MICAAI 2014 - Computational Brain Tumor Cluster of Events

I. **Workshop: Computational Precisian Medicine**
II. **Imaging Challenge: BRATS 2014**
III. **Digital Pathology Challenge**

The increase in volume and variety of multi modal data, including genomics, biomarkers, pathology and imaging data, together with advances in computational power and analytics have given rise to challenges and opportunities in determining optimal strategies for development of systems for personalized clinical decision support and advancement of precision medicine. Although this topic may be considered for many clinical problems, brain cancer is especially of interest because it is an area where a wealth of imaging and clinical data, computational tools, the severity of the disease (viz., high grade glioma), and lack of effective clinical treatment come to a head. MICCAI 2014 provides an excellent opportunity for a day long cluster of events in Brain Tumor computation, composed of a Workshop, radiologic and pathology image processing Challenges, to discuss and showcase the value of open science in addressing the challenges of Big Data in the context of brain cancer. Please see the last page (page 8) for a preliminary agenda for the Computational Brain Tumor Cluster.

The advantage of clustering these events is four-fold: (1) To demonstrate the link between computational aspects and clinical implication of such technologies, (2) To showcase Challenges as case examples of topics discussed in the workshop, (3) To lay the foundation for future expansion of Challenges to link various aspects of diagnosis and treatment planning, including genomics, digital pathology, and imaging, and (4) To offer a comprehensive full day activity to interested participants.

The proposed Imaging Challenge (MICCAI-BRATS 2014 – Challenge on Multimodal Brain Tumor Image Segmentation), and Digital Pathology Challenge will make use of data currently available through data archive resources of the National Institutes of Health (NIH), namely, the Cancer Genome Atlas (TCGA) and the Cancer Image Archive (TCIA) –see Figure 1. The proposed Digital Pathology challenge will use digital slides related to patients whose genomics data are available from TCGA. Similarly, BRATS 2014 Challenge will use clinical MRI image data, also from the TCGA study subjects. The common approaches taken by both of these Challenges are scientifically important in a number of ways - First we will be using high quality publicly available data for which the corresponding genomics data are also available. Second, targeting pathology and imaging data from the same patient cohort explores a connection between the Digital Pathology Challenge and BRATS Challenge, which joins two key drivers of clinical decision making, i.e., pathologic and radiologic diagnoses, as well as support for neurosurgical, radiotherapy and neuro-oncologic treatment planning. Third, these dual brain tumor challenges proposed for 2014 will set the stage for future MICCAI challenges which will further explore connections between multimodal data (genomics, pathology, and imaging).

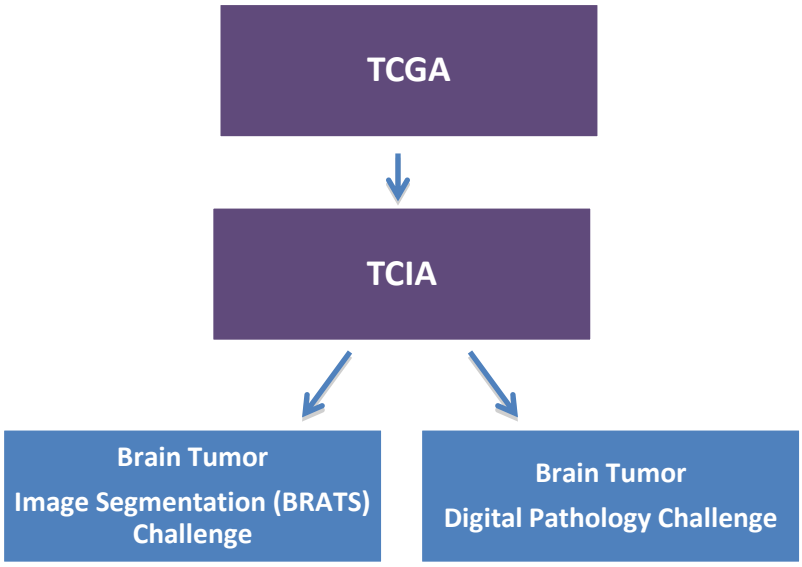

Figure 1 – *The Cancer Genome Atlas (TCGA) contains tissue samples, pathology and imaging data of clinical cases of brain tumors. Anonymized imaging and digital pathology data corresponding to TCGA data will be available for the BRATS and Digital Pathology Challenges on the Cancer Image Archive (TCIA).*

I. Workshop: Computational Precisian Medicine

The goal of the workshop is to present and discuss basic requirements and current recourses for open science development of systems in support of computational precision medicine in brain tumor diagnosis and treatment planning. Presentations in this half-day workshop (8:30 am – 12:30 pm) will include a report of a recent National Cancer Institute (NCI) workshop on imaging and genomics by organizers of that workshop; invited presentations by leading field experts; open science approaches, including Grand Challenges, for assessment of technologies in computer-aided interventions; and discussion of NCI computational resources available to the scientific community. The workshop will also include a 1-hour session for oral presentation of proffered papers, selected by the organizers. Other meritorious paper submissions may be presented at a poster session.

