

Neuroimaging Predictors of Survival, Pathology and Molecular Profiles in TCGA Glioblastomas

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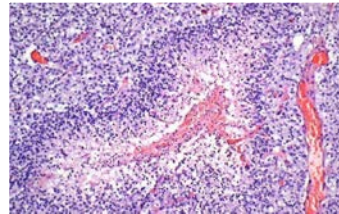
Emory University¹, Thomas Jefferson University²



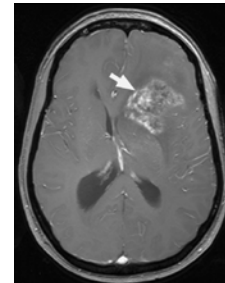
In Silico research using public data



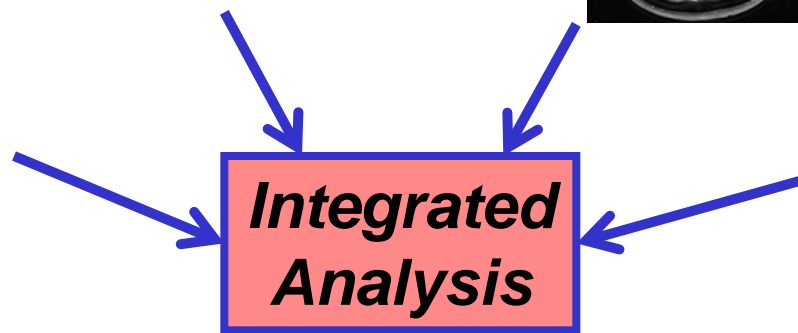
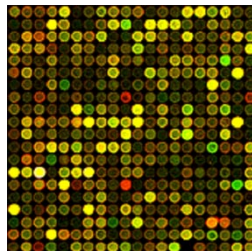
histology



radiology



molecular



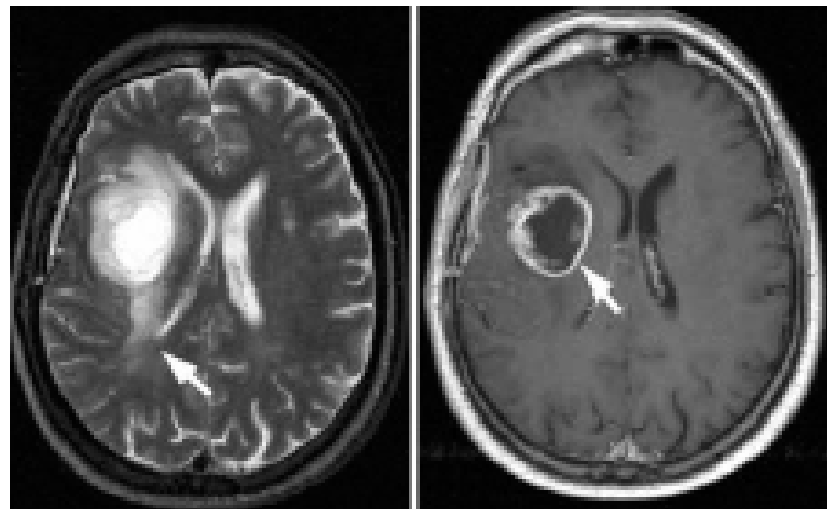
clinical/pathology

	A	B	C	D	E
1	Age at Dx	Gender	Survival	Disease	
2	30-34	F	>60M	OLIGODENDROGLIOMA	
3	50-54	M	--	GBM	
4	50-54	M	--	GBM	
5	50-54	F	30-36M	GBM	
6	20-24	M	--	UNKNOWN	
7	65-69	M	12-18M	UNKNOWN	
8	55-59	F	--	ASTROCYTOMA	



Glioblastoma Multiforme (GBM)

- Most common form of primary brain tumor
- Grade IV Astrocytoma
- 14 month median survival
- First tumor in NCI's *The Cancer Genome Atlas* (TCGA)
 - 500 patients from participating hospitals
 - mRNA transcription, CGH, sequence, DNA methylation
 - Neuroimaging
 - Whole slide pathology images





