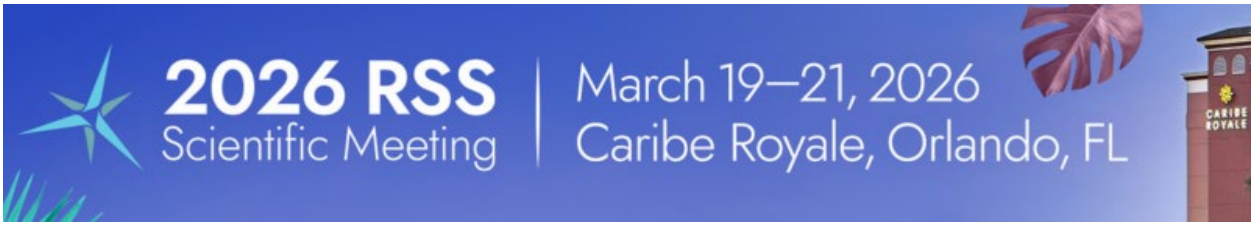

Prediction of Long-Term Clinical Outcomes After Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations Based on Early Hemodynamic Response as Measured by 4D Flow MRI

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Objectives: Stereotactic radiosurgery (SRS) is a standard treatment for unresectable cerebral arteriovenous malformations (AVMs). However, obliteration can take years to occur, and outcome prediction is challenging. Here we assess whether early changes in blood flow through feeding arteries after SRS are predictive of time to future obliteration and hemorrhage events using a novel functional magnetic resonance imaging (MRI) technique, 4D Flow MRI. We hypothesized that greater hemodynamic changes at early timepoints would be associated with earlier obliteration and lower hemorrhage risk.

Methods: Eighteen prospectively enrolled AVM patients underwent 4D Flow MRI prior to, 6-months post-, and one-year post-SRS. Blood flow was measured using FDA-cleared software for clinical 4D flow analysis. At each timepoint, mean blood flow over the cardiac cycle was measured at the same point in a proximal feeding artery. Treatment response at 6 months and 1 year was defined as the fractional flow at that timepoint compared to before SRS. Patients were followed clinically thereafter with annual serial imaging. The association between fractional response and time to obliteration was analyzed using the Fine-Gray approach, with hemorrhage or death treated as competing events. AVM volume and standard dosimetric variables were assessed using the same approach.

Results: Median follow-up was 1,236 days (range 280–2,577). Median flow response was 0.72 at 6 months (0.38–0.93) and 0.58 at 1 year (0.12–1.04). Median volume was 0.73cc (0.20–10.3cc). Median (range) was 18.4Gy (13.7-20.7Gy) for Dmin, 26.9Gy (23.2-32Gy) for Dmax, 23.4Gy (21.6-26.5Gy) for Dmean, and 19.7Gy (16-22Gy) for D99%. There were 12 obliterations and 2 hemorrhages. Four patients remain at risk. On univariate regression, 1-year response, D99, and Dmin demonstrated a trend toward significance with respect to obliteration ($p < 0.2$), with patients demonstrating a deeper 1-year response trending towards earlier obliteration. Both 6-month and 1-year responses were significant predictors of competing hemorrhage (both $p< 0.05$). Neither nidus volume nor any of the dosimetric variables were predictive of hemorrhage.

Conclusion(s): With over 3 years median follow-up, early hemodynamic response in feeding arteries after SRS, as measured by 4D flow MRI, shows promise as a predictor of post-SRS hemorrhage and

may also have predictive value for time-to-obliteration. Larger cohorts are needed to validate these findings.