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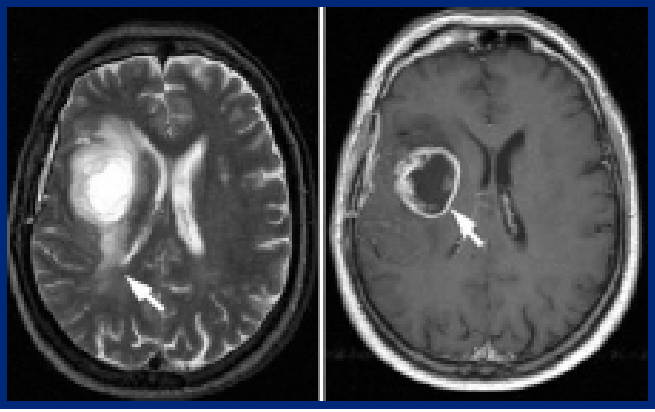

Neuroimaging Predictors of Survival, Pathology and Molecular Profiles in TCGA Glioblastomas

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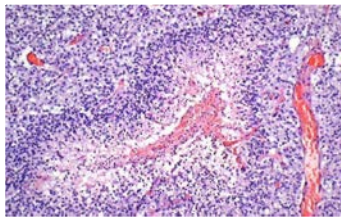
In Silico research using public data

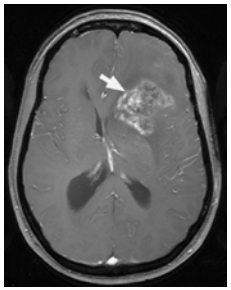
THE CANCER GENOME ATLAS

REMBRANDT

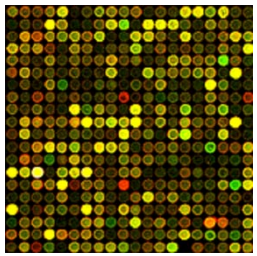
histology



radiology



molecular



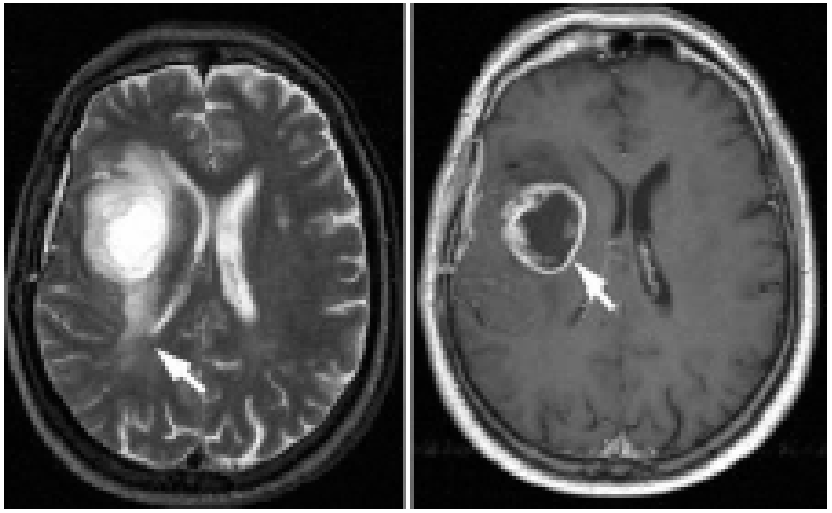
Integrated Analysis

clincal\pathology

	A	B	C	D	E
1	Age at Dx	Gender	Survival	Disease	
2	30-34	F	>60M	OLIGODENDRO	
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