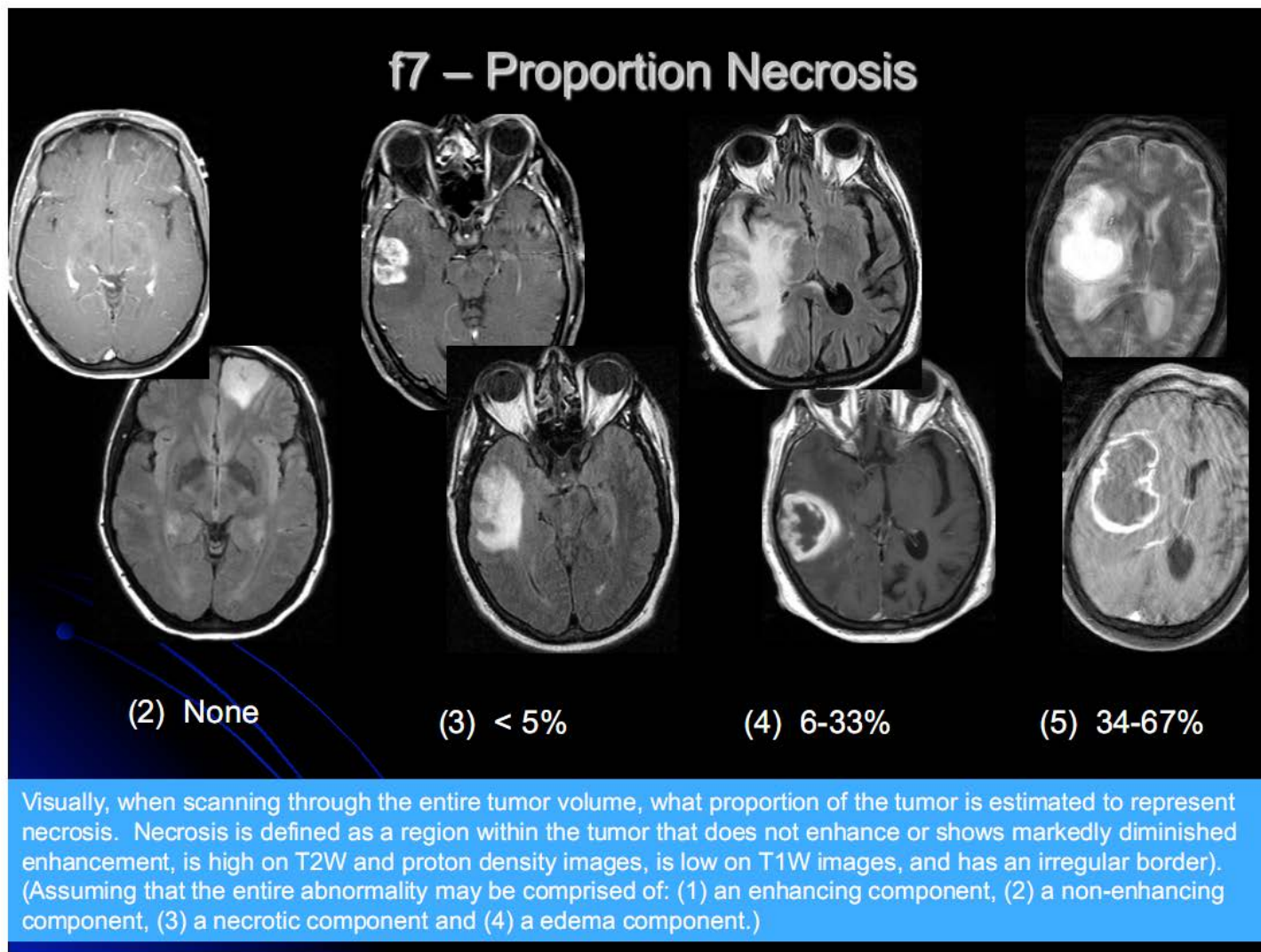
General Methodology Employed in our In Silico Center

