Vascular Targeting Causing Thrombosis in an Arteriovenous Malformation Animal Model

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Introduction: Despite current treatments, ⅓ of brain arteriovenous malformations (AVMs) are untreatable. Previous work has identified the potential target phosphatidylserine (PS) externalised in the plasma membrane of the endothelium in AVMs that have undergone treatment with focused irradiation. We hypothesise that treatment of AVMs with gamma knife radiosurgery (GKS) and vascular targeting of PS with a thrombotic compound will cause localised thrombosis within the AVM vessels.

Methods: A rat animal model was used by performing an end-to-side anastomosis of the external jugular vein (EJV) to the common carotid artery. The AVM was treated with a dose of focused radiation of 20 Gy using a Leksell Gamma Knife. At 3 weeks following GKS a dose of a conjugate of Annexin V and thrombin was administered intravenously. Comparison groups of saline and thrombin alone were included. At 4 weeks following conjugate administration, an angiogram was performed with tissue harvested for histology.

Results: There was occlusion of the AVM on angiography in 69% of conjugate-treated animals (**p=0.002**). AVM occlusion occurred in 63% of the GKS group treated with conjugate (**p=0.03**), and in 75% of the sham-GKS conjugate treated group (**p=0.009**). Both control arms had preserved AVM flow on angiogram. Histological evidence of occlusive thrombus was present within the EJV and nidus of 62.5% of animals in the GKS with conjugate group (**p=0.026**). A non-significant trend of histological thrombus within the EJV was noted in animals in the GKS with conjugate group (62.5%) compared to animals with conjugate alone (37.5%) (p=0.37).

Conclusion: This study demonstrates a significant association between use of an Annexin V/Thrombin conjugate and thrombosis of AVM vessels both radiologically and histologically and may demonstrate a potential new treatment for AVMs. This finding is the first of its kind in the treatment of AVMs. Further work is needed to confirm the findings in a larger sample and to explore other potential targets.