II. Imaging Challenge: BRATS 2014

The goal of the imaging Challenge in multi-modal Brain Tumor Image Segmentation (BRATS) is to gauge the current state-of-the-art in automated brain tumor segmentation and compare different methods. This will be a continuation of efforts with BRATS in MICCAI 2012 and continued in MICCAI 2013. Twenty groups have participated in previous BRATS challenges. An annotated data set containing 60 low and high grade gliomas was generated which is publicly available through the Virtual Skeleton Database (VSD)[1] and MIDAS[2] websites, two online platforms for hosting and evaluating image segmentation benchmarks. A related manuscript by Menze, et. al., describing the results of these efforts has been submitted to the IEEE Transactions in Medical Imaging journal.[3]

BRATS 2014 will continue with image segmentation challenges and add to the variety of sub-challenge tasks, including analysis of longitudinal data sets and classification of tumor grades. We will invite researchers, primarily past BRATS participants, to automatically annotate MRI data sets from the National Cancer Institute (NCI) image archive, the Cancer Image Archive (TCIA)[4]. The TCIA contains MR images, acquired with different weightings, from over 200 clinical cases, some acquired pre-/post-therapy or at multiple time points. We will fuse 5-10 segmentations to arrive at an approximate Ground Truth. We will then manually annotate a subset of the data set to estimate automated segmentation quality and make the necessary corrections, at least for the Test data. The processed (coregistered, resampled to 1 mm^3 resolution, skull stripped) images will be publicly available in spring via VSD, complementing existing training data sets from MICCAI-BRATS 2012 and 2013.

BRATS-2014 Sub-Challenges

BRATS-2014 Challenge will contain three sub-challenges:

Sub-Challenge 1: Segmentation – General evaluation of over 50 cases, similar to previous BRATS Challenges.

Sub-Challenge 2: Longitudinal Evaluation – Segmentation of time series images, representing a sub-set of Test data.

Sub-Challenge 3: Classification – Automatic classification of data into one of the three classes of Lo Grade II, Low Grade III, and High Grade IV (glioblastoma multifome or GBM).

Sub-challenge 1 and 2 will use segmentation evaluation metrics as implemented in VSD. Performance scores for sub-challenge 1 and 2 will be evaluated for every segmentation entry. Sub-challenge 3 will be optional. We will use the same Test data sets cases for the BRATS Challenge and Digital Pathology Challenge (next section) to encourage discussions between groups participating in these challenges and to compare the diagnostic value of automated classification of MRI and pathology images.

[1] https://vsd.unibe.ch/WebSite/BRATS/Start2013
[2] http://challenge.kitware.com/midas/folder/102
[3] A preliminary draft is available here: www.vision.ee.ethz.ch/~bmenze/tmp/brats_manuscript_3.pdf
[4] www.cancerimagingarchive.net

III. Brain Tumor Digital Pathology Challenge

Brain tumor diagnosis, as traditionally performed by pathologists, involves examination of tissue sections on glass slides with a light microscope. As the technology for digital imaging has advanced, there is now increasing use of digital images ("virtual slides") for pathologic analysis of surgical specimens. Automated tumor segmentation, by defining tumor regions with critical histologic features has the potential to increase both the speed and accuracy of diagnosis by pathologists and/or computer software. Key features in digital pathology diagnosis of brain tumors, which lend themselves well to computer-aided detection and automation, as means of supporting clinical decision making by pathologists, include, (a) differentiation of high and low grade gliomas, and (b) segmentation of necrotic zones – both of which have significant implications for downstream tissue sample genetic testing.

A critical dividing line in brain tumor diagnosis is separating glioblastoma multiforme (GBM, WHO Grade IV) from lower grade glioma (LGG, defined as WHO grade II or III for purposes of the TCGA), since GBM compared to LGG has worse prognosis and may be treated more aggressively by neuro-oncologists. Diffusely infiltrating astrocytic tumors with necrosis are, by definition, glioblastoma. Necrosis, therefore, is a critical histopathologic variable in separating GBM from LGG.