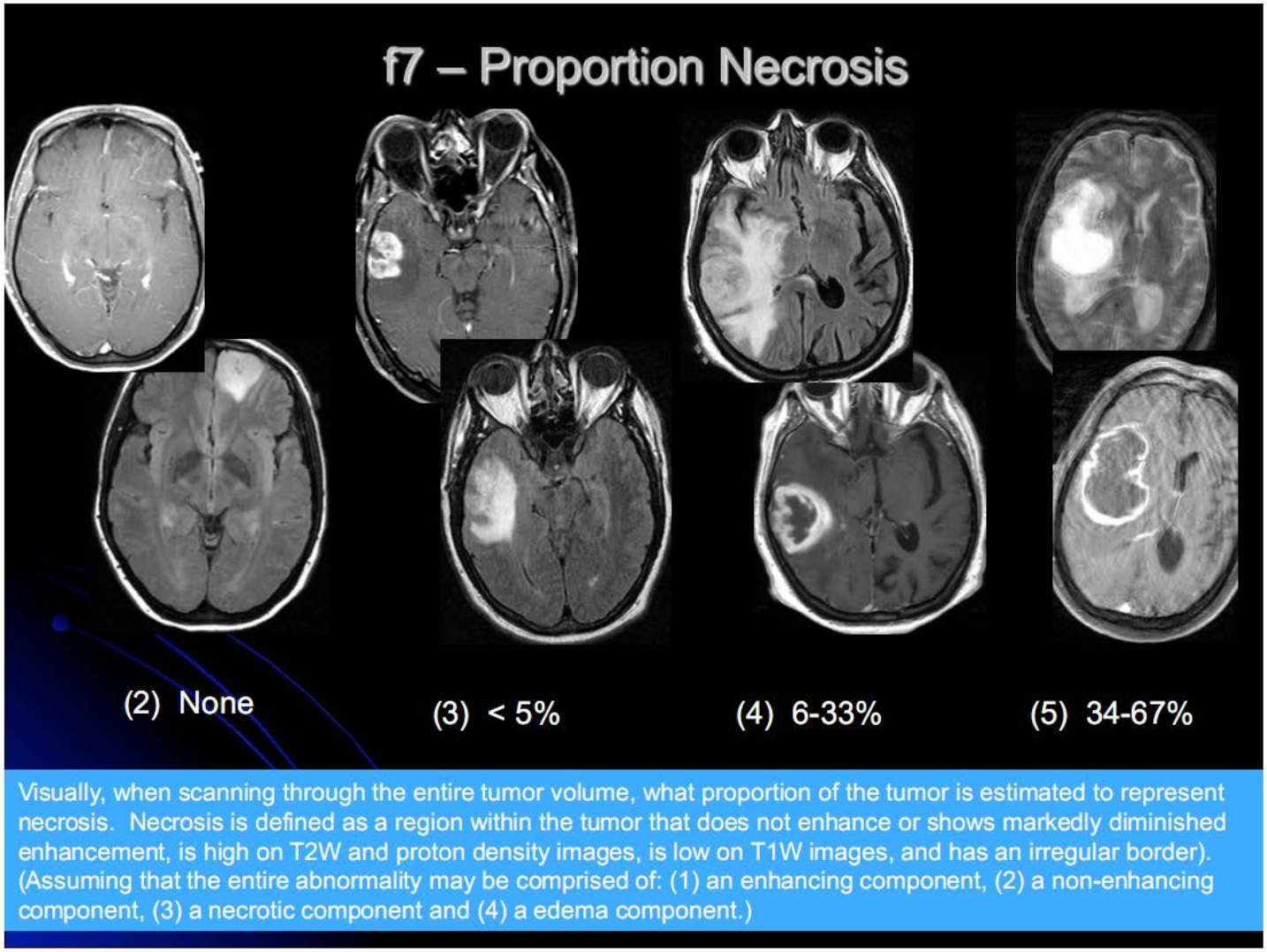


- First tumor in NCI's *The Cancer Genome Atlas* (TCGA)
  - 500 patients from participating hospitals
  - mRNA transcription, CGH, sequence, DNA methylation
  - Neuroimaging
  - Whole slide pathology images

