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Brainstem Radiosurgery: Analysis of Dose and Radiographic Adverse Events

Eric J. Lehrer [1] , Matthew H. Snyder [2] , Sonam Sharma [3] , David Schlesinger [2] , Daniel M. Trifiletti [4] , Jason Sheehan [5]

1. Department of Radiation Oncology, Ichan School of Medicine at Mount Sinai, New York, USA 2. Department of Neurological Surgery, University of Virginia, Charlottesville, USA 3. Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York City, USA 4. Department of Radiation Oncology, Mayo Clinic Florida, Jacksonville, USA 5. Neurological Surgery, University of Virginia , Charlottesville , USA

Corresponding author: Eric J. Lehrer, ericjlehrer@gmail.com

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Abstract

Objectives: The brainstem is a highly eloquent area of the central nervous system (CNS). As a result, treatment options for these lesions are often limited, conferring a poorer prognosis compared to similar lesions in other CNS locations. Conservative estimates by the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) indicate that the risk for adverse events increases when the maximum brainstem dose exceeds 12.5 Gy. The objective of this study is to analyze the association between dose-volume relationships and adverse effects in brainstem lesions treated with stereotactic radiosurgery (SRS).

Methods: Treatment plans were generated on BrainLab Elements and GammaPlan software with aid of magnetic resonance imaging (MRI). Dosimetric data from dose-volume histograms were extracted as continuous variables for patients who received SRS to brain metastases (BrM) or arteriovenous malformations (AVM) within or on the brainstem margin. Dosimetric parameters included V5Gy, V25Gy, V50Gy, V75Gy, V95Gy, D5%, D25%, D50%, D75%, and D95% to the brainstem. Adverse effects were analyzed as a dichotomous categorical variable and were defined as both clinical (new cranial nerve palsy or limb paresis) and radiographic radiation-related changes on follow-up MRI (new edema, radiation necrosis, cystic change, > 20% lesion volume expansion from baseline, or hemorrhage [AVM only]). Logistic regression was utilized to assess the relationship between dosimetric parameters and incidence of radiographic adverse effects.

Results: Sixty patients who underwent single fraction Gamma Knife (GK) radiosurgery at the University of Virginia from 2007-2018 for BrM or AVM were retrospectively analyzed. Mean patient age was 60.9 years (range: 12-92 years) and median prescription dose was 18 Gy (range: 13-25 Gy). The mean brainstem dose ranged from 2.7-5.6 Gy and the maximum dose ranged from 0.4-44.6 Gy. The median follow-up was 4.3 months for all patients. On logistic regression, increasing D5% (OR: 1.21; p=0.013) and D25% (OR: 1.54; p=0.03) were found to be associated with a higher incidence of clinical or radiographic complications. The mean D5% was 8 Gy and the mean D25% was 3 Gy. Increasing V25Gy was found to be associated with clinical complications post-GK (OR: 0.1; p=0.05). The mean V25Gy was 0.09cc. The remainder of the

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dosimetric parameters were not found to be associated with radiographic adverse effects.

Conclusions: In this series of patients with brainstem lesions treated with stereotactic radiosurgery, increasing dose to the hottest 5% and 25% of the brainstem volume and increasing brainstem volume receiving 25 Gy or higher is associated with a higher incidence of adverse effects. Changes in other dose-volume parameters were not found to be associated with increasing toxicity. Therefore, brainstem dose tolerances may be greater than those estimated by QUANTEC. Further investigation is needed to validate these findings.