- Goal is to develop human and/or machine based assessments of image features
- A standardized imaging feature (dubbed VASARI) was developed
- Feature set consists of 30 features that describe the size, location and appearance of the MRI image set
- MRI image provides a global view of the tumor
 - Small tumor adjacent to motor area (e.g. eloquent cortex) has vastly different outcome than a small tumor in frontal lobe





Examples of the feature set

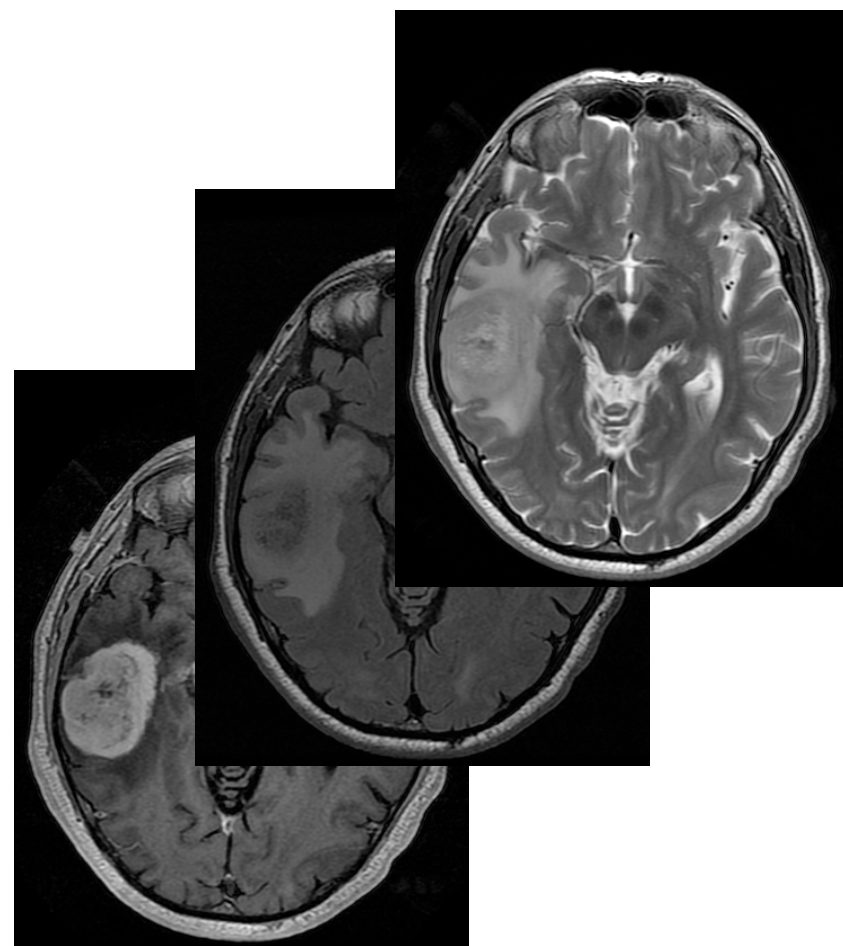




Proportion Enhancing Tumor



1-5%



68-95%



Capturing structured annotations and markups AIM Data Service

The screenshot displays the AIM TCGA on ClearCanvas Workstation 3.0 interface. The main window shows an axial T1 MRI scan of a brain with two yellow dashed lines indicating tumor measurements. The left sidebar contains a table of available AIM annotations:

Name:	TCGA-06-0164_trr_2...
AE:	Temporal lobe
IO:	mass

Below the table is a [Show Study](#) link with a red arrow pointing to it, labeled "An existing AIM instance".

The main window displays the following information:

- TCGA-06-0164 125307
- AXIAL T1 SIG AD
- 12-Jan-1885
- Acq: -
- Se: 10/13
- Im: 3/4
- Loc: H34.0

Two tumor measurements are shown:

- TCGA-06-0164_trr_2011-03-28 13:21 PM 4.28 cm
- TCGA-06-0164_trr_2011-03-28 13:21 PM 3.20 cm

Technical details at the bottom left: 256 x 192, ET: 0, TR: 500.00 ms, TE: 14.00 ms, HEAD, Thk: 15.0 mm, Zoom: 2.87x, W:976 L:488 (Auto). Technical details at the bottom right: 15000.0T, BAY1OC0, DFOV: 24.0 x 24.0 cm.