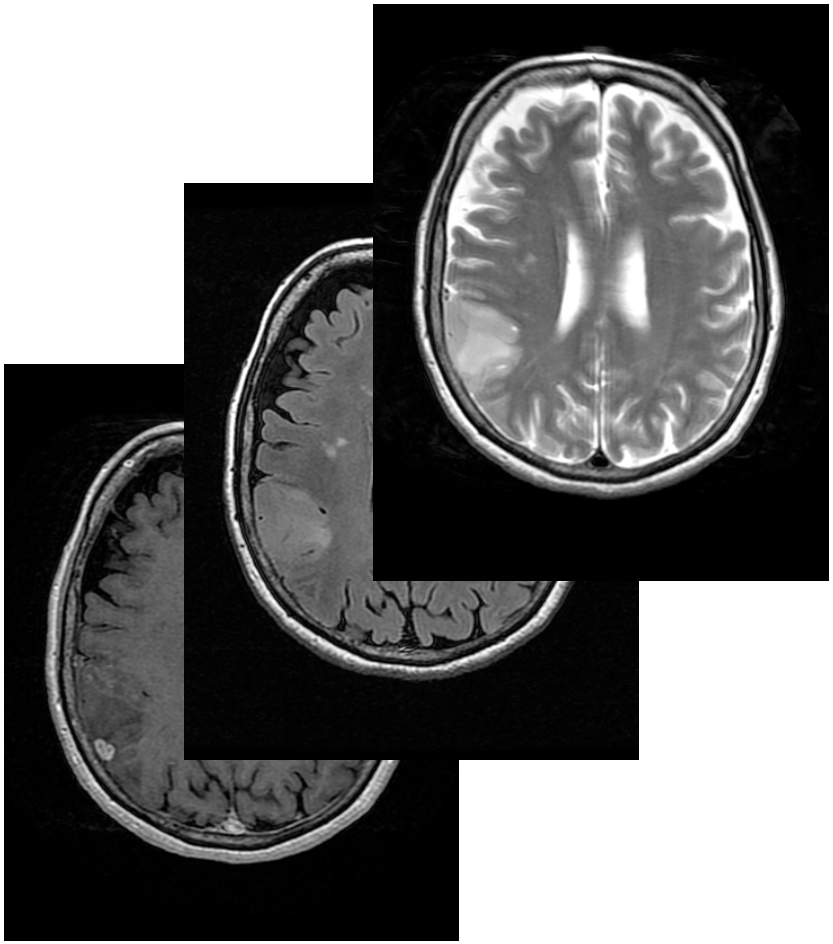
General Methodology Employed in our In Silico Center

- Goal is to develop human and/or machine based assessments of image features
- A standardized imaging 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

