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# Reductions in Brain Pericytes are Associated with Arteriovenous Malformation Vascular Instability

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## Introduction

Brain arteriovenous malformations (bAVMs) are a rupture-prone tangle of blood vessels with direct shunting between arterial and venous circulations. The mechanisms contributing to bAVM pathogenesis in sporadic lesions remains elusive. Studies have focused on endothelial cells and the contributions of other cell types have yet to be studied. Pericytes are multi-functional cells which regulate brain angiogenesis and vascular stability. Here, we analyze the abundance of brain pericytes and their association with vascular changes in human bAVMs.

## Methods

bAVMs and non-vascular lesion epilepsy tissue were surgically resected. Immunofluorescent staining was performed to quantify pericytes (platelet derived growth factor receptor beta (PDGFRbeta) and N-aminopeptidase (CD13)) and hemoglobin. Hemosiderin deposits were quantified with Prussian blue staining. Syngo-iFlow processing was utilized to measure blood flow on pre-intervention angiograms.

## Results

Immunofluorescent analysis demonstrated a 68% reduction in vascular pericyte number in bAVMs ($p < 0.01$). Analysis demonstrated 52% and 50% reduction in the vascular surface area covered by CD13- and PDGFRbeta-positive pericyte cell processes, respectively, in bAVMs ($p < 0.01$). Reductions in pericyte coverage were greatest in ruptured bAVMs ($p < 0.05$), and correlated negatively with microhemorrhage-derived extravascular hemoglobin in unruptured cases (CD13: $r = -0.93$, $p<0.01$; PDGFRbeta: $r = -0.87$, $p<0.01$). A similar negative correlation was observed with pericyte coverage and Prussian-blue positive hemosiderin deposits. Pericyte coverage correlated positively with mean transit time of blood flow through the bAVM nidus (CD13:$r = 0.60$, $p < 0.05$; PDGFRbeta:$r = 0.63$, $p < 0.05$).

## Conclusions

Pericytes are reduced in sporadic bAVMs and are lowest in cases with prior rupture or with greatest mircohemorrhage burden. Pericytes also correlate with rate of blood flow through the bAVM nidus. This suggests that pericytes are associated with and may contribute to vascular fragility and hemodynamic changes in bAVMs. Future studies are needed to better characterize the role of pericytes in AVM pathogenesis.

## Learning Objectives

By the conclusion of this session, participants should be able to: 1)Describe the importance of vascular pericytes in cerebrovascular biology; 2) Understand the hypothesized role of pericytes in vascular destabilization of brain arteriovenous malformations; 3) Identify the novel potential of therapeutic targeting of vascular mural cells in the treatment of brain vascular lesions.