–FLAIR mismatch sign on routine clinical MRI is highly predictive of the *IDH*-mutant 1p/19q non-codeleted glioma molecular subtype, with 100% positive predictive value. The T2–FLAIR mismatch sign is associated with a survival profile that is similar to that of the *IDH*-mutant 1p/19q non-codeleted glioma subtype and more favorable to that of *IDH*-wild-type gliomas. Conventional imaging features that distinguish between the two molecular subtypes of *IDH*-mutant glioma (1p/19q codeleted and 1p/19q non-codeleted) with high specificity are lacking, and such correlates may be clinically meaningful given the distinct prognoses between these two cohorts. Identification of this simple and robust MRI biomarker may enable a more informed pretreatment management plan and patient counsel.

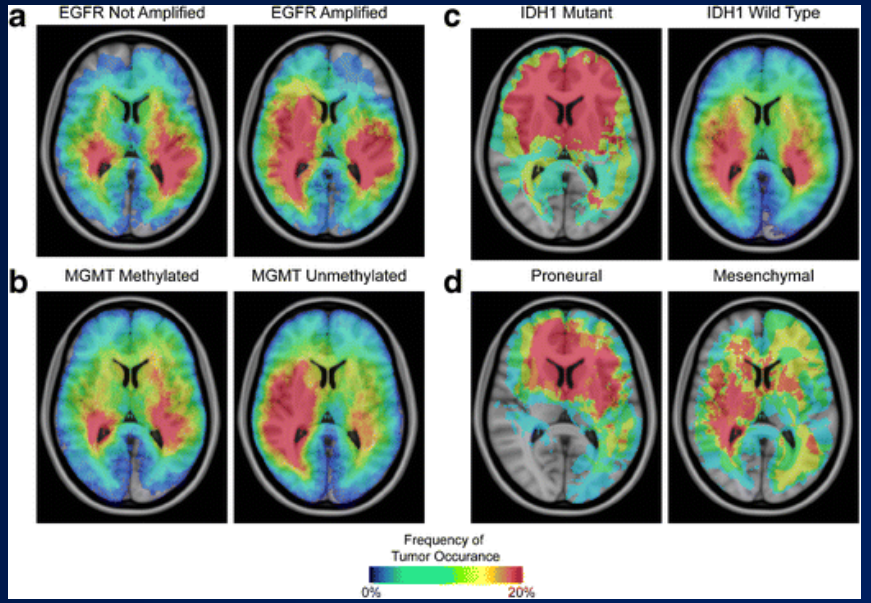


Radiomics & Habitat Imaging

- *Radiomics:*
  - Images Are More than Pictures, They Are Data
    - A high-throughput process in which a large number of shape, edge, & texture metrics are extracted & quantified in a reproducible form.
- *Habitat Imaging:*
  - These quantitative metrics can provide important insights into tumor phenotype & as well as the interaction of the tumor with its microenvironment, defined as “habitat imaging”.

Radiogenomics: what it is & why it is important.

- A new direction in cancer research that focuses on the relationship between imaging phenotypes & genomics.
  - Referred to as *radiogenomics* or *imaging genomics*.
- Significance?
  - *Assessing tumor heterogeneity*
  - Improved decision making
  - Improved patient outcomes.

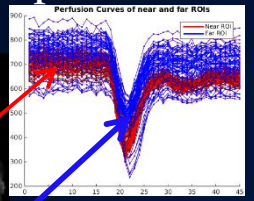


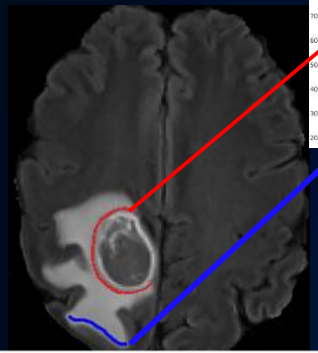
Ellingson BM. Radiogenomics & imaging phenotypes in glioblastoma: novel observations & correlation with molecular characteristics. Curr Neurol Neurosci Rep. 2015; 15(1): 506.

In Vivo Detection of EGFRvIII in GBM using MR perfusion
Heterogeneity in peri-tumoral tissue reflecting high/low degree of infiltration

T_1-Gad, T_2-FLAIR, DSC-MRI → Annotation of Near & Far ROIs (T1 Gad & T2 FLAIR) → Statistical Analysis of Perfusion Dynamics (DSC-MRI)

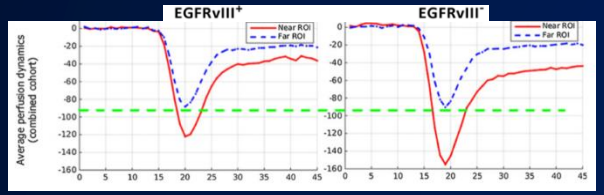
142 *de novo* GBM patients





The Φ index!