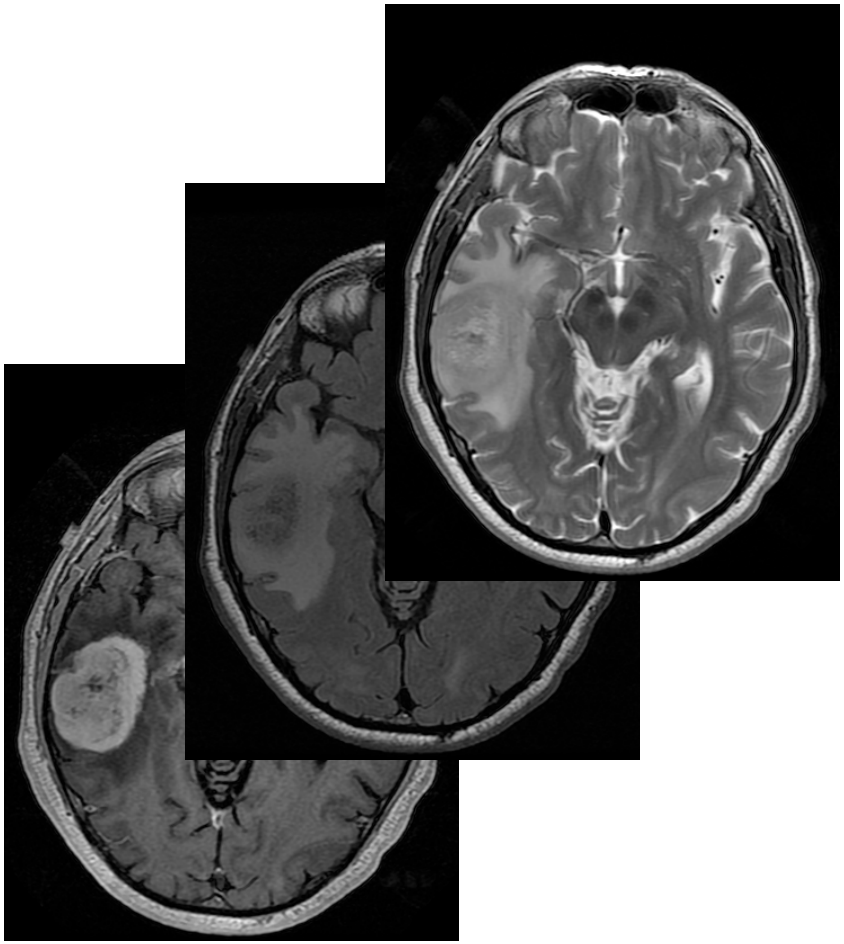
Examples of the feature set



Proportion Enhancing Tumor

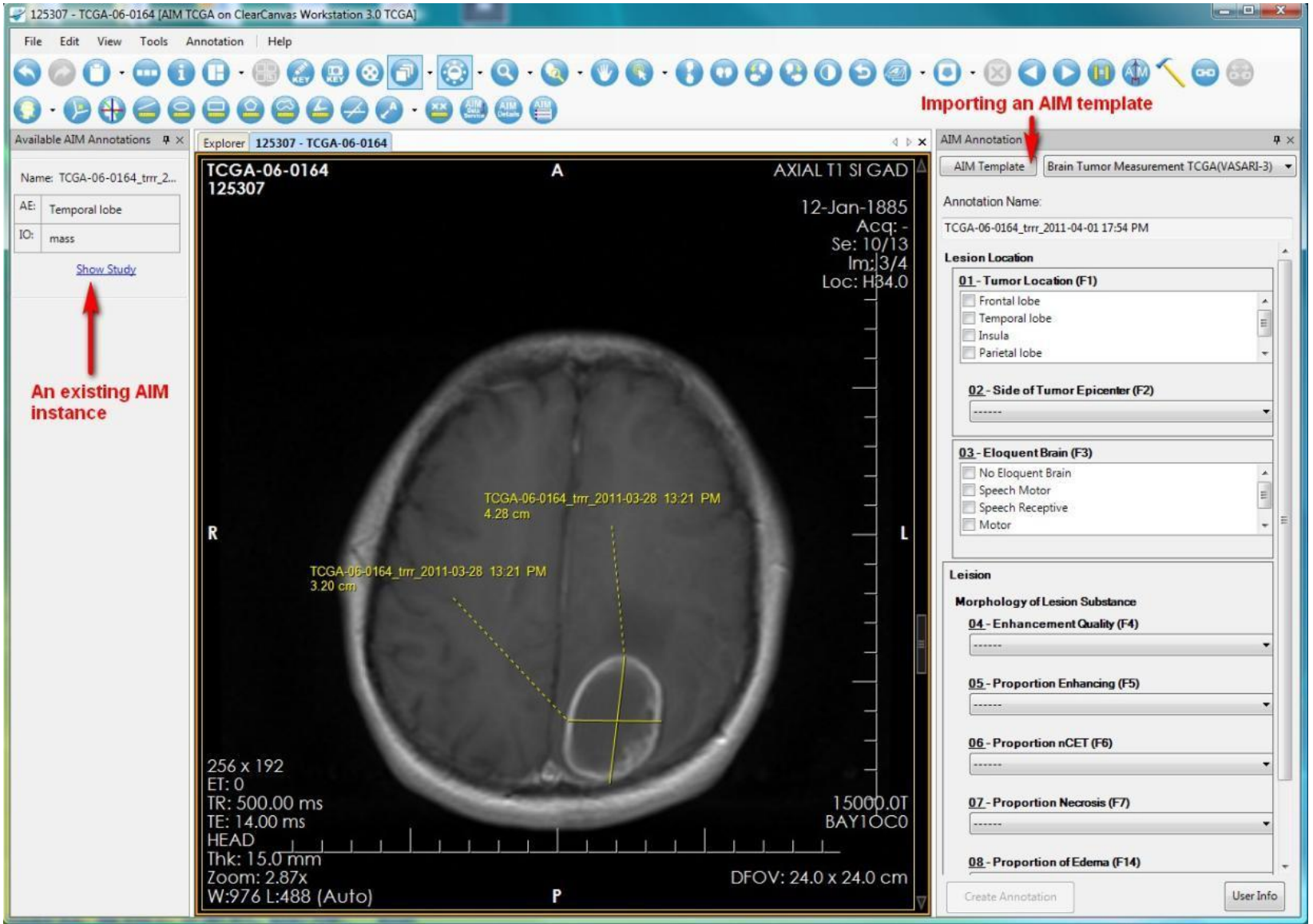


1-5%



68-95%

Capturing structured annotations and markups
AIM Data Service



Systematic assessment of tumor imaging properties

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

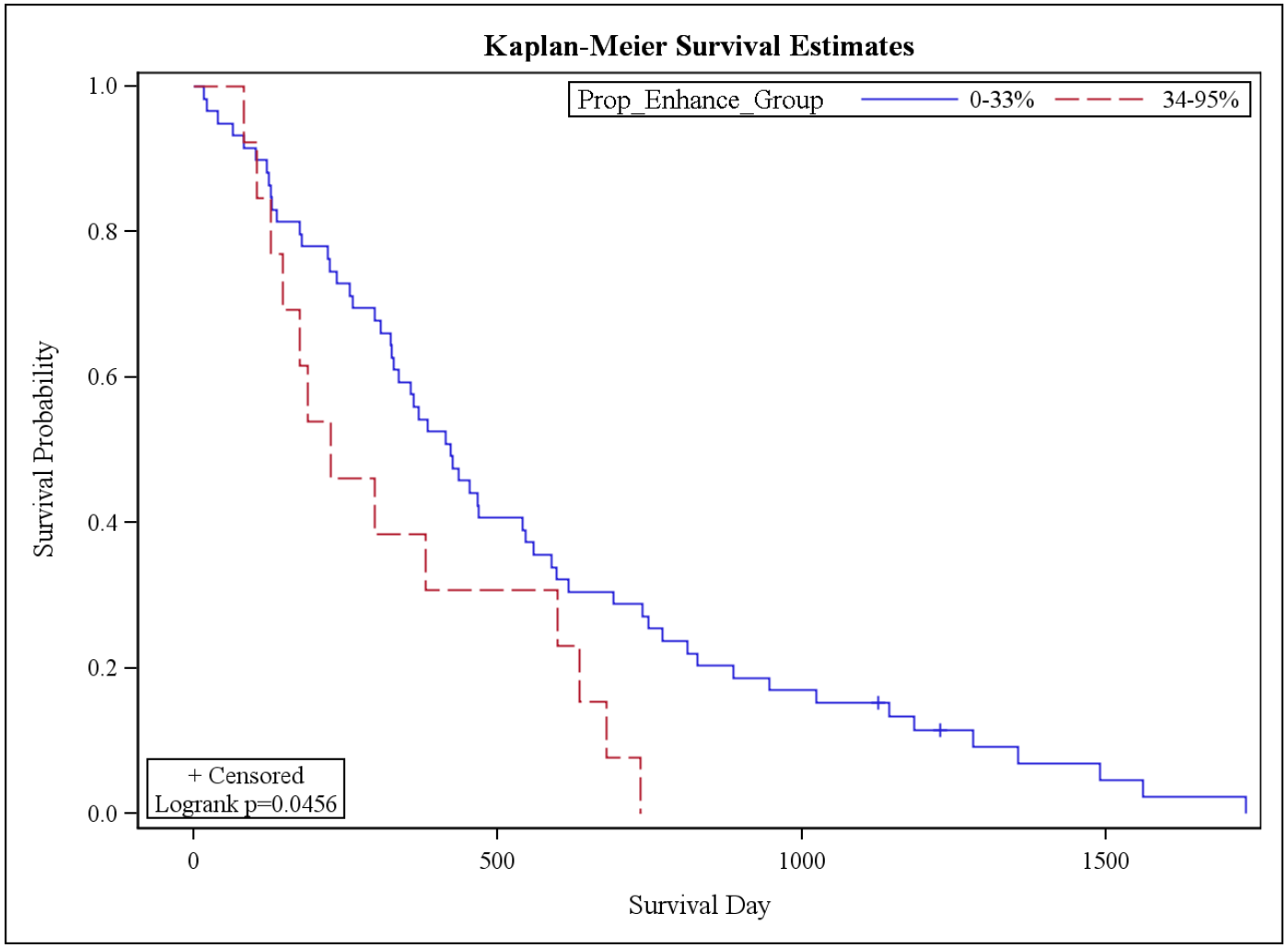
- Current data set is from 72 patients
- Data is now available from ~125 GBM patients that were part of the TCGA data collection
