

Brain Cancer Modeling and Forecasting in Patients



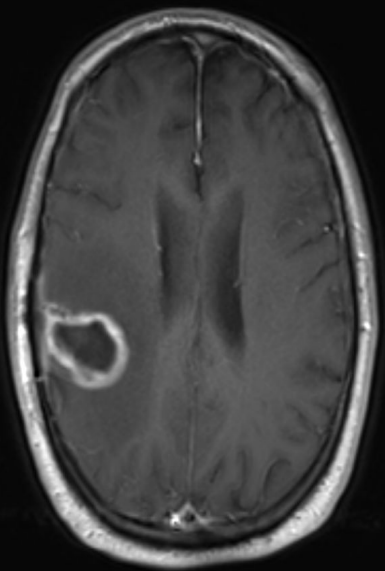
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Patrick Hoover, Ashley Nichols

Mentor: Dr. Kostelich; Duane Harris

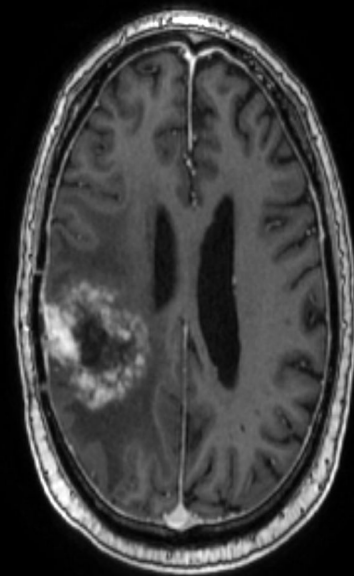


Background


- GBM (Glioblastoma Multiforme) is an aggressive brain cancer with a low survival rate.
- Different treatments include radiation, chemotherapy, and surgical resection
- Patients usually die within 15 months of diagnosis
- Our goal is to create a way for doctors to better counsel GBM patients through accurate simulations of brain tumor proliferation.
- Several parameters to consider (proliferation rate, diffusion rate, model type, etc.)
- GBM has both diffusive and growth behaviors (Neumann boundaries)
- There is still a degree of uncertainty when it comes to these simulations



Scan 1



Scan 6



Harris-Kuang Model

$$\begin{aligned}\frac{\partial p}{\partial t} &= \nabla * (D \nabla p) + \rho g(p + q)p - k\delta(p + q)p \\ \frac{\partial q}{\partial t} &= k\delta(p + q)p\end{aligned}$$

- Representative of a 2 Cell Population Model
 - Proliferating cells
 - Quiescent cells
 - Necrotic - dead
 - Hypoxic - lack of oxygen
- G is a decreasing function of population
- Δ is an increasing function of population



Image Processing

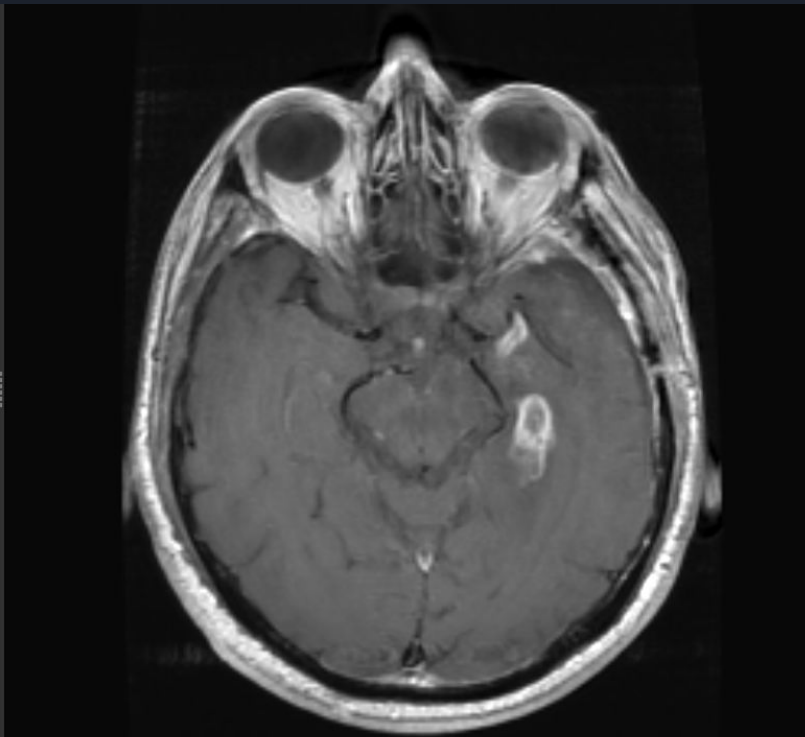
- Preprocessing
 - MATLAB code - SPM12
 - Bias Correction - 3D Slicer
 - MATLAB code - SPM12
 - Reduce dimensions, align the scans, tissue classification
- Segmentation



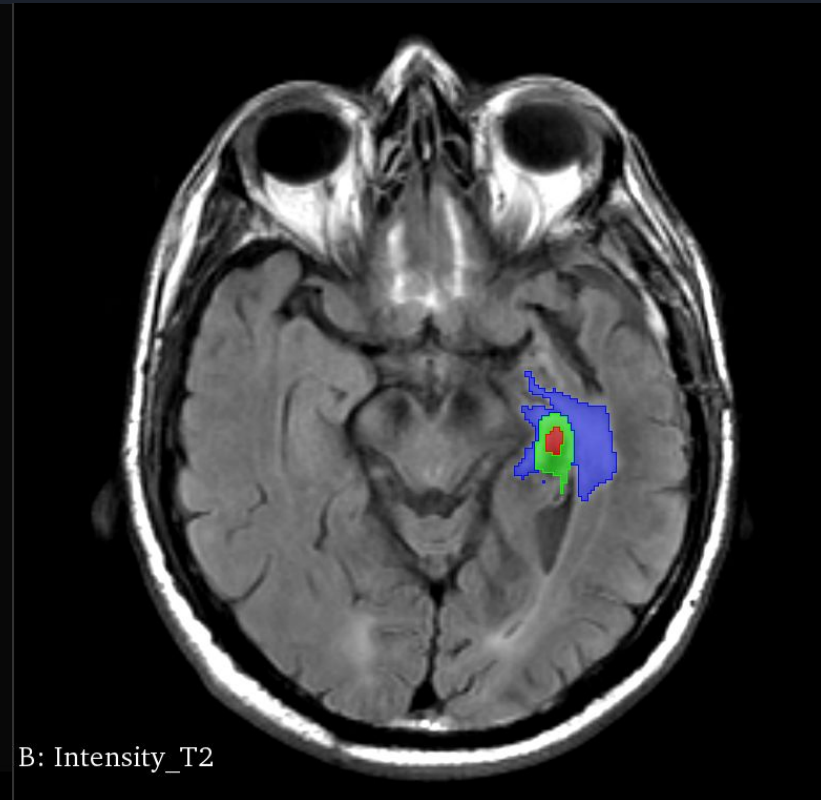
Segmentations

- 3D Slicer
- We look for high intensity regions in every scan and label them:
 - Rim, core, and edema
- Each scan is a resection of the patient's tumor
- Variability of scans in each person
- We were helped by Dr. Preul and Dr. Mignucci

