

In vitro Aneurysm Modeling and Improved Treatment using Genipin Coated Coils

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Clinical Need

- Intracranial aneurysms (ICA) are a life-threatening medical condition characterized by the weakening of blood vessels in the brain, which can then fill with blood, causing the vessel to balloon and bulge.



Figure 1: Image of healthy blood vessel (left) and diseased blood vessel

- 6.4 million people in the United States will be affected by intracranial aneurysms¹.
- Aneurysms pose a life threatening risk in the event of rupture because they have the potential to cause hemorrhagic stroke.
- With the current platinum coiling treatment, there is a 34% chance of aneurysm recurrence after the first 6 months².
- There is a need for a novel solution that reduces aneurysm recanalization rates, which our project aims to do by coating the platinum coils with genipin to crosslink and stabilize the aneurysm.

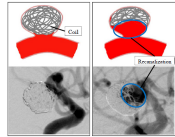


Figure 2: Image of aneurysms before (left) and after ICA treatment

Prototype Design

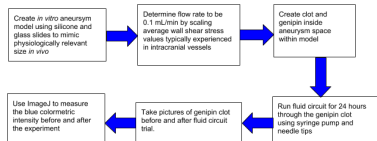


Figure 3: Flowchart Describing the Groups Objectives Throughout the Project



Figure 4: Final in vitro ICA Prototype Design

Table 1: Summary of Prototype Dimensions

Prototype Part	Size (mm)
Vessel Diameter	.25
Aneurysm Space Diameter	.9
Total Length	75
Total Width	25

Design Description



Figure 5: Experimental Setup of Fluid Circuit

- A fluid circuit was set up to model blood flow across the aneurysm space over a set period of time
- Genipin, a natural, biocompatible crosslinker, was tested to be used as a crosslinking agent to stabilize the clotting of the ICA

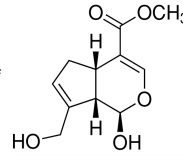


Figure 6: Structure of Genipin



Figure 7: Image of Genipin/Fibrin Clot Complex after 24 hours

- The total amount of genipin is correlated with the intensity of the blue color
- A colorimetric assay is utilized to determine relative genipin concentration at different times, which is used as a metric for clot degradation.

Reaction-Diffusion Model for the Genipin-Clot Interaction

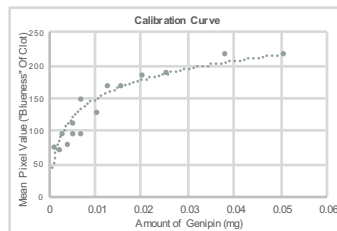
- The aneurysm space was modeled as a Continuously Stirred Tank Reactor (CSTR)
- The concentration of theoretically reacted genipin can be calculated via integrating the reaction rate in equation 1.
- The amount of genipin diffusing from the model is assumed to be any unreacted genipin

Equation 1: Reaction rate for genipin in fibrin

$$\frac{d[G]}{dt} = 3.10 \times 10^{-10} [G]^2 [A]^{1.4}$$

Initial Amount of Genipin (mg)	Amount of Genipin Reacted (mