**IGKRF Retrospective Study: Volume-Stage Stereotactic Radiosurgery for Large Arteriovenous Malformations**

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**Abstract**

Unlike small arteriovenous malformations (AVMs), which may be treated effectively with surgery, embolization, or radiosurgery, large AVMs remain difficult to treat. The generally accepted goal of SRS for AVMs is complete obliteration without associated adverse radiation effects (AREs). Select small AVMs (< 10 ml) have a 3-year obliteration rate of 70%–95%.\(^3\,^6\) Total obliteration appears to reduce the cumulative lifetime risk of hemorrhage to approximately 1%, in comparison to an annual hemorrhage risk for these large lesions which is estimated between 5-7% annually with approximately a 40% mortality rate per hemorrhage.\(^4\,^8\) Radiation dose and treatment volume play important roles in the rates of AVM obliteration; Pan et al. reported only a 25% overall obliteration rate at 40 months for single-stage SRS to treat AVM volumes larger than 15 ml using doses less than 17.5 Gy.\(^5\)

Volume-staged radiosurgery (VS-SRS) is an approach to large volume targets potentially improve rates of obliteration and decrease the normal tissue 12-Gy volume by 27.3% and the overall 12-Gy volume by 11% compared with a hypothetical single session of SRS which may allow for necessary dose escalation to the lesions.\(^7\) Volume staging also allows for sub-lethal damage repair in the adjacent normal brain, possibly further decreasing the risk of a symptomatic ARE. The rates of obliteration in the volume-staged setting have varied, and predictors of response include as total AVM volume, volume per stage, dose per stage, and AVM architecture.\(^1\,^8\)

Initial reports of VS-SRS reveal low rates of obliteration likely due to inadequate volume-staging by not reducing the volume of stage to allow for adequate dose delivery. Seymour et al. reported rates of at least near obliteration by MRI as high as 74% at 5 years when volume stages were increased in order to ensure 17 Gy per stage compared to 23% in patients treated with <17 Gy (univariate: p = <0.001; multivariate: p = 0.01, hazard ratio 5.34, 95% confidence interval 1.5-8.95).\(^8\) Kano et al. notes similar findings suggesting a continued dose-response curve with VS-SRS as had previously been document in single session SRS with higher rates of obliteration in patients treated to ≥17 and ≥18 Gy (margin dose ≥17 Gy P 0.001 and ≥18 Gy p < 0.001) and reported a 63% total obliteration rate when treating with ≥17 Gy per volume-stage.\(^1\)

Estimates of ARE have been demonstrated based on the size of the treatment volume, location of the target and the 12 Gy volume in the treatment of AVMs in the single session setting.\(^2\) However, we are unsure the degree to which we are able to successfully dissociate the inherent correlation of dose and volume with a volume-staged approach. Seymour et al noted a trend to decreased ARE in spite of higher treatment dose when utilizing more volume-stages per lesion and higher doses per volume stage suggesting that some dissociation is occurring (29% vs 13%).\(^8\)

The purpose of this multi-center project is to evaluate factors associated with obliteration, risks of bleeding, ARE, delayed cyst formation, and the utilization of salvage therapy in patients with large AVMs which were treated by repeat VS-SRS approach. Specifically, we will 1) descriptively describe the current treatment paradigm with estimates for good outcomes with response and avoidance of ARE and 2) evaluate the frequency of ARE compared with patients treated with a single volume stage from prior NAGKC/IGKRF reviews and models estimating ARE with those with multiple
stages to assess the ability of a VS-SRS approach in dissociating dose and volume to develop guidelines for future prospective dose-escalation with a volume staged approach.

References:


