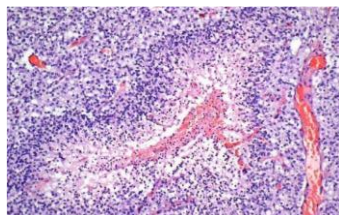


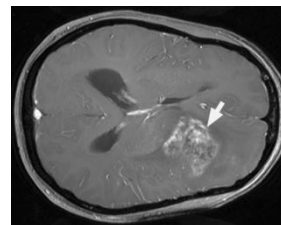
Overview of Web-based Tools to Support Imaging Based In Silico Research

David A Gutman MD PHD
 9/26/2011

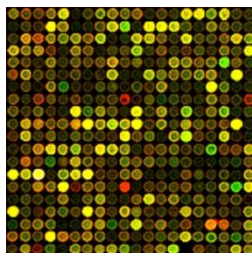
histology



radiology



molecular



clinical\pathology

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

Integrated Analysis

Brief Overview

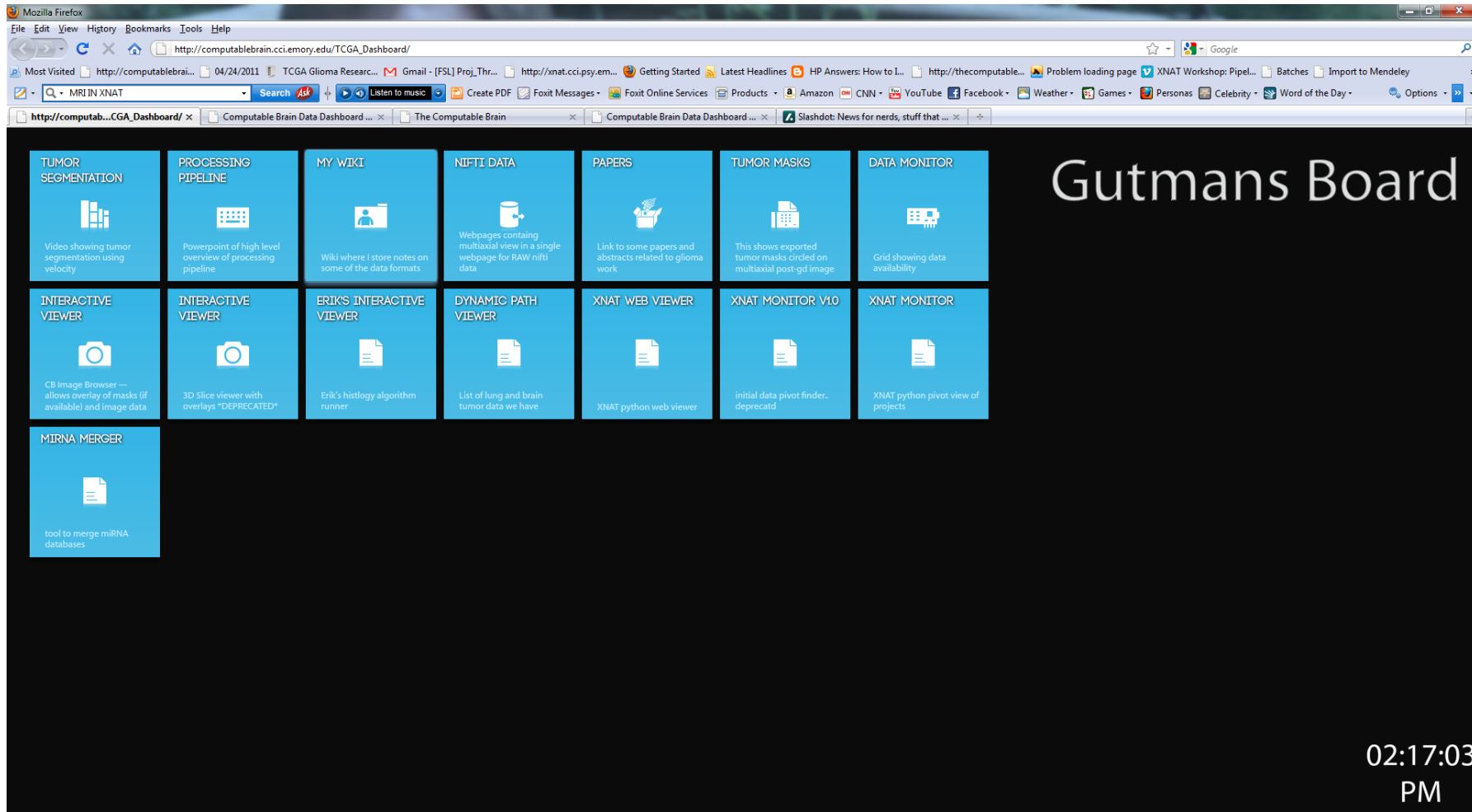
- TCGA Portal is very OMICs focused
- To support our *in silico* work we have developed a number of web-based tools to support informatics integration as well as visualization of results
- Prototypes roughly fall into 3 domains
 - Radiology workflow tools
 - Portals to find common data sets across imaging pipelines
 - Pathology image analysis work/ QA


















Apps are available
online... Brief
descriptions on
following slides

http://computablebrain.cci.emory.edu/TCGA_Dashboard/

Has a general base link... number of active sites are here



Gutmans Board

| | | | | | | |
|--|---|---|--|--|--|--|
| TUMOR SEGMENTATION  Video showing tumor segmentation using velocity | PROCESSING PIPELINE  Powerpoint of high level overview of processing pipeline | MY WIKI  Wiki where I store notes on some of the data formats | NIFTI DATA  Webpages containing multiaxial view in a single webpage for RAW nifti data | PAPERS  Link to some papers and abstracts related to glioma work | TUMOR MASKS  This shows exported tumor masks circled on multiaxial post-gd image | DATA MONITOR  Grid showing data availability |
| INTERACTIVE VIEWER  CB Image Browser — allows overlay of masks (if available) and image data | INTERACTIVE VIEWER  3D Slice viewer with overlays *DEPRECATED* | ERIK'S INTERACTIVE VIEWER  Erik's histlogy algorithm runner | DYNAMIC PATH VIEWER  List of lung and brain tumor data we have | XNAT WEB VIEWER  XNAT python web viewer | XNAT MONITOR V1.0  initial data pivot finder. deprecated | XNAT MONITOR  XNAT python pivot view of projects |
| MIRNA MERGER  tool to merge miRNA databases | | | | | | |

02:17:03
 PM

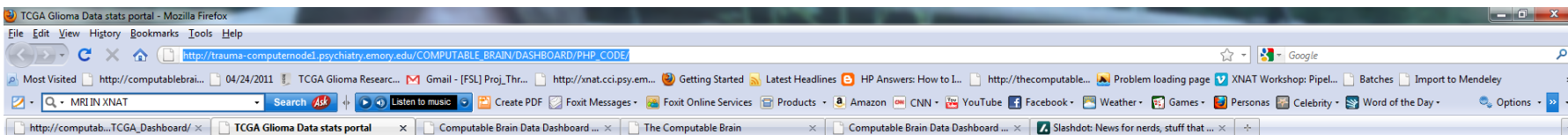
http://thecomputablebrain.com/DASHBOARD/DASHBOARD_IMAGES/
Can quickly view summary images of data belonging to a given image type (i.e. see all the images labeled AXIAL T1 PRE GD)

Center for Comprehensive Informatics



http://trauma-computernode1.psychiatry.emory.edu/COMPUTABLE_BRAIN/DASHBOARD/PHP_CODE/