There will be two sub-challenges in the proposed Brain Tumor Digital Pathology Challenge:

> **<u>Sub-Challenge I: Classification</u> - Automated classification of LGG and GBM from a collection of 30 high-resolution digital pathology slide clinical cases.**
>
> **<u>Sub-Challenge II: Segmentation</u> – Automated segmentation of necrotic and normal brain regions on regions of digital pathology slides from a collection of 20 GBM cases.**

This challenge and a related challenge (MICCAI-BRATS 2014 – Challenge on Multimodal Brain Tumor Image Segmentation, proposed by Menze, et. al.), will make use of data currently available through data archive resources of the National Institutes of Health (NIH), namely, the Cancer Genome Atlas (TCGA) and the Cancer Image Archive (TCIA) –see Figure 1. The proposed Digital Pathology challenge will use digital slides related to patients whose genomics data are available from TCGA. Similarly, BRATS 2014 Challenge will use clinical MRI image data, also from the TCGA study subjects. The common approaches taken by both of these Challenges are scientifically important in a number of ways - First we will be using high quality publicly available data for which the corresponding genomics data are also available. Second, targeting pathology and imaging data from the same patient cohort explores a connection between the Digital Pathology Challenge and BRATS Challenge, which joins two key drivers of clinical decision making, i.e., pathologic and radiologic diagnoses, as well as support for neurosurgical, radiotherapy and neuro-oncologic treatment planning. Third, these dual brain tumor challenges proposed for 2014 will set the stage for future MICCAI challenges which will further explore connections between multimodal data (genomics, pathology, and imaging).

Evaluation of Computer Algorithm Results

Computer algorithms that participate in the challenge will be required to output their results as image masks and associated annotations. The resolution of the mask is the same as the source image/tile. An image mask is a 2D array of integers where integers of the same value represent the region segmented by the computer algorithm. Different integer values represent different regions. The integer value 0 (zero) means background (or the region that was not segmented by the algorithm). A region is annotated by a tuple (integer value, annotation) where the integer value corresponds to the integer value in the mask marking the region. The masks will be used to compute the metrics for comparing algorithm output with the expert markups and annotations in the segmentation sub-challenge.

Classification sub-challenge: The score for each contestant in the Classification sub-challenge will be computed as the number of correctly classified cases divided by the number of total cases. There will be guidelines, to be posted on the challenge website, outlining how issues related to a tie or lucky guesswork will be resolved.

Segmentation sub-challenge: The metrics will include: (1) the amount of overlap between a region segmented by an algorithm and the region marked by the pathologist, (2) the number and area of regions that were missed by the algorithm, (3) the number and area of regions segmented and annotated by the algorithm, but not by the pathologist.

Evaluation of individual results in the Leader Board and Test phases of the Brain Tumor Digital Pathology Challenge will be automated through a web site submission.

Logistics

Timeline for Imaging and Digital Pathology Challenges

Figure 2 shows the timeline for brain tumor Challenges. In Phase 1 (Training) prospective contestants can train their algorithm to perform the required tasks. No evaluation of results will be available in this phase. In Phase 2 (Leader Board) prospective contestants may submit their algorithm results for evaluation against sequestered Ground Truth data. In Phase 3 (Test) contestants will submit their results for evaluation and ranking. We would like to hold the Test phase “off-site” and on-line a week prior to the date for MICCAI Challenges. This will allow for timely download of large amounts of data, processing and uploading of results.