EGFR VIII - | EGFR VIII +



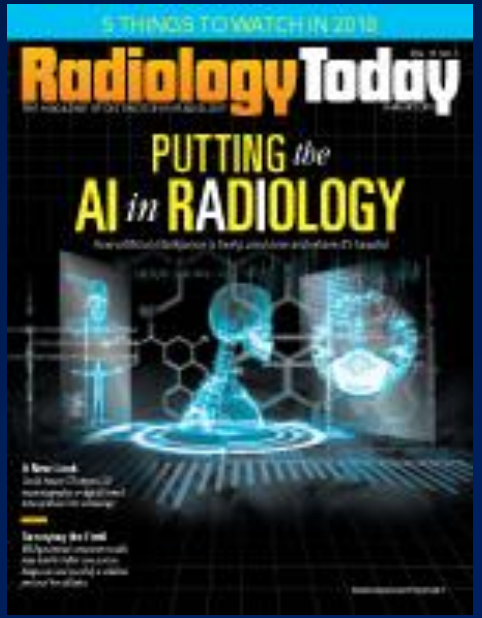
- *Non-invasive imaging signature of EGFRvIII expression.*
- ROIs were drawn within on near & far regions of peritumoral edema, to assess tumor cell infiltration.
- PCA to summarize the perfusion signal within the ROI's through the PHI/ϕ index.
- More aggressive infiltrative pattern seen in EFGFRvIII+ tumors, the perfusion signal was more similar between near and far ROI's in EGFRvIII+ tumors.

Bakas S, ..., O'Rourke DM, Davatzikos C. In Vivo Detection of EGFRvIII in Glioblastoma via Perfusion Magnetic Resonance Imaging Signature Consistent with Deep Peritumoral Infiltration: The ϕ-Index. Clin Cancer Res. 2017 Aug 15;23(16):4724-4734.

Advances in Radiology: What's new in 2018!

5 Things to Watch in 2018

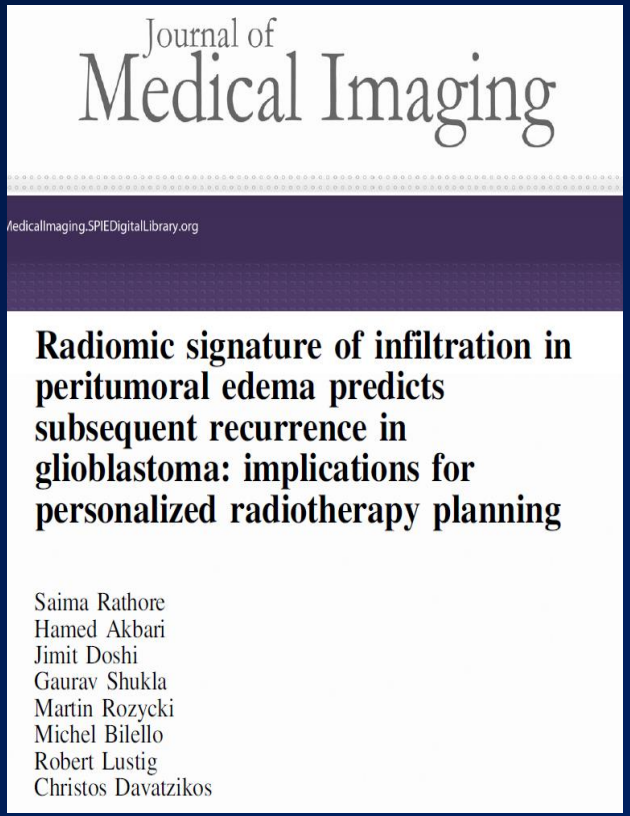
1. Artificial Intelligence
2. Artificial Intelligence
3. Artificial Intelligence
4. Artificial Intelligence
5. Artificial Intelligence



