TITLE: Continuous Tissue Plasminogen Activator Infusion Using a Minimally Invasive Irrigating Catheter for the Treatment of Intraparenchymal Hemorrhage: Preclinical Model

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Intracerebral hemorrhage (ICH) is a stroke subtype which poses one of the greatest treatment challenges affecting about 2 million people yearly worldwide. About 45 percent of ICH extend into the ventricles resulting in intraventricular hemorrhage (IVH), which is associated with a 50-80 percent mortality and high morbidity.[1] Historically, surgical clot evacuation has failed to significantly improve functional outcomes.[2] Minimally invasive approaches using an external ventricular drain with intermittent dosing of alteplase have shown to be a safe and viable method of reducing clot volume.[3,4] Despite not improving functional outcomes, a subgroup of patients may benefit from this approach provided that the clot burden is reduced by at least 50 percent.[3] We hypothesize that continuous irrigation with a minimally invasive dual lumen catheter (IRRAflow) will achieve a clot volume reduction of *at least* 50 percent in the preclinical model that we developed.

We created a system using a brain agar phantom[5] with an embedded clot made of blood products.[6] We tested four conditions: control without intervention, external ventricular drain

(EVD) with rt-PA bolus every eight hours, IRRAflow irrigation with saline, and IRRAflow irrigation with rt-PA. Clots were treated and monitored for 72 hours with CT images taken every 24 hours. Volumetric measurements were taken every 24 hours and rate of reduction in clot volume was then calculated.

Our results show that constant irrigation with rtPA using the IRRAflow device is the most effective technique for reducing clot volume by more than 50 percent. This preclinical study will serve as a basis for the use of IRRAflow in the next iterations of clinical trials evaluating minimally invasive approaches for intracranial clot lysis. Word count: 270

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