The right sidebar shows the "AIM Annotation" panel with the following settings:

- AIM Template: Brain Tumor Measurement TCGA(VASARI-3)
- Annotation Name: TCGA-06-0164_trr_2011-04-01 17:54 PM
- Lesion Location:
 - 01 - Tumor Location (F1):
 - Frontal lobe
 - Temporal lobe
 - Insula
 - Parietal lobe
 - 02 - Side of Tumor Epicenter (F2):
 - 03 - Eloquent Brain (F3):
 - No Eloquent Brain
 - Speech Motor
 - Speech Receptive
 - Motor
- Lesion:
 - Morphology of Lesion Substance
 - 04 - Enhancement Quality (F4):
 - 05 - Proportion Enhancing (F5):
 - 06 - Proportion nCET (F6):
 - 07 - Proportion Necrosis (F7):
 - 08 - Proportion of Edema (F14):

Buttons at the bottom right: Create Annotation, User Info.

A red arrow points to the "Importing an AIM template" button in the top right corner of the interface.



Systematic assessment of tumor imaging properties

Data was obtained from the Cancer Imaging Archive
<http://cancerimagingarchive.net>

- Current data set is from 72 patients
- Data is now available from ~125 GBM patients that were part of the TCGA data collection
- Each case was reviewed and scored independently by 3 neuroradiologists
- Consensus measures were obtained and used for this analysis