By Dave Yeager
Radiology Today
Vol. 19 No. 1 P. 22

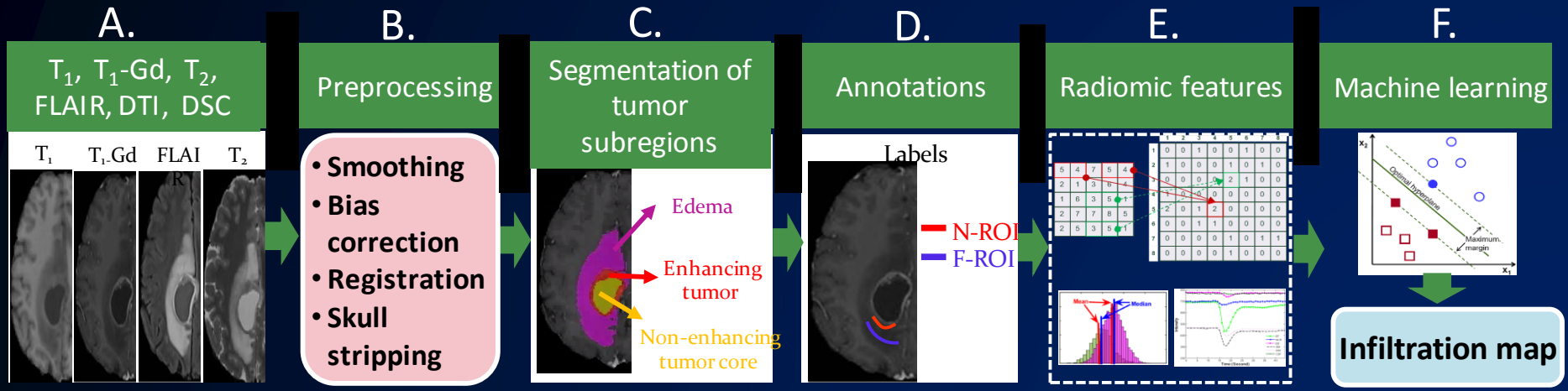
Artificial intelligence in neuro-oncology

- Combine advanced multi-parametric MRI with ML
  - To predict tumor recurrence beyond the tumor margins
- By leveraging these advances in computational neuro-oncology and by conjoining the ultra-high field properties of 7Tesla MRI and AI.
- To develop a plan for precision diagnostics and predictive modeling for GBM patients.



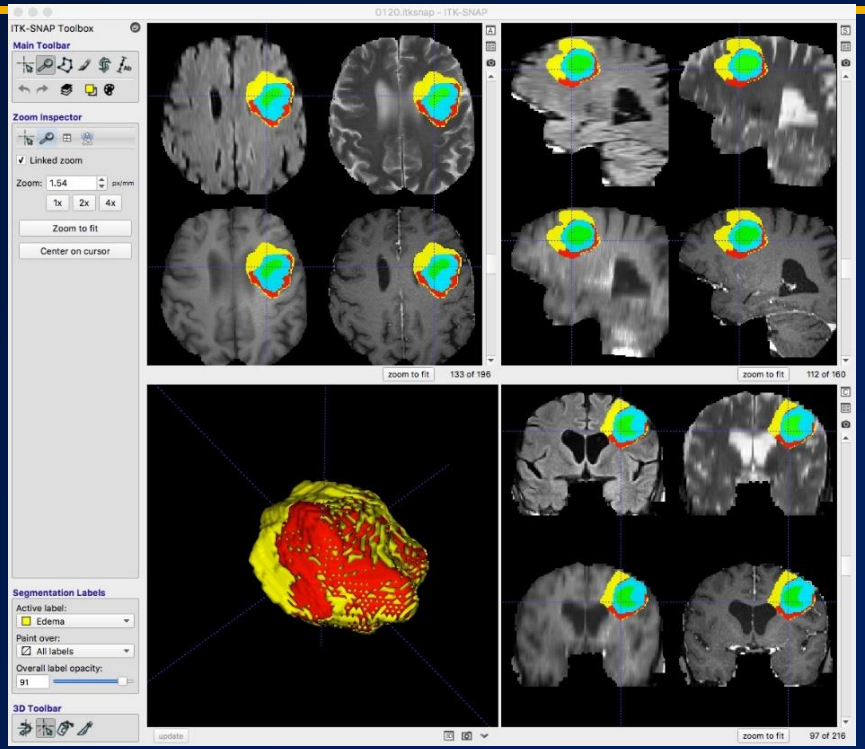
Machine Learning: Prediction of location of recurrence

- Non-invasive *in vivo* delineation of the areas of tumor infiltration and prediction of early recurrence
  - A method for estimating peritumoral edema infiltration using radiomic signatures



Robust segmentation algorithms: ITK-SNAP

- Minimal operator input
- Imaging informatics
  - Prognostic & predictive models & noninvasive disease monitoring.