Basic Portal helps me figure out which patients have which imaging data



Welcome to the Computable Brain TCGA Glioma Data stats portal

| Patient_ID | ADC-MAP | AXIAL-T1-POST-GD | AXIAL-T1-PRE-GD | AXIAL-T2-FLAIR | FA-MAP | POST-GD-MASK |
|------------|---------|------------------|-----------------|----------------|--------|--------------|
| HF2665 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2591 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2582 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2579 | 1 | 1 | 1 | 0 | 0 | 0 |
| HF2566 | 1 | 1 | 1 | 1 | 0 | 0 |
| HF2562 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2560 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2548 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2537 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2519 | 1 | 1 | 1 | 1 | 0 | 0 |
| HF2503 | 1 | 0 | 0 | 0 | 1 | 0 |
| HF2501 | 1 | 1 | 0 | 1 | 1 | 0 |
| HF2485 | 1 | 1 | 0 | 1 | 1 | 0 |
| HF2472 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2414 | 1 | 1 | 1 | 1 | 1 | 0 |
| HF2371 | 1 | 1 | 1 | 1 | 0 | 0 |
| HF2366 | 1 | 1 | 1 | 1 | 1 | 0 |

<http://computablebrain.cci.emory.edu/Monitor/>

Previous version was static--- this one pulls data directly from local XNAT instance I have up and running

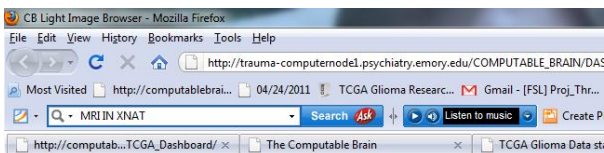
Center for Comprehensive Informatics

Displaying XNAT Data for

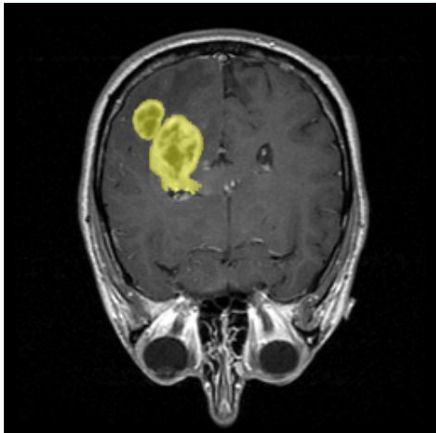
| PatientID | Experiment | AXIAL T1 PRE GD | | AXIAL T1 POST GD | | AXIAL T2 FLAIR | |
|--------------|----------------------|-----------------|------|------------------|------|----------------|------|
| | | Scan | Mask | Scan | Mask | Scan | Mask |
| TCGA-02-0087 | CCL_XNAT_PROD_E00039 | 1 | | 1 | | 0 | |
| TCGA-02-0086 | CCL_XNAT_PROD_E00038 | 1 | | 1 | | 0 | |
| TCGA-06-0878 | CCL_XNAT_PROD_E00165 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00166 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00167 | 1 | | 1 | | 1 | |
| TCGA-06-0238 | CCL_XNAT_PROD_E00459 | 1 | | 1 | | 1 | |
| TCGA-06-1801 | CCL_XNAT_PROD_E00182 | 0 | | 0 | | 0 | |
| | CCL_XNAT_PROD_E00183 | 0 | | 0 | | 0 | |
| | CCL_XNAT_PROD_E00180 | 1 | | 1 | | 0 | |
| | CCL_XNAT_PROD_E00187 | 0 | | 0 | | 1 | |
| | CCL_XNAT_PROD_E00185 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00179 | 0 | | 1 | | 0 | |
| | CCL_XNAT_PROD_E00178 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00177 | 1 | | 1 | | 1 | |
| TCGA-06-1802 | CCL_XNAT_PROD_E00188 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00190 | 1 | | 1 | | 1 | |
| | CCL_XNAT_PROD_E00192 | 1 | | 1 | | 1 | |
| TCGA-14-0817 | CCL_XNAT_PROD_E00417 | 0 | | 0 | | 0 | |
| | CCL_XNAT_PROD_E00401 | 0 | | 0 | | 0 | |
| TCGA-14-0813 | CCL_XNAT_PROD_E00407 | 0 | | 0 | | 0 | |
| | CCL_XNAT_PROD_E00433 | 0 | | 0 | | 0 | |
| TCGA-14-0812 | | | | | | | |

Quick sanity check... part of workflow is to mask the tumor region--- below allows web based overlay of mask on base image (can adjust opacity so can see underlying structure as well)

http://trauma-computernode1.psychiatry.emory.edu/COMPUTABLE_BRAIN/DASHBOARD/PHP_CODE/PNG_DEPOT/cb_light_image_viewer.php



▼



27

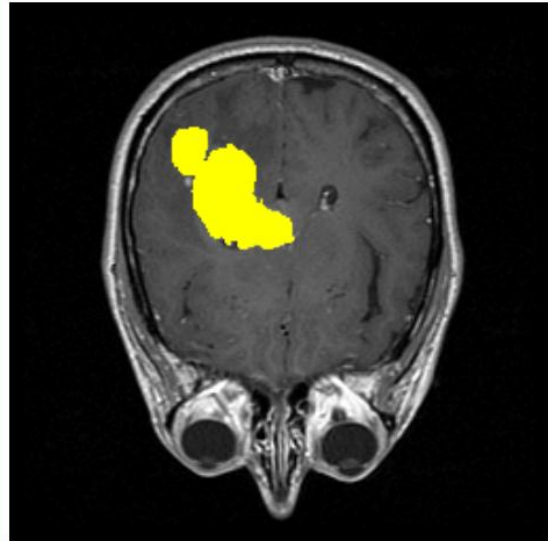
CURRENT PATEINT IS DISPLAYED HERE

Toggle Mask:

Mask transparency

TITLE BOX GOES HERE

▼



29

CURRENT PATEINT IS DISPLAYED HERE

Toggle Mask:

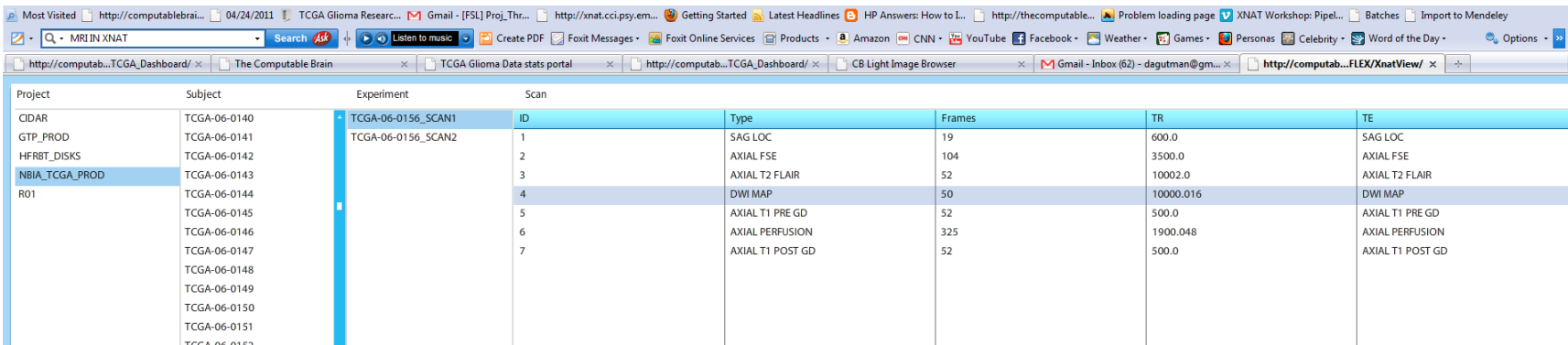
Mask transparency

TITLE BOX GOES HERE

Want to visualize data based on Scan Tags..

http://computablebrain.cci.emory.edu/CB_FLEX/XnatView/

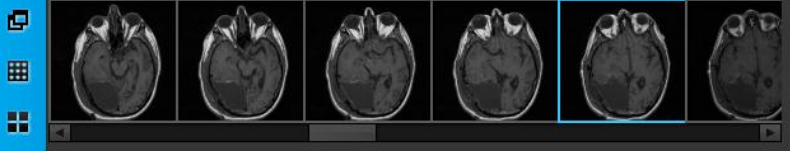
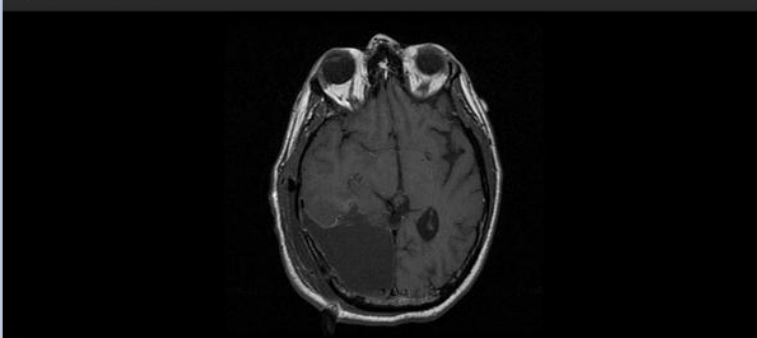
Can also see/view TR/TE/ other scan parameters to really find ideal data set; want to eventually integrate ability to see masks overlaid as well.. Can also pull data from other PACS if we wanted



| Project | Subject | Experiment | Scan | ID | Type | Frames | TR | TE |
|----------------|--------------|--------------------|------|----|------------------|--------|-----------|------------------|
| CIDAR | TCGA-06-0140 | TCGA-06-0156_SCAN1 | | 1 | SAG LOC | 19 | 600.0 | SAG LOC |
| GTP_PROD | TCGA-06-0141 | TCGA-06-0156_SCAN2 | | 2 | AXIAL FSE | 104 | 3500.0 | AXIAL FSE |
| HFBT_DISKS | TCGA-06-0142 | | | 3 | AXIAL T2 FLAIR | 52 | 10002.0 | AXIAL T2 FLAIR |
| NBIA_TCGA_PROD | TCGA-06-0143 | | | 4 | DWI MAP | 50 | 10000.016 | DWI MAP |
| RO1 | TCGA-06-0144 | | | 5 | AXIAL T1 PRE GD | 52 | 500.0 | AXIAL T1 PRE GD |
| | TCGA-06-0145 | | | 6 | AXIAL T1 POST GD | 325 | 1900.048 | AXIAL T1 POST GD |
| | TCGA-06-0146 | | | 7 | AXIAL T1 POST GD | 52 | 500.0 | AXIAL T1 POST GD |

[Project: NBIA_TCGA_PROD] [Subject: TCGA-06-0156] [Experiment: TCGA-06-0156_SCAN1] [Scan: 5]

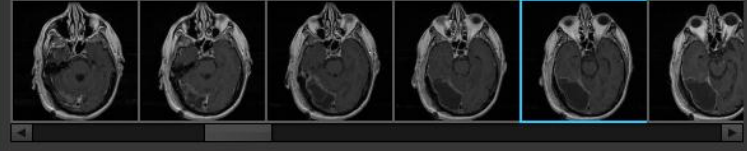
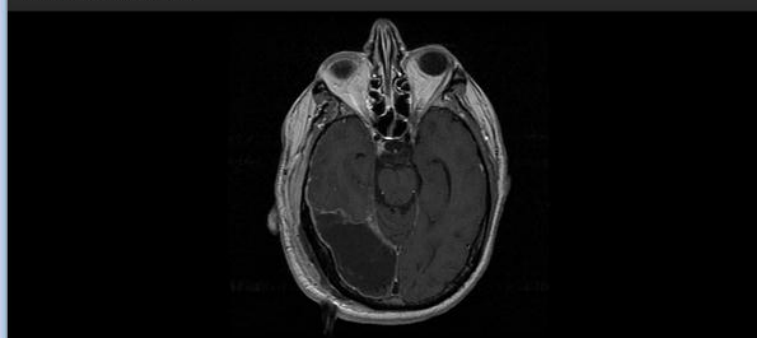
MR5.23.19960727.2KS727



Zoom Brightness Contrast

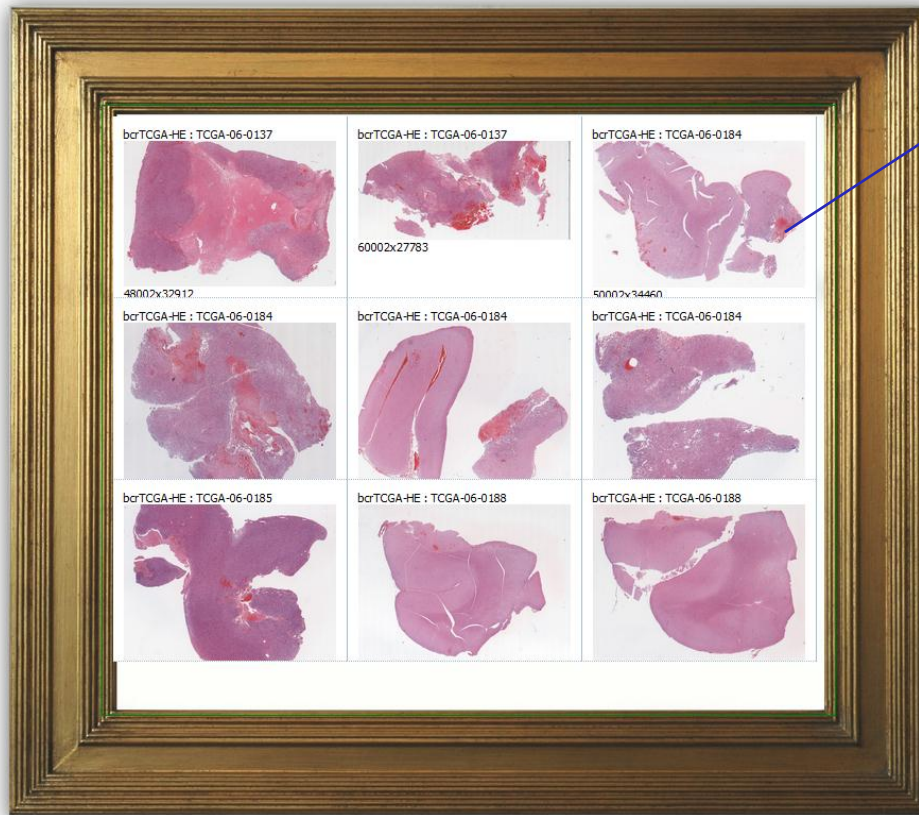
[Project: NBIA_TCGA_PROD] [Subject: TCGA-06-0156] [Experiment: TCGA-06-0156_SCAN1] [Scan: 7]

MR7.18.19960727.1CLIT6K



Zoom Brightness Contrast

http://thecomputablebrain.com/PATH_VIEWER/
 Allows me to filter/find patients matching given criteria and with path



Current slide_count 480
 Current patient_count 167

Sort by type [asc](#) | [desc](#)
 Sort by name [asc](#) | [desc](#)
 Sort by size [asc](#) | [desc](#)

[Filter by TCGA ID](#)
 [Filter by Slide group](#)
[Clear All Filters](#)

Note: Must click Filter by to actually filter

Filter By Clinical or MR Data
 MRI IN XNAT
 MRI, Path and Survival and Genetics
[Minimum Patient Age](#)
 Filter by Verhaak Type Any
 Filter by slide group

[Clear All Filters](#)
Note: Must click Filter by to actually filter

Slide Group: bcrTCGA-HE
 PT ID: TCGA-06-0137
 Gender:undefined MR_Count:2
 KarnScore:null Verhaak Type:Classical
 Days to progression 487
 VASARI READS:3
 VITALSTATUS DEAD_
 days to death 812 days to last followup 701

Slide Group: bcrTCGA-HE
 PT ID: TCGA-06-0184
 Gender:undefined MR_Count:1
 KarnScore:80 Verhaak Type:Mesenchymal
 Days to progression null
 VASARI READS:3
 VITALSTATUS ALIVE_HF_C
 days to death null days to last followup 1228

Slide Group: bcrTCGA-HE
 PT ID: TCGA-06-0188
 Gender:undefined MR_Count:1
 KarnScore:100 Verhaak Type:Neural
 Days to progression null
 VASARI READS:3
 VITALSTATUS DEAD_
 days to death null days to last followup 866

Note: Can also view patient metadata about a slide

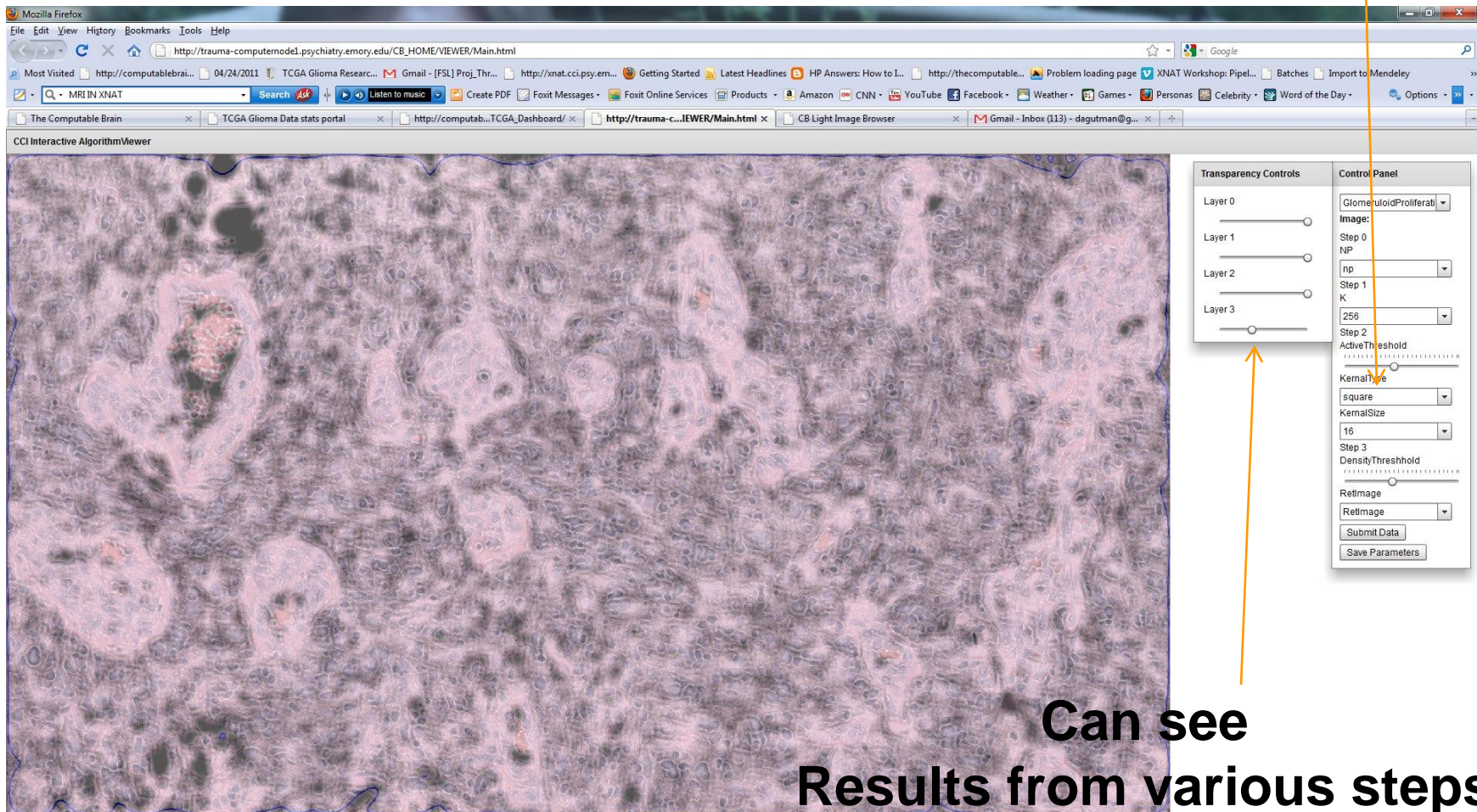
Interactive Algorithm Runner, can run and tune

multi-step algorithm

Select params

Note: This is particularly buggy

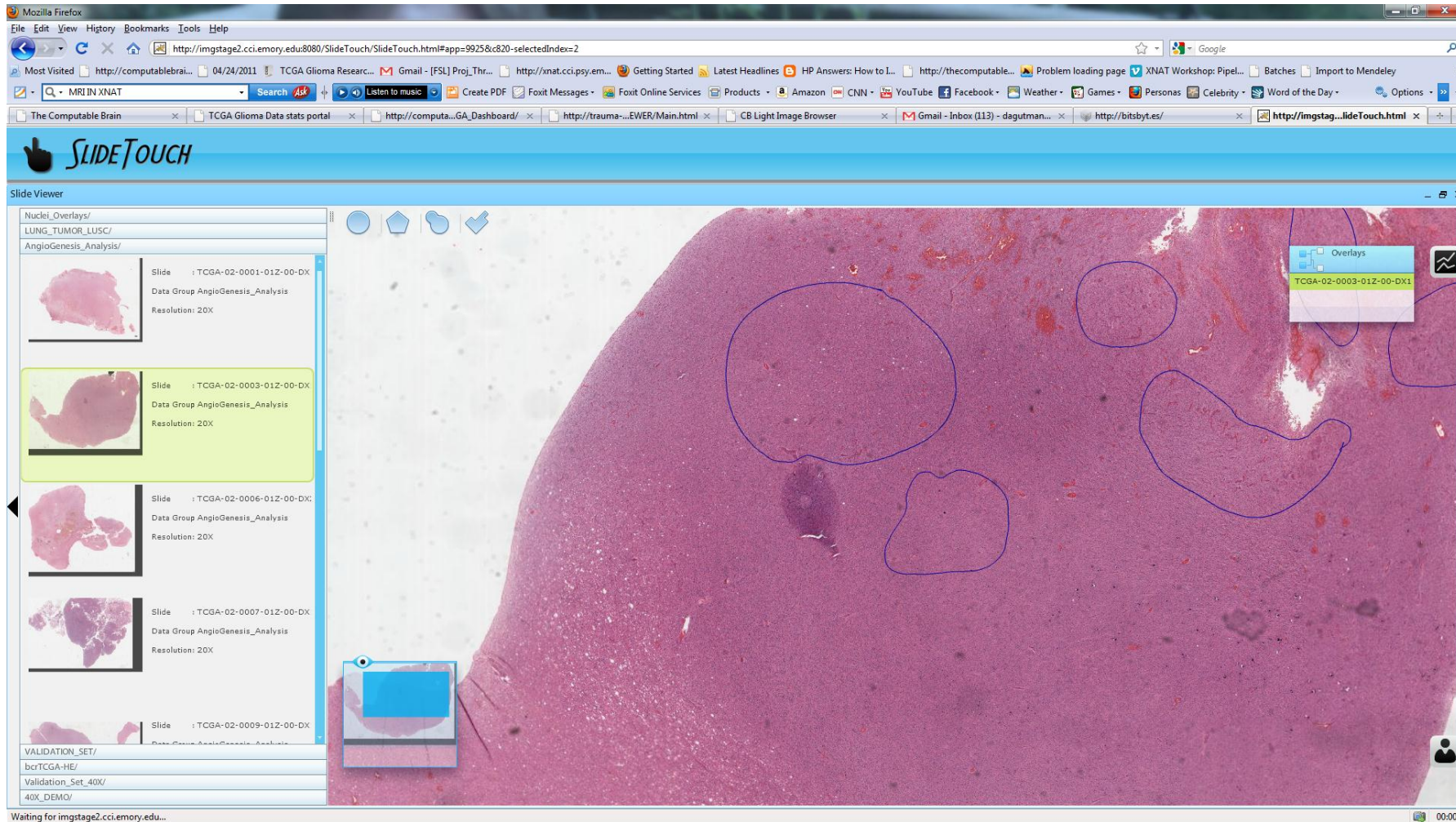
http://trauma-computernode1.psychiatry.emory.edu/CB_HOME/VIEWER/Main.html



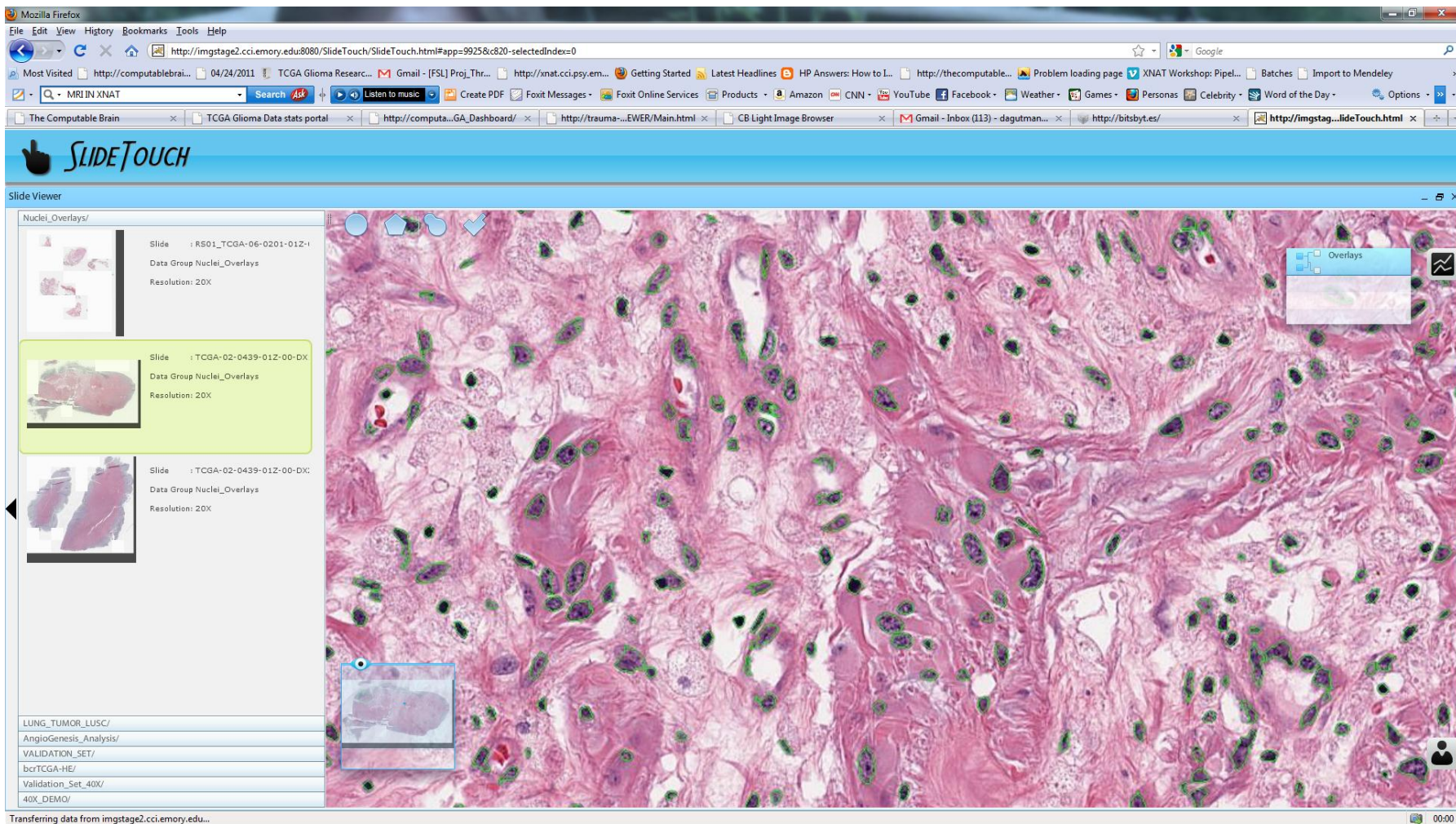
Can see
Results from various steps

Whole Slide Viewing app showing ROI selected

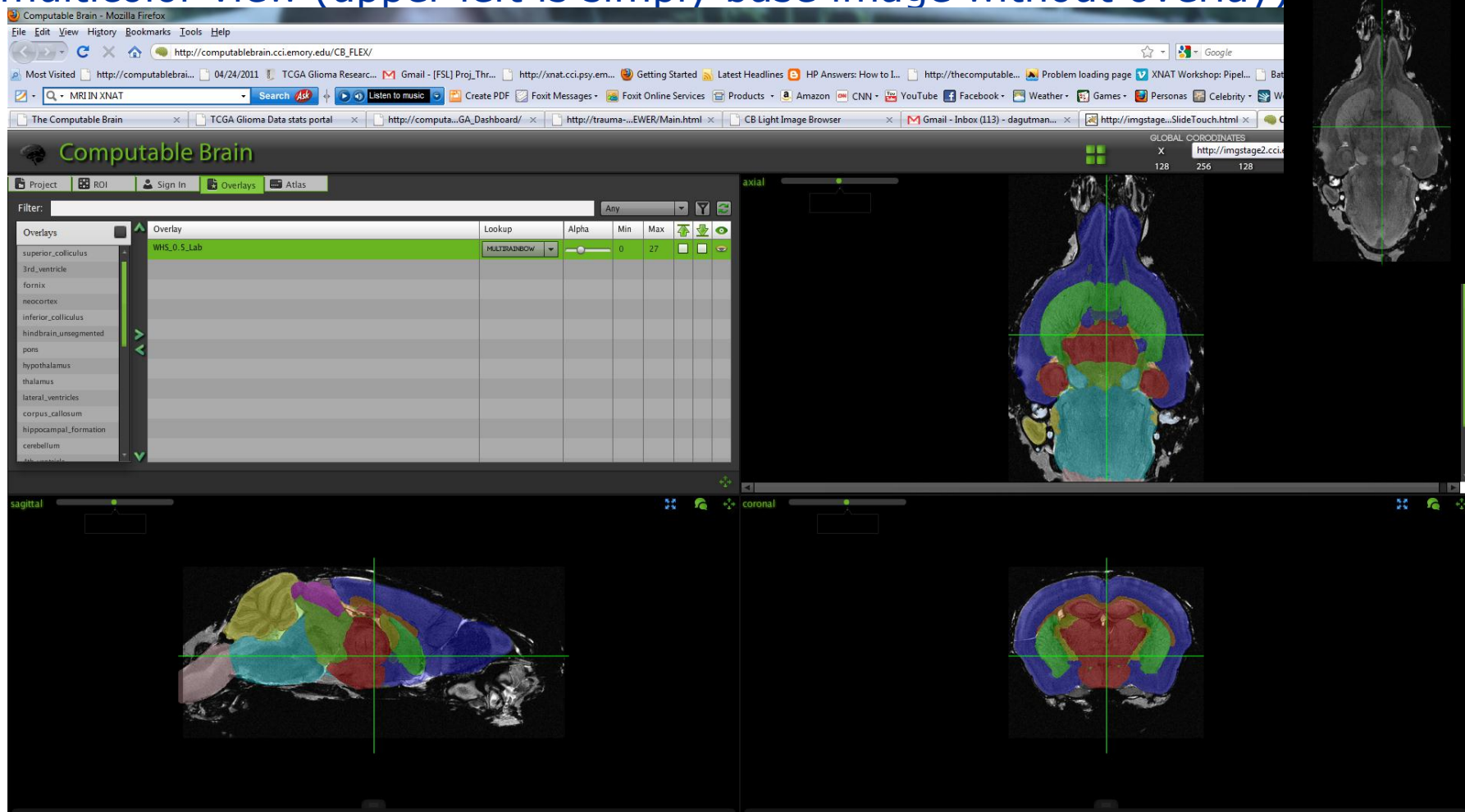
<http://imgstage2.cci.emory.edu:8080/SlideTouch/SlideTouch.html#app=9925&c820-selectedIndex=2>