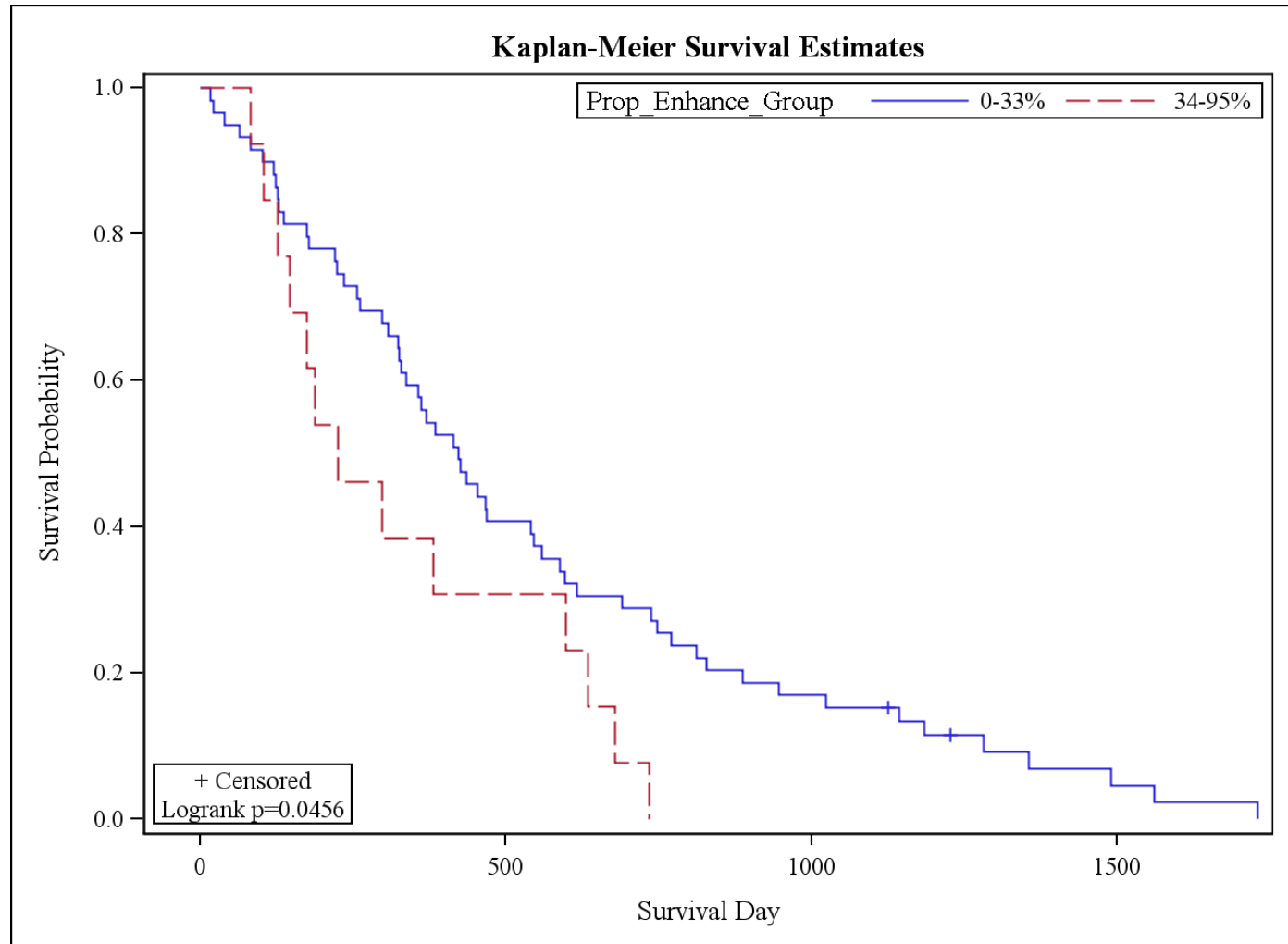
Imaging Predictors of Survival

Neuroimaging Feature	p value
Edema	0.48
Contrast Enhancing Tumor	0.004
Necrosis	0.37
Non-contrast Enhancing Tumor	0.83

Variable		Hazard Ratio (95% Confidence Limits)	p value
Karn Score		0.955 (0.933, 0.978)	0.0001
Contrast Enhancing Tumor	06-33% vs 0-5%	0.528 (0.196, 1.425)	0.025
	34-95% vs 0-5%	1.446 (0.485, 4.312)	



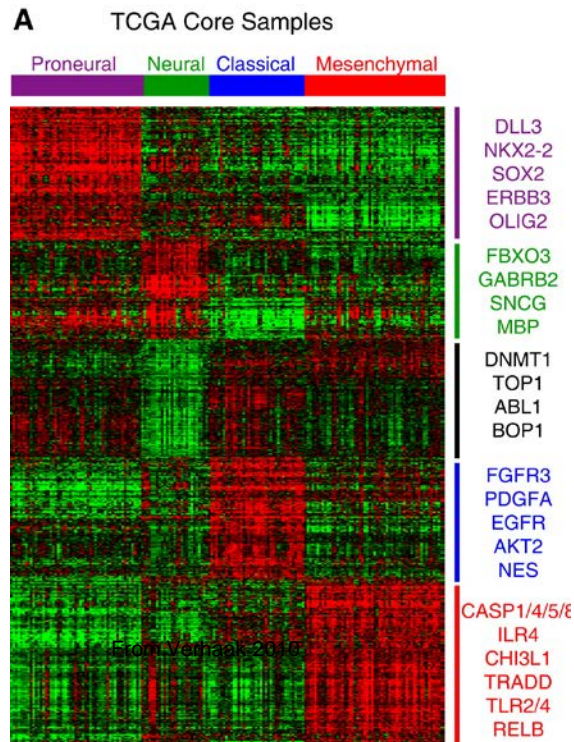
Percent of Contrast Enhancement was significantly associated with shorter survival





Tumor Subtypes and Imaging Features

Do tumor genotypes “look” different?



- The Mesenchymal subtype were noted to have significantly lower rates of non-contrast enhancement compared to other tumor subtypes ($p < 0.01$).



MR Imaging Results

- The Proneural subtype was associated with a low degree of contrast enhancement (0-5%) ($p < 0.01$).