Segmentation Example - Pt 17



B: Intensity_T1C

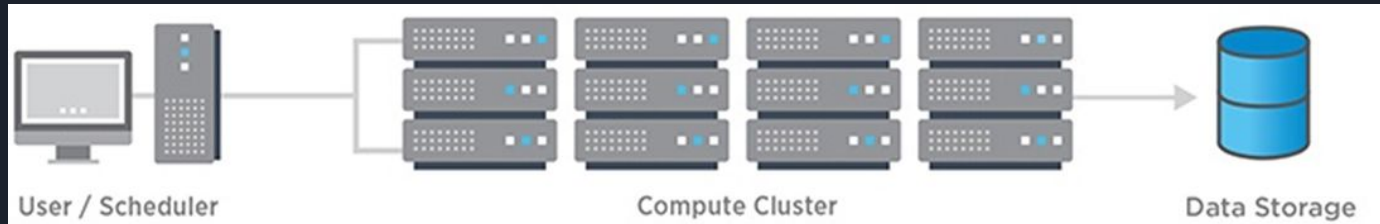


B: Intensity_T2



Agave

- High-Performance Computing (HPC) cluster
- Cluster has computer servers to help user optimize research
 - High memory computation and storage (>34TB RAM)
 - Separate server rather than local computer
 - Parallel programming



Source:
researchcomputi
ng.asu.edu
“Core Facilites”

Agave Simulation Predictions

Name/Model

Population

Parameters

```
&NAME  
model_name='harris'
```

```
! Unspecified values are zero  
&POPULATION  
pmin_edema = 0.01 ! proliferating cells  
pmax_edema = 0.05  
pmin_t1c = 0.05  
pmax_t1c = 0.75  
qratio_edema = 0  
qratio_t1c = 0.0625  
qmin_core = 0.75 ! quiescent cells  
qmax_core = 0.99  
pratio_core = 0.125
```

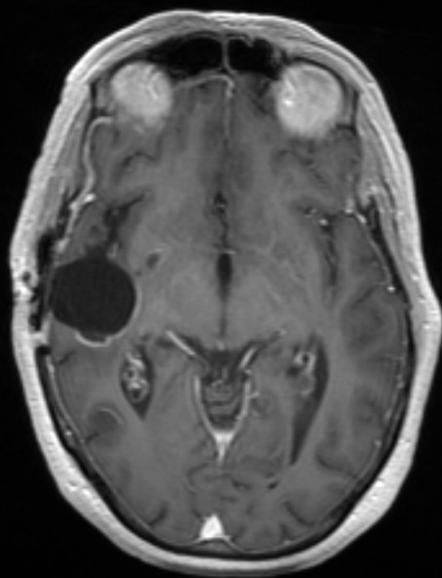
```
&BASEPARAM  
d0(1,1)=0.4 ! white matter diffusion rate, proliferating cells  
d0(2,1)=0.2 ! gray matter diffusion rate, proliferating cells  
d0(3,1)=0.2 ! edema diffusion rate, proliferating cells  
d0(4,1)=0.2 ! enhancing rim diffusion rate, proliferating cells  
d0(5,1)=0.2 ! tumor core diffusion rate, proliferating cells  
d0(1,2)=0.04 ! white matter diffusion rate, quiescent cells  
d0(2,2)=0.02 ! gray matter diffusion rate, quiescent cells  
d0(3,2)=0.02 ! edema diffusion rate, quiescent cells  
d0(4,2)=0.02 ! enhancing rim diffusion rate, quiescent cells  
d0(5,1)=0.02 ! tumor core diffusion rate, quiescent cells  
r0(1,1)=0.028 ! white matter growth rate, proliferating cells (rho1 in paper)  
r0(2,1)=0.032 ! gray matter growth rate, proliferating cells (rho2 in paper)  
r0(3,1)=0.04 ! edema growth rate, proliferating cells (rho1 in paper)  
r0(4,1)=0.02 ! enhancing rim growth rate, proliferating cells  
r0(5,1)=0.02 ! tumor core growth rate, proliferating cells  
q0(1,1)=0.01 ! quiescence rate, white matter (k1 in paper)  
q0(2,1)=0.01 ! quiescence rate, gray matter (k1)  
q0(3,1)=0.01 ! quiescence rate, edema (k1)  
q0(4,1)=0.02 ! quiescence rate, enhancing rim (k2)  
q0(5,1)=0.04 ! quiescence rate, core (k3)  
beta_g = 1, 3 ! Taken from Lifeng's paper  
beta_d = 2, 2 ! see Fig. 4 in Lifeng's paper  
hmax = 1 ! initial maximum time step  
verblev = 2 ! verbose  
days = 56 ! update
```