Can also visualize analysis results (nuclei circled in green)



Other pet project: Computable Brain
 Can store imaging results online, as well as overlays/processed intermediates/etc
 Showing canonical mouse atlas with atlas based ROI's shown in multicolor view (upper left is simply base image without overlay)



The screenshot displays the 'Computable Brain' web application interface. The browser window shows the URL http://computablebrain.cci.emory.edu/CB_FLEX/. The application interface includes a navigation menu with 'Project', 'ROI', 'Sign In', 'Overlays', and 'Atlas'. A list of brain regions is shown on the left, with 'superior_colliculus' selected. The main display area shows three views of a mouse brain atlas: 'axial' (top right), 'sagittal' (bottom left), and 'coronal' (bottom right). Each view shows the brain with various regions highlighted in different colors (e.g., blue, green, red, yellow, cyan). A table of overlays is visible in the center-left, with columns for 'Overlay', 'Lookup', 'Alpha', 'Min', and 'Max'. The 'WHS_0.5_Lab' overlay is currently selected, with a 'MULTIRAINBOW' lookup and an alpha value of 0. The 'GLOBAL COORDINATES' section shows X: 128, Y: 256, and Z: 128.

| Overlay | Lookup | Alpha | Min | Max |
|---------------------|--------------|-------|-----|-----|
| superior_colliculus | MULTIRAINBOW | 0 | 27 | |

Also supports atlas lookups--- so can register "my" data to a reference space and do lookups to help figure out what local anatomy I am looking at



The screenshot displays the 'Computable Brain' web application interface. On the left, there is a table for atlas lookups. The main area shows three MRI brain scan views: axial, sagittal, and coronal. The axial view is currently selected and shows a cross-section of the brain with a green crosshair. The sagittal and coronal views are also visible below it. The interface includes a navigation menu with options like Project, ROI, Sign In, Overlays, and Atlas. A status bar at the bottom indicates 'Transferring data from computablebrain.cci.emory.edu...' and a memory usage of 337 MB.

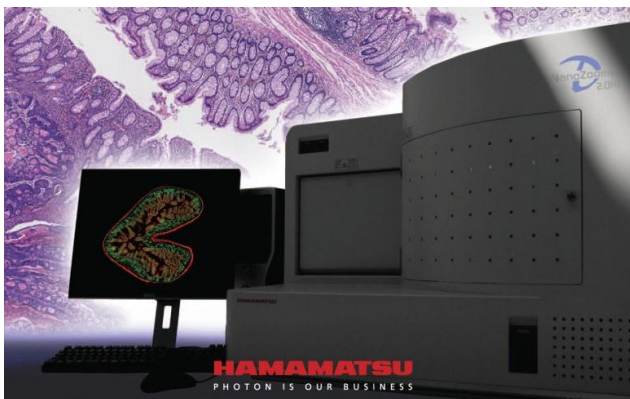
| Atlas | Atlas | Description | Intensity |
|-------|----------------------------------|--|-----------|
| | Harvard Oxford Cortical Index | | |
| | Harvard Oxford SubCortical Index | Right Cerebral White Matter Right Cerebral Cortex | 48 50 |
| | JHU Tract Labels | | |
| | JHU Tracts | | |

Other slides from presentation—

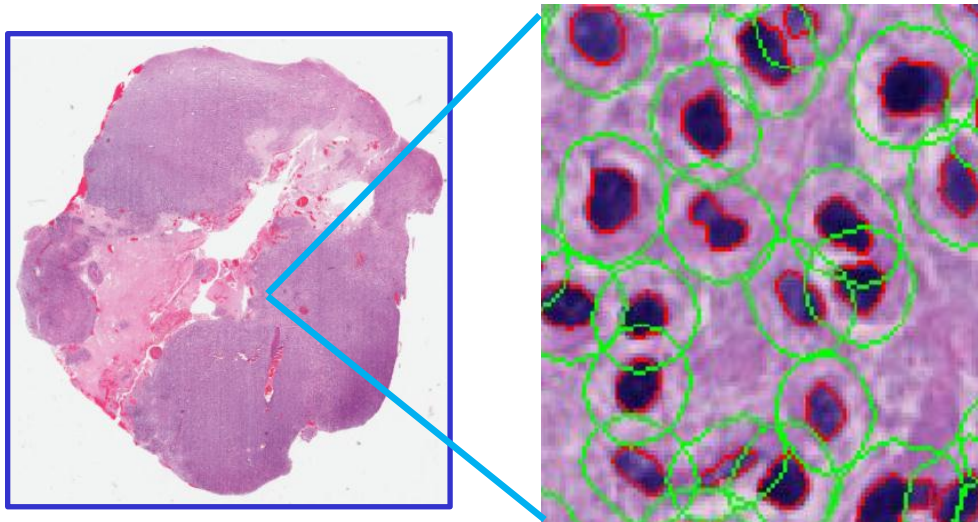
**Basically our group is interested in human generated
And computer generation annotations and using that
For correlative analysis of outcome... as well as building
Tools and pipelines to assist this process.**