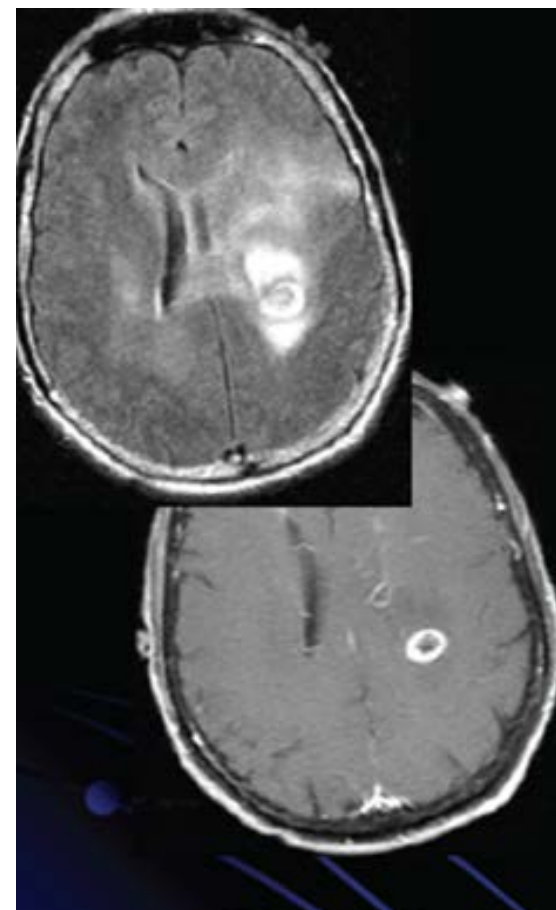
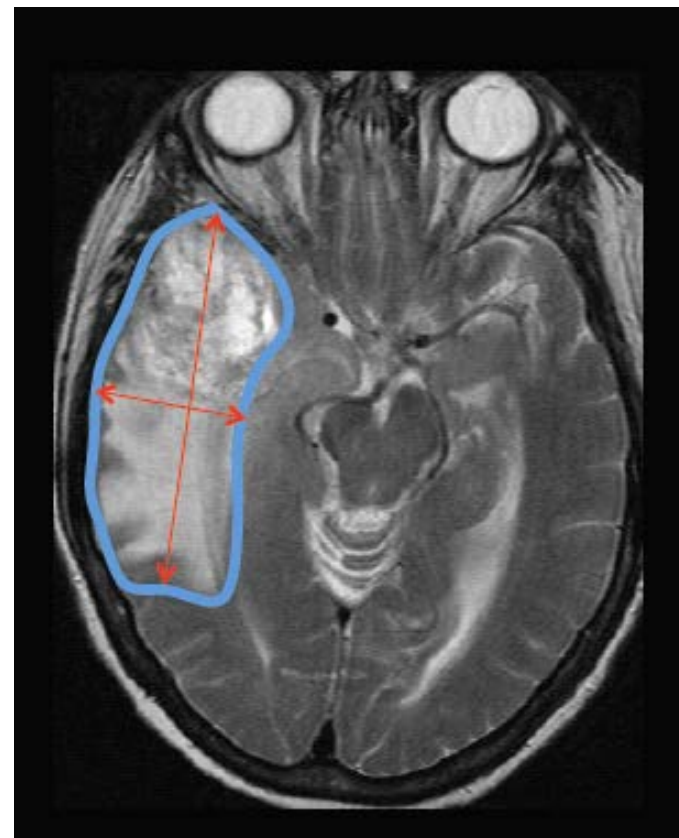




Image based-features and mutation status

- *EGFR* mutant GBMs (11/49) were *larger* based on the T2-weighted FLAIR images than wild type *EGFR* GBMs ($p < 0.05$).
- *TP53* mutant GBMs (9/49 patients) were *smaller* than those that were wild type ($p < 0.006$)





Conclusions

- Imaging based features can provide important prognostic information, even after accounting for other clinical variables
- Current qualitative work suggests genotypes may be associated with imaging phenotypes

Future Work:

- Increase sample size (in progress)
- Move from ordinal assessments (0-5%, 6-33%, 34-67%) to continuous based assessments of tumor compartments (e.g. volumetrics)
- More sophisticated feature extraction to include texture/size/location and voxel-based assessments



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The TCGA Glioma Research Group

If you have imaging data for TCGA contributed cases available and would like to contribute, please contact kirbyju@mail.nih.gov (Justin Kirby) or John Freymann (john.freymannj@mail.nih.gov) as we can help with deidentification and sharing

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