- Each case was reviewed and scored independently by 3 neuroradiologists
- Consensus measures were obtained and used for this analysis

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

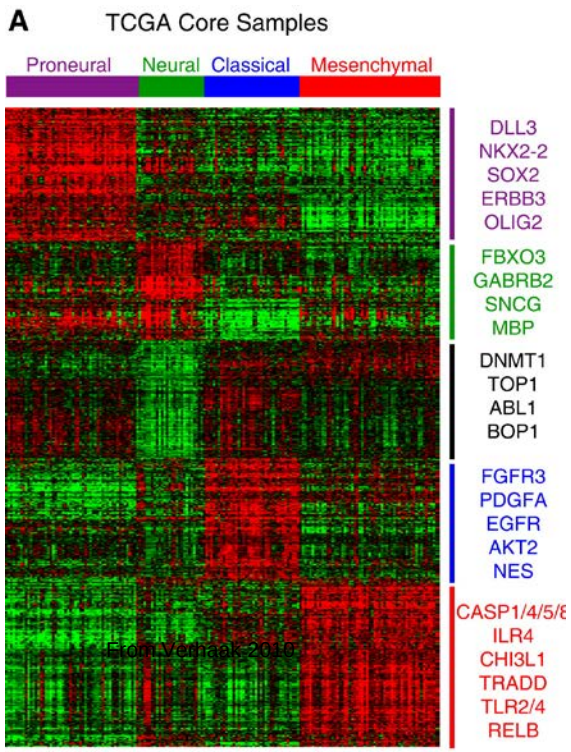
Variable		Hazard Ratio (95% Confidence Limits)	p value
Karn Score		0.955 (0.933, 0.978)	**0.0001**
Contrast Enhancing Tumor	06-33% vs 0-5%	0.528 (0.196, 1.425)	**0.025**
	34-95% vs 0-5%	1.446 (0.485, 4.312)	