Morphological subtypes study: cellular features

Whole Slide Imaging



Nuclei Segmentation



Cellular Features

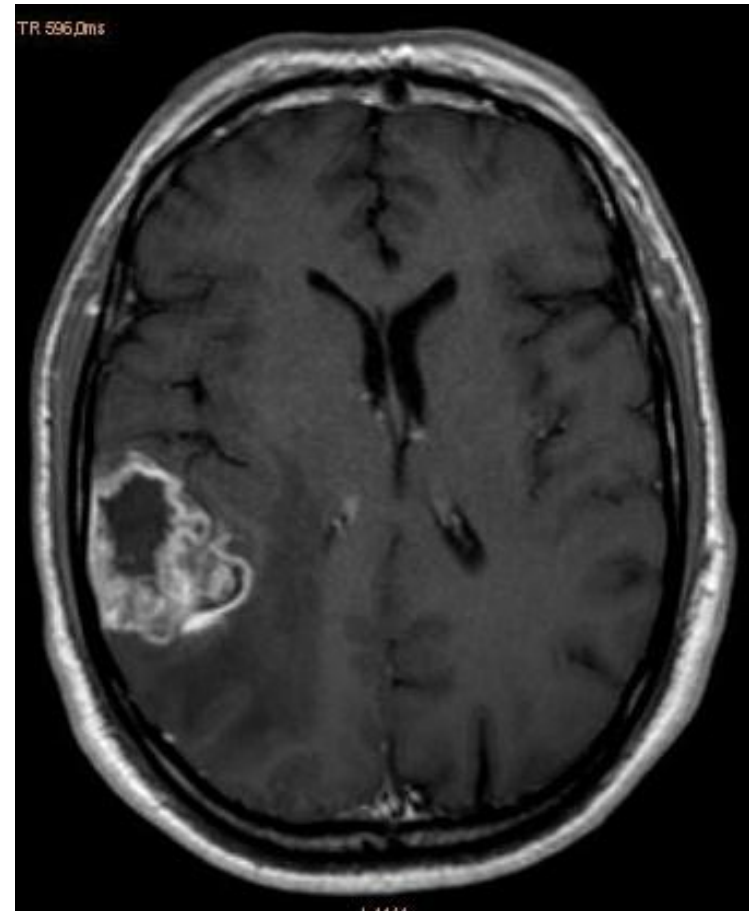
| Nuclear Morphometry | | | |
|-----------------------|------------------|----------------------|--------------------------|
| Nuclei Area | Nuclei Perimeter | Eccentricity | Circularity |
| Major Axis | Minor Axis | Extent Ratio | Fourier Shape Descriptor |
| Intensity Information | | Texture Information | |
| Avg Inty | Std Inty | Entropy | Energy |
| Max Inty | Min Inty | Skewness | Kurtosis |
| Gradient Statistics | | | |
| Avg GM | Std GM | Entropy GM | Skewness GM |
| Energy GM | Kurtosis GM | Edge Pixel Summation | Edge Pixel Percentage |

Mechanisms Underlying Glioma Progression

Diagnostic Improvement

Molecular Classification

Predictors of Progression



TCGA and REMBRANDT Datasets

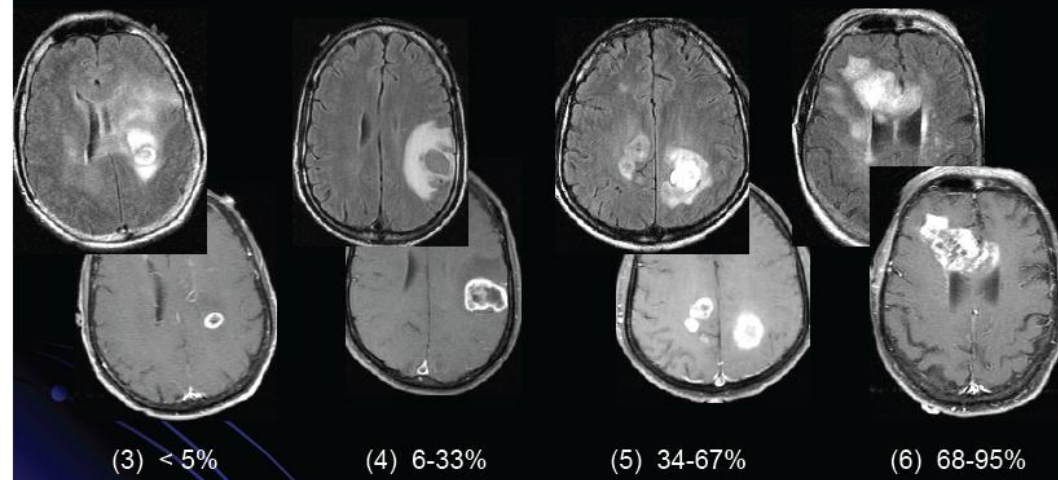
| University/Project | Modality | # Patients | Total # of slides |
|----------------------------|--------------------|------------|-------------------|
| TCGA Public Repository | 20X Digital Slide | 167 | 480 |
| EMORY TCGA Cases | 40X Digital Slide | 52 | 195 |
| Henry Ford TCGA Cases | 40X Digital Slide | *,**70 | 198 |
| Henry Ford REMBRANDT Cases | 40X Digital Slides | **199 | 335 |
| TJU Rembrandt Cases | 40X Digital Slides | ***63 | 230 |

*Some overlap with TCGA main repository but rescanned at 40X

** Data obtained by generosity of Lisa Scarpace/Tom Mikkelsen @ HF

***Thanks to Adam Flanders/Mark Curtis @ TJU

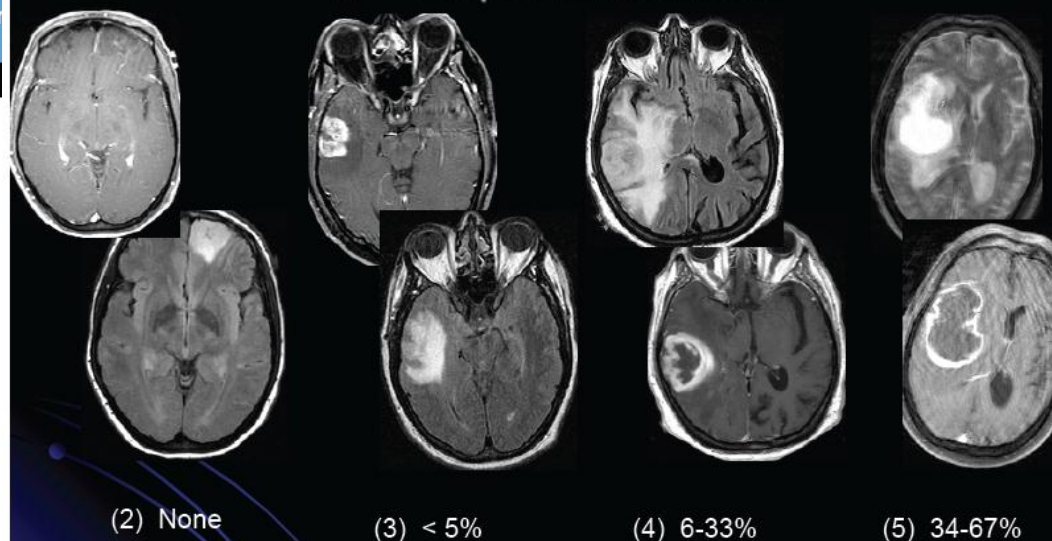
f5 – Proportion Enhancing



Visually, when scanning through the entire tumor volume, what proportion of tumor would you estimate is enhancing. (Assuming that the entire abnormality is comprised of: (1) an enhancing component, (2) a non-enhancing component and (4) a edema component.)