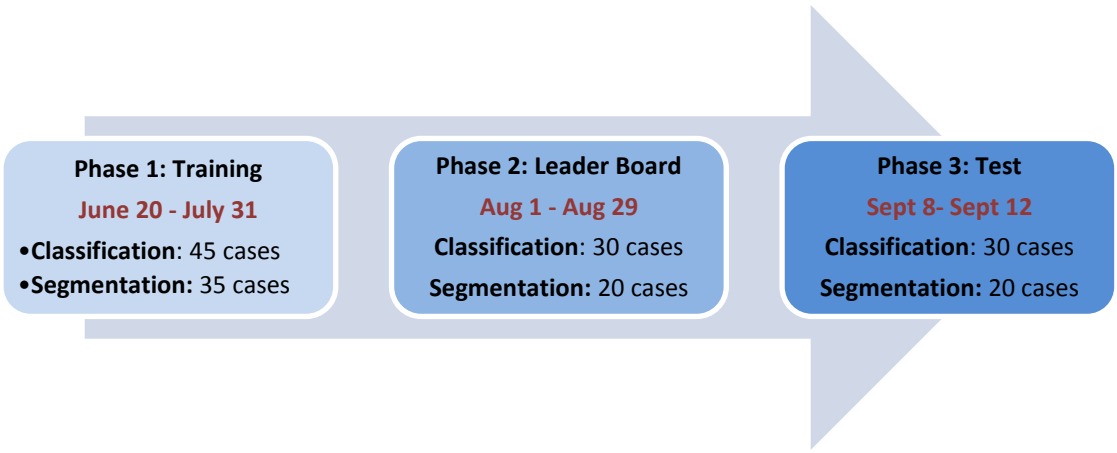

Figure 2 – *Timeline and number of unique cases for each phase of Classification and Segmentation sub-challenges. GBM cases used for the Segmentation sub-challenge will be a subset of the combined LGG and GBM cases used for the Classification sub-challenge. All data will be anonymized and available on the NCI TCIA Website for download. The proposed time line may be adjusted in consideration of MICCAI registration requirements.*

Manuscript and Poster Submissions

Participants in each of the two Challenges will be required to submit short manuscripts outlining their approach and preliminary results on the training data in July. Respective Challenge organizers will review all submissions and submitters will be notified of the results. Challenge Test (Phase 3) results will be announced at the workshop and the top three scoring teams will be invited to give 12 min presentations of their methodology and results. All participants will be invited to submit posters for exhibition at MICCAI 2014. Reports may be prepared by the respective organizers of each Challenge after MICCAI 2014 for submission to appropriate peer reviewed journals.

Announcements and Anticipated Number of Participants

We will publicize the Computational Brain Tumor Cluster of events through appropriate email distributions, including imageworld, machine learning, visionlist, and NCI Cancer Imaging Program website and listserv. Based on past experience with similar challenges we expect about 10 groups (more than 20 registrants) to participate in the Brain Tumor Digital Pathology Challenge.

MICCAI Resource Needs

Space for 60+ people with one projector and one screen (or multiple large screen display monitors), wireless Internet access. Due to the clinical relevance of topics in the Brain Tumor Workshop and Challenge Cluster we request holding these events at the Harvard Medical School. This will encourage participation by clinicians and their research staff.

Computational Brain Tumor Cluster: Organizers and Contacts

Workshop Organizing Committee:

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Keyvan Farahani, National Cancer Institute, and Johns Hopkins University (Farahani@nih.gov)
John Freymann, Leidos Biomedical Res, Inc. (freymanj@mail.nih.gov)
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Workshop Speakers (tentative and subject to final confirmation):

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Rivka Colen, MD Anderson Cancer Center
Keyvan Farahani, National Cancer Institute
Robert Gillies, Moffitt Cancer Center
Carl Jaffe, Boston University
Ron Kikinis, Harvard Medical School
Simon Mercer, Microsoft Research
Joel Saltz, Stony Brook Cancer Center
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MICCAI 2014- Computational Brain Tumor Cluster

8:30 am – 12:30 pm Workshop

[Chairs: Clarke (NCI), Farahani (NCI), Jaffe (BU)]

8:30-8:45 am	Introduction
8:45-10:00 am	Invited talks (3-4) – on computation and/or path correlation, plus • Report: NCI 2013 Workshop on Imaging and Genomics • Open science platforms for assessment of technologies
10:00-10:20 am	Break
10:20-11:50 am	Proffered papers
11:50 am-12:30 pm	Presentation of NCI resources: TCGA, TCIA, HubZero, etc.

1:00 pm – 5:30 pm	**Brain Tumor Challenges**
1:00 – 3:00 pm	**Brain Tumor Image Segmentation Challenge (BRATS)** [Chairs: Menze (TU Munich), Kalpathy-Cramer (MGH), Reyes (Bern U)]
1:00 – 1:30 pm	Presentation of results by chairs and discussion of results
1:30 – 2:15 pm	Presentations by top 3 challenge winners (12 min each + 3 min discussion)
2:15 – 3:00 pm	General discussion
3:00 – 3:30 pm	Break

3:30 – 5:30 pm	**Brain Tumor Digital Pathology Challenge**
	[Chairs: Saltz (Stony Brook), Brat (Emory)]
3:30 – 4:00 pm	Presentation of results by chairs and discussion of results
4:00 – 4:45 pm	Presentations by top 3 challenge winners (12 min each + 3 min discussion)
4:45 – 5:30 pm	General discussion and wrap-up
5:30 pm	Adjourn