Capstone for Impact Submission | GY2020

Project Title: Metabolic Tumor Volume Response Assessment Using (11)C-Methionine Positron Emission Tomography Identifies Glioblastoma Tumor Subregions That Predict Progression Better Than Baseline or Anatomic Magnetic Resonance Imaging Alone

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Advisor Names(s): Michelle Kim, MD

Branch: Patients and Populations

Path of Excellence: Scientific Discovery

If this project can be continued by another UMMS student, please include your contact information or any other details you would like to share here:

Purpose

To evaluate whether response assessment of newly diagnosed glioblastoma at 3 months using ^{11}C-methionine-positron emission tomography (MET-PET) is better associated with patient outcome compared with baseline MET-PET or anatomic magnetic resonance imaging alone.

Methods and Materials

Patients included were participants in a phase I/II trial of dose-escalated chemoradiation based on anatomic magnetic resonance imaging. Automated segmentation of metabolic tumor volume (MTV) was performed at a threshold of 1.5 times mean cerebellar uptake. Progression-free (PFS) and overall survival were estimated with the Kaplan-Meier method and compared with log-rank tests. Multivariate analysis for PFS and overall survival was performed using Cox proportional hazards, and spatial overlap between imaging and recurrence volumes were analyzed.

Results

Among 37 patients, 15 had gross total resection, of whom 10 (67%) had residual MTV, 16 subtotal resection, and 6 biopsy alone. Median radiation therapy dose was 75 Gy (range, 66-81). Median baseline T1 Gd-enhanced tumor volume (GTV-Gd) was 38.0 cm^3 (range, 8.0-81.5). Median pre-CRT MTV was 4.9 cm^3 (range, 0-43.8). Among 25 patients with 3-month MET-PET, MTV was only 2.4 cm^3 (range, 0.004-18.0) in patients with uptake. Patients with MTV = 0 cm^3 at 3 months had superior PFS (18.2 vs 10.1 months, P = .03). On multivariate analysis, larger 3-month MTV (hazard ratio [HR] 2.4, 95% confidence interval [CI], 1.4-4.3, P = .03), persistent MET-PET subvolume (overlap

of pre-CRT and 3 month MTV; HR 2.0, 95% CI, 1.2-3.4, *P* = .06), and increase in MTV (HR 1.8, 95% CI, 1.1-3.1, *P* = .09) were the only imaging factors significant for worse PFS. GTV-Gd at recurrence encompassed 97% of the persistent MET-PET subvolume (interquartile range 72%-100%), versus 71% (interquartile range 39%-93%) of baseline MTV, 54% of baseline GTV-Gd (18%-87%), and 78% of 3-month MTV (47%-95%).

Conclusions

The majority of patients with apparent gross total resection of glioblastoma have measurable postoperative MTV. Total and persisting MTV 3 months post-CRT were significant predictors of PFS, and persistent MET-PET subvolume was the strongest predictor for localizing tumor recurrence.

Reflection/Impact Statement:

This project allowed me to engage in the research process from start to finish. I helped with the initial image processing to obtain the necessary volumes for the study. I then helped perform the various analyses with the help of statisticians in the Department of Radiation Oncology at the University of Michigan. Finally, I wrote a manuscript with the assistance of Michelle Kim, MD – an Assistant Professor of Radiation Oncology at Michigan. I also presented this work at the 2019 ASTRO meeting. This project shed light on the usefulness of 11C-Methionine PET scans for glioblastoma. This modality appears to identify a radioresistant portion of tumor. Ideally, we will be able to identify this portion of tumor using a more widely applicable modality such as advanced MRI. This is where future studies should be directed.

As far as recommendations for future students, they should identify a mentor early who is accustomed to working with medical students and who has a track-record of publishing. Then they should remain focused and follow through the project to completion, even if this takes many years (as long as it looks like it will ultimately be publishable).