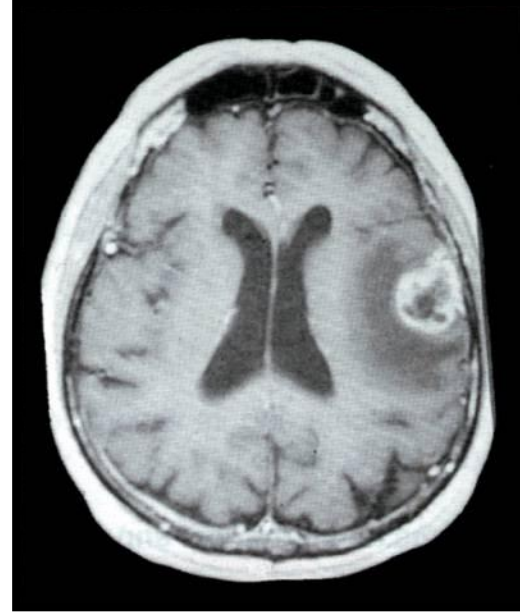
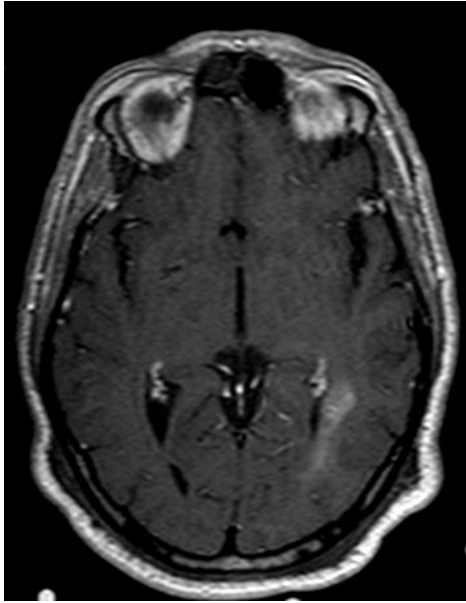
VASARI Feature Set

f7 – Proportion Necrosis



Visually, when scanning through the entire tumor volume, what proportion of the tumor is estimated to represent necrosis. Necrosis is defined as a region within the tumor that does not enhance or shows markedly diminished enhancement, is high on T2W and proton density images, is low on T1W images, and has an irregular border). (Assuming that the entire abnormality may be comprised of: (1) an enhancing component, (2) a non-enhancing component, (3) a necrotic component and (4) a edema component.)

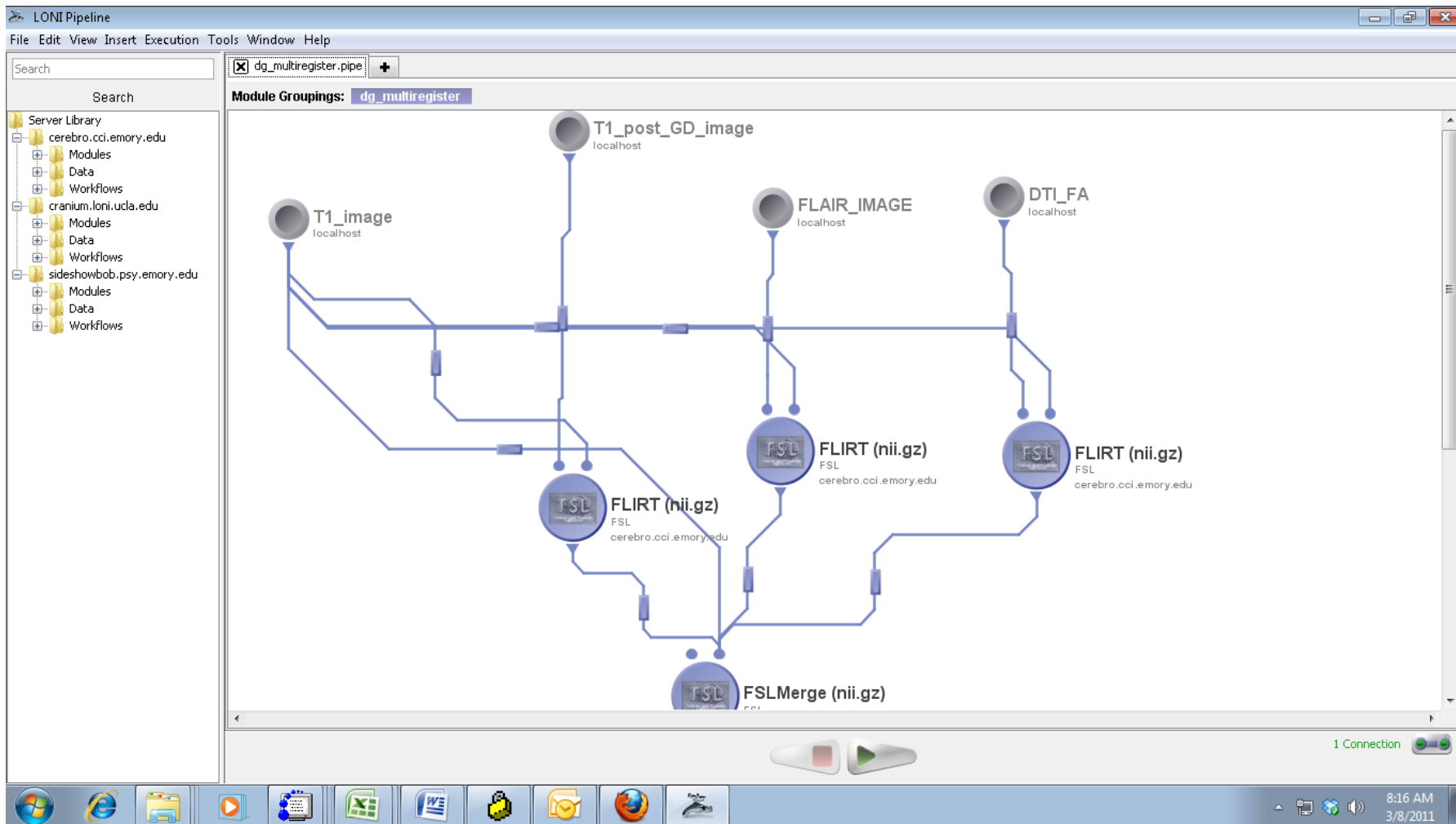
Molecular and Pathologic Correlates of MR Features



MRI of 75 TCGA GBMs reviewed by 3 neuroradiologists using VASARI feature set

MR Features compared to TCGA Neuropathology Classes, Transcriptional Classes, Genetic Alterations

Automated feature extraction pipeline also being developed for MRI

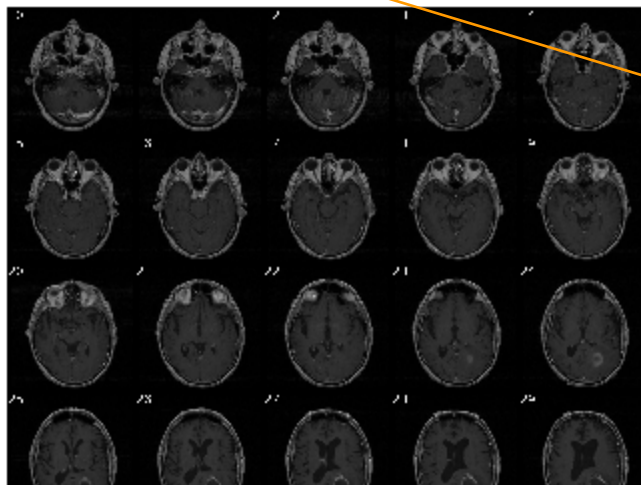


notes:

Basically the descriptions are often duplicated or nonsensical-- to parse this we need to manually tag the sequences from within a given MRI session

Scans

| Scan | Type | Usability | Files | Note |
|------|-------------------------------|-----------|-------------|------|
| + 1 | SAG LOCAL | usable | Show Counts | |
| + 2 | AXIAL FSE | usable | Show Counts | |
| + 3 | AXIAL T2 FLAIR | usable | Show Counts | |
| + 4 | DWI MAP | usable | Show Counts | |
| + 5 | AXIAL T1 PRE GD | usable | Show Counts | |
| + 6 | AXIAL GRE | usable | Show Counts | |
| + 7 | AXIAL T1 PRE GD | usable | Show Counts | |
| + 8 | NEW AXIAL PERFUSION/20S-DELAY | usable | Show Counts | |
| - 9 | AXIAL T1 POST GD | usable | Show Counts | |



Image

