Automatic Segmentation and Longitudinal Tracking of Brain Metastatic Lesions on MRI

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Introduction
In current clinical practice, patients with brain metastases (BM) receive surgery, radiation, and/or chemotherapy, and undergo magnetic resonance (MR) scans at regular intervals throughout their therapy. To assess efficacy of the current treatment regimen, neuroradiologists track individual lesion sizes across time points. If BM enlarge overtime, a different treatment option may be needed. However, as some patients can have more than ten lesions, manual delineation of all metastatic lesions is prohibitively time-consuming. As a result, most radiographic response criteria restrict response to a select number of target lesions, which can fail to capture the full extent of the disease burden. To overcome these challenges and enable applications in a clinical setting, we propose a robust deep learning approach to automatically segment all BM on MR, and furthermore, enable tracking of individual lesions across time points.

Hypothesis
We hypothesize that a deep learning approach can be used to automatically segment brain metastatic lesions on post contrast MR, which will enable longitudinal volumetric tracking of individual lesions.

Methods
182 longitudinal MRIs from 82 patients with MPRAGE-post contrast imaging protocol were prospectively obtained from Massachusetts General Hospital (MGH). An expert neuro-oncologist with 10+ years of experience provided ground truth segmentations for all patients. We split our data into training (46 patients, 118 timepoints), validation (18 patients, 32 timepoints), and testing (18 patients, 32 timepoints) sets. Using the training set, a 3D U-Net architecture (implemented in DeepNeuro, a software package for machine learning in neuroimaging) with input patch size of 32x32x32 was trained with weighted cross-entropy loss function. Training was stopped when validation set Dice score plateaued to prevent overfitting. To enable individual lesion tracking, all time-points per patient were affinely registered to each other. Every lesion was subsequently classified based on its growth rate (responder: overall lesion shrinkage; inconclusive: 0% to 40% lesion growth; non-responder: more than 40% lesion growth). Characterization of global lesion growth rate patterns was accomplished by affinely registering all time-points to the MNI brain atlas. Segmented lesions were projected onto the atlas, which was qualitatively analyzed to identify spatial regions composed primarily of one class of lesion.

Results
For automatic segmentation, we report a mean dice score of 0.778, 0.737, and 0.704 on training, validation, and testing sets respectively. Furthermore, we find that the largest BM with the highest average growth rate (non-responders) tend to

Figure 1. Red lesion represents high growth rate metastases. This lesion was not present during time point one but grows to a significant size over the patient visits. Yellow lesion represents slow growth rate metastases. This lesion was also not present during time point one but does not grow to as large of a volume, nor grow as quickly as the red-labeled lesion. Green lesion represents a shrinking metastasis. This lesion shrinks in size over the course of treatment.
be located in the posterior frontal/parietal lobes, while smaller, lower growth rate lesions (responders) tend to be localized in the frontal lobes. The posterior fossa was found to be heterogeneous in lesion size and growth rate.

**Conclusion**
We developed longitudinal metastatic lesion tracking and identified brain regions associated with differing growth rate lesions.

**Statement of Impact**
Our segmenter accurately tracks BM longitudinally during treatment facilitating individual tumor response assessment in a disease where multiple tumors are common. Identification of regions associated with non-responding tumors may improve our understanding of local microenvironment drivers of response and may enable use of focal targeted therapies (i.e. resection or radiation) to augment treatment.

**Keywords**
deep learning, metastatic lesions, segmentation