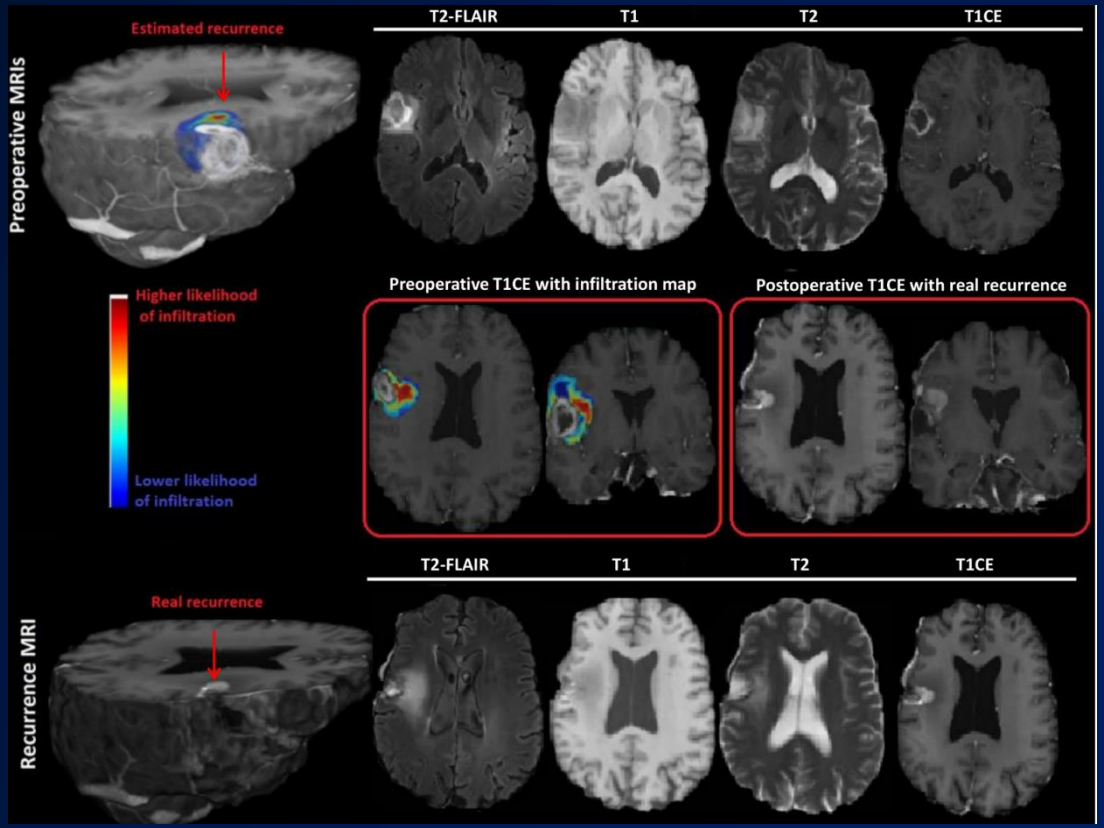


Courtesy: Joel Stein MD, Ph.D & Penn Image Computing & Science Lab

Neuroinformatics: Accepted

Machine Learning techniques & predictive modelling

- Application of ML to multi-parametric advanced MRI can predict GBM recurrence.
  - 3T MRI studies prospectively validated on 34 GBM patients.
- Regions predicted pre-operatively to present early neoplastic recurrence were 10 times more likely to recur, based on follow-up MRIs & pathology-proven recurrence.



7T clinical protocol for management of GBM

Precision diagnostics:

- Noninvasive in vivo delineation of invisible tumor infiltration
- Prediction of recurrence
  - Utilizing 7Tesla MRI & radiomic signatures determined via ML.

Personalized therapeutics:

- Targeted intensification of local therapies
- *Super-total resection* &/or *intensification of postoperative radiation* thereby paving way to personalize treatment.

Longer-term goal: Potentially delaying recurrence
Prolonging overall survival (OS)
Improve outcomes

Looking Beyond the Visible: Precision Diagnostics for GBM Coupling Ultra-High Field Capabilities of 7-Tesla with Machine Learning








Donald M. O'Rourke, MD
Neurosurgery

Christos Davatzikos, PhD
Radiology

MacLean Nasrallah, MD, PhD
Neuro-Pathology

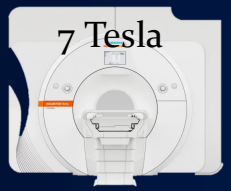
Saima Rathore PhD
Radiology

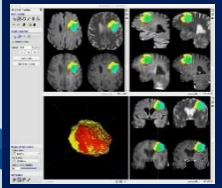
Robert Lustig, MD
Radiation Oncology

Ravinder Reddy, PhD
Radiology

Sumei Wang, MD
Radiology

Sanjeev Chawla, PhD
Radiology





PCPM Accelerator Fund Proposal

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Radiology:

- Mitchell Schnall, MD, PhD
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- Laurie Loevner, MD
- Ronald Wolf, MD, Ph.D
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