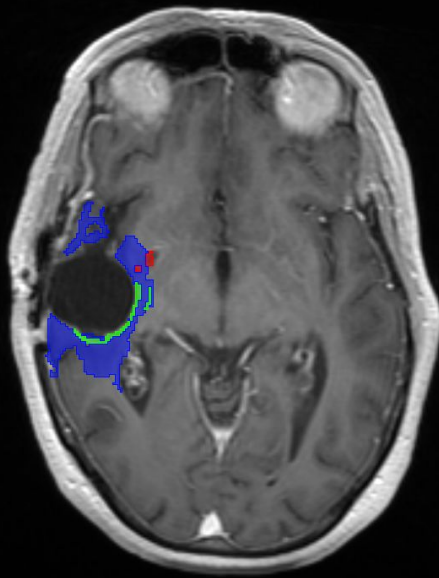
Comparing Our Results

- Agave gives a prediction based on the parameters
- Compare Agave prediction to our own segmented scans
- Segmentations are up to interpretation, segmentations may not be 100% accurate

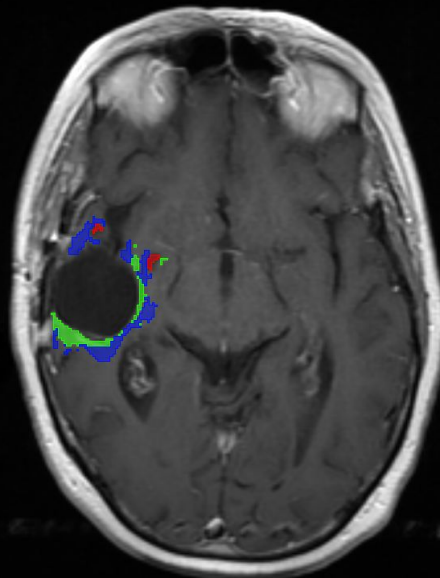
Patient 48: 68 Day Simulation



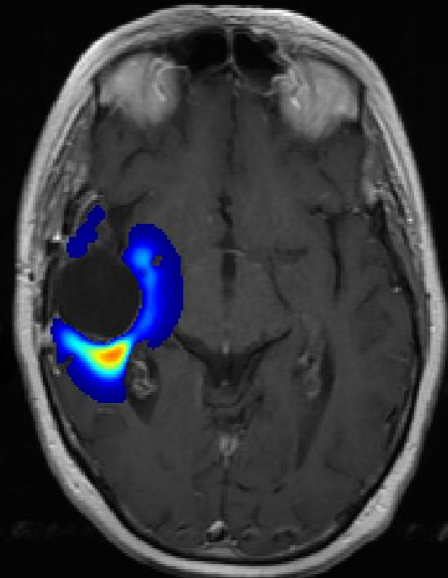
Scan 1
No Segmentation



Scan 1
Segmentation

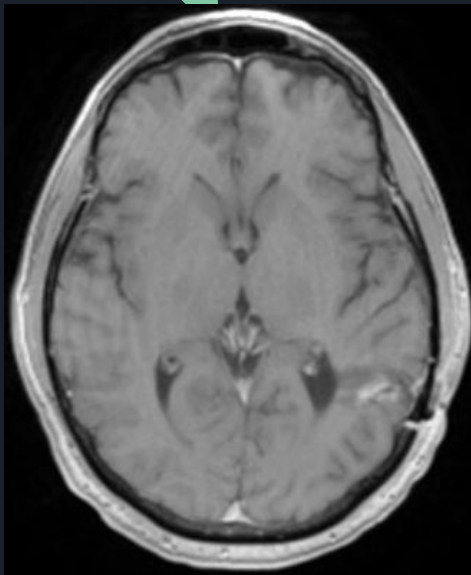


Scan 2
Segmentation

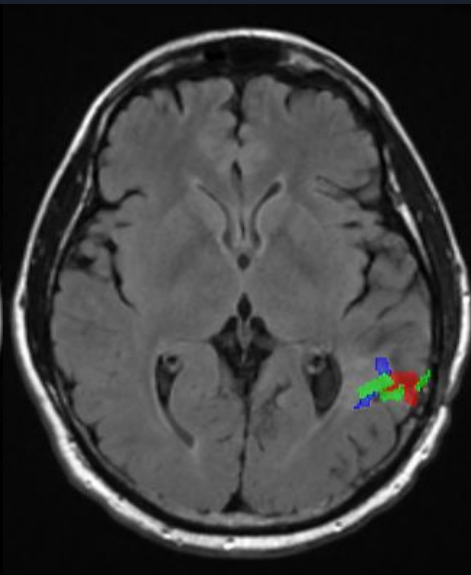


Scan 2
Harris-Kuang Model

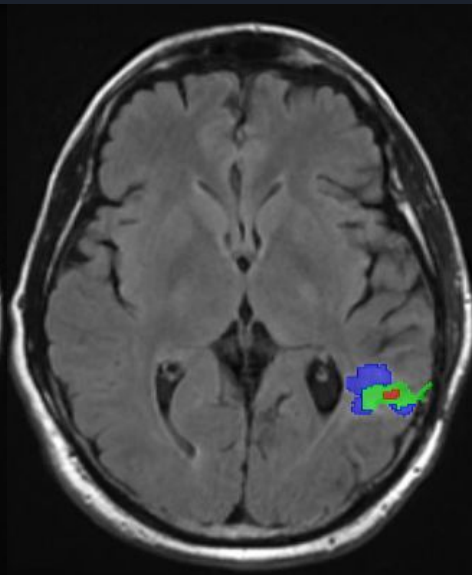
Patient 15: 56 Day Simulation



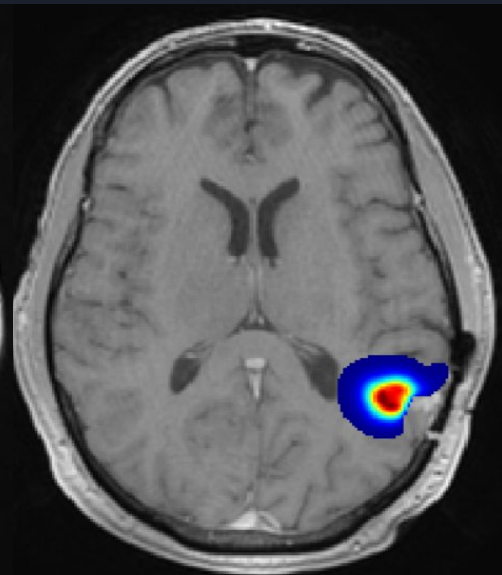
Scan 1
No Segmentation



