

# Focused Ultrasound-Mediated Blood-Brain Barrier Opening Enables Amyloid- $\beta$ Immunotherapy in Cerebral Amyloid Angiopathy Without Microhemorrhage Risk

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## Abstract

Cerebral amyloid angiopathy (CAA) complicates Alzheimer's immunotherapy due to vessel-associated amyloid and microhemorrhage risk. We employed MRI-guided focused ultrasound (FUS) with microbubbles to achieve localized, reversible blood-brain barrier (BBB) opening in Tg-SwDI mice modeling CAA. FUS-enhanced delivery of aducanumab resulted in 70% reduction of vascular amyloid without increased cerebral microbleeds observed in systemic high-dose regimens. Histological analysis confirmed reduced perivascular macrophage activation and preserved vascular integrity. FUS-mediated BBB opening offers a safe, spatially targeted approach for immunotherapeutic intervention in CAA and other vascular pathologies.

**Keywords:** focused ultrasound, blood-brain barrier opening, cerebral amyloid angiopathy, aducanumab, microhemorrhage, MRI-guided delivery



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