Percent of Contrast Enhancement was significantly associated with shorter survival



Tumor Subtypes and Imaging Features

Do tumor genotypes “look” different?



From Verhaak 2010

- 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%) ($p<0.01$).

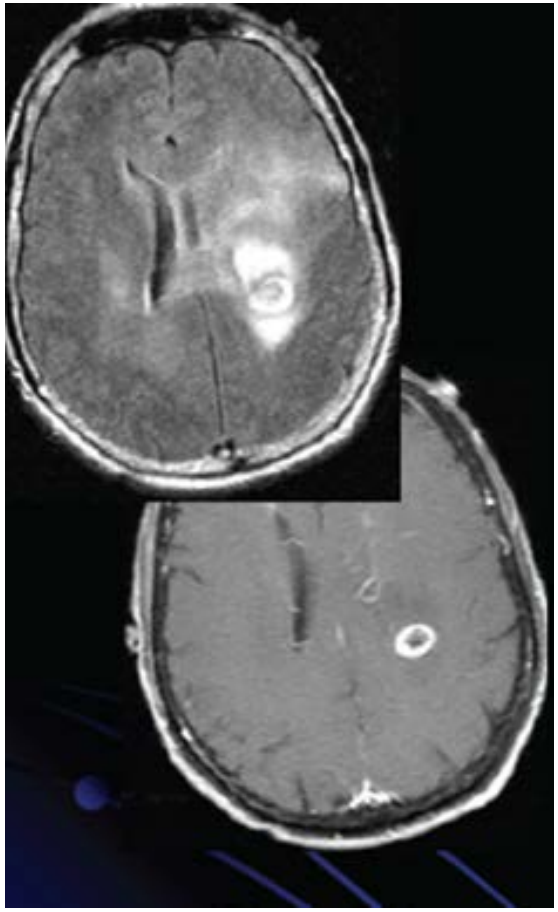
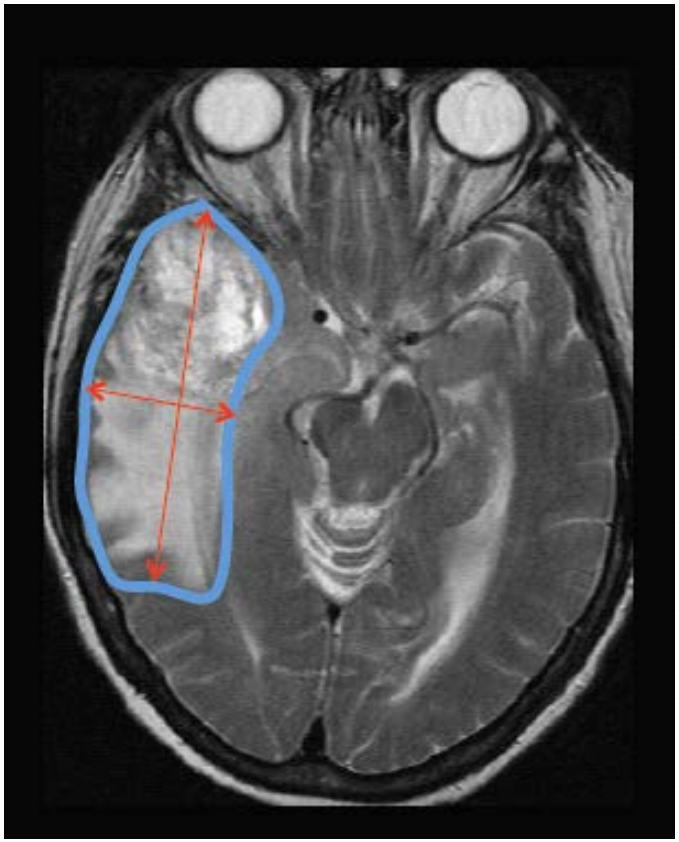


Image based-features and mutation status

- *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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