Scan 1
Segmentation

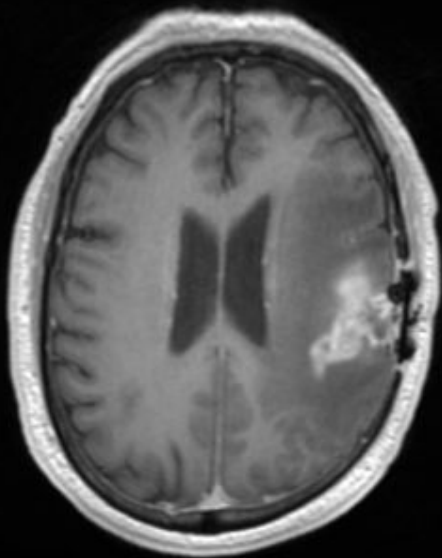


Scan 2
Segmentation

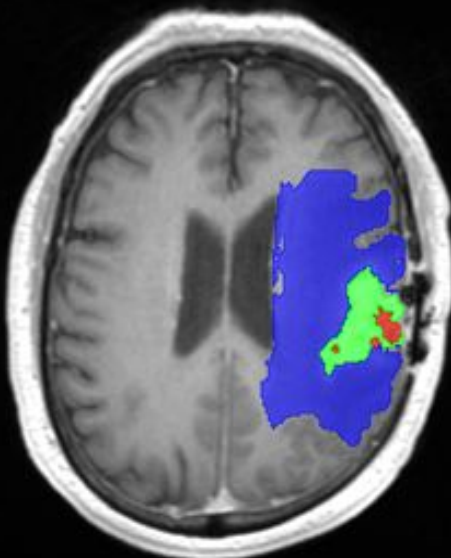


Scan 2
Harris-Kuang Model

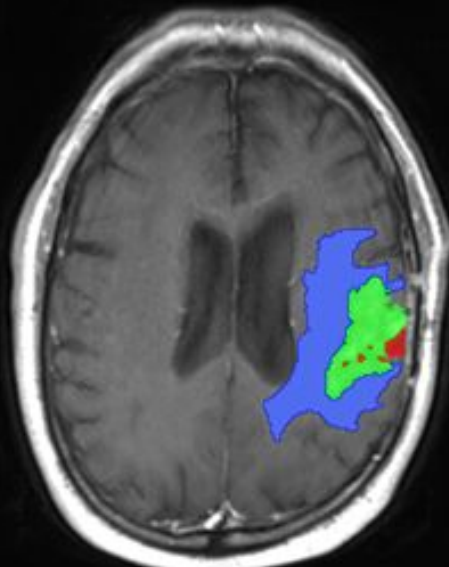
Patient 38: 56 Day Simulation



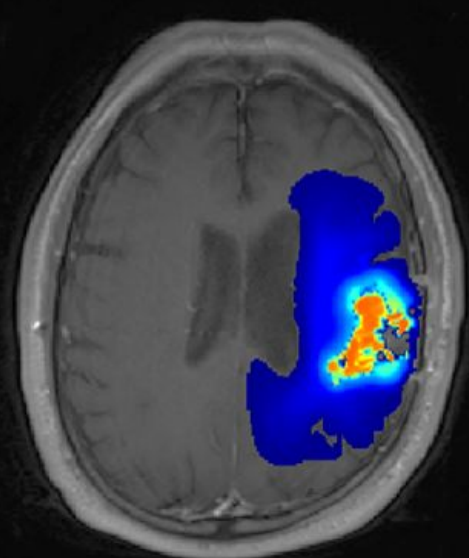
Scan 2
No Segmentation



Scan 2
Segmentation

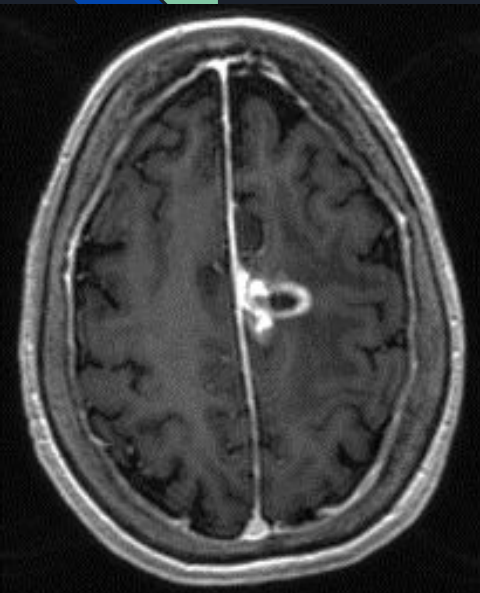


Scan 3
Segmentation

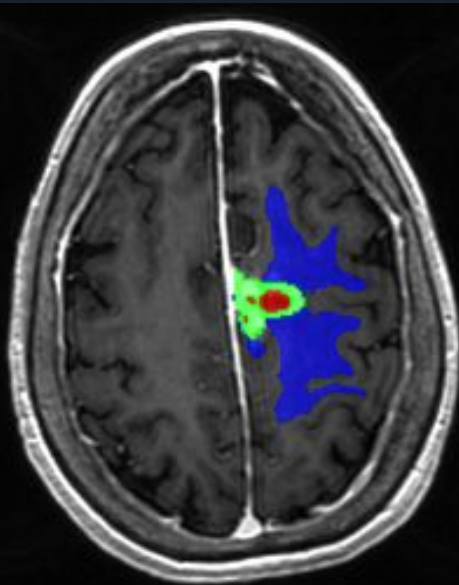


Scan 3
Harris-Kuang Model
Modified

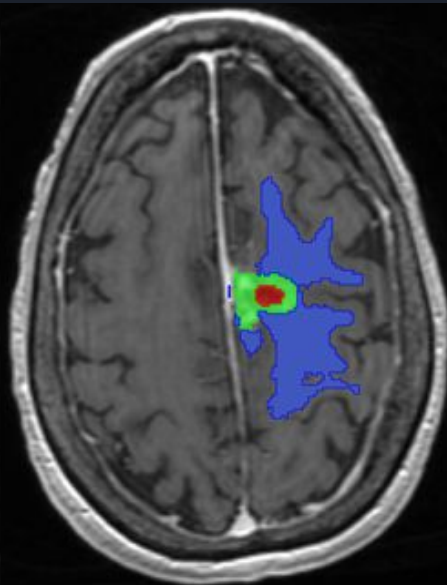
Patient 40: 31 Day Simulation



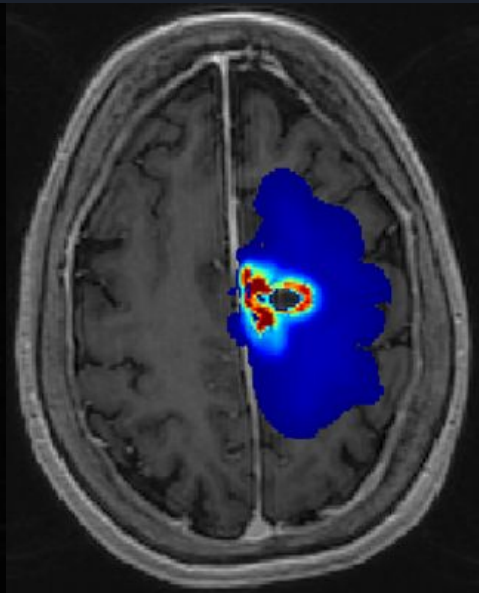
Scan 1
No Segmentation



Scan 1
Segmentation



Scan 2
Segmentation



Scan 2
Harris-Kuang Model
Modified



Image Subtraction

- Use image subtraction to find the difference between the *Agave* prediction and our own segmentation
 - Gives us an idea of how accurate the prediction was
- An accurate prediction = an accurate set of parameters (model, rate of diffusivity, etc.)



Image Subtraction Results

Patient	Rim Agreement	Core Agreement
Patient 48	9.75%	0%
Patient 15	14.39%	5.22%
Patient 38	26.47%	2.96%
Patient 40	35.60%	43.21%

*Note: “Rim” = Proliferating cells, “Core” = Quiescent cells



Limitations of Image Subtraction

- The subtraction method does not take into account the cell density at each location
- Different parameter values will produce different results
- Consider both proliferating and quiescent regions whereas a tumor/high intensity region radius may be more accurate for our purposes



Future Work and Improvements

- More trials of the Agave program in order to find a set of parameters that gives the best outcome
- If we find an accurate set of parameters that works from scan 1 to scan 2:
 - Will it work from scan 2 to scan 3 and so on?
 - Will it work for different patients?
- More biologically accurate segmentations and models



Thanks for listening!

Any questions?

Acknowledgments: Dr. Kostelich, Duane Harris, Dr. Preul, Dr. Mignucci

Thank you to the NSF (National Science Foundation)
and Arizona Biomedical Research Center
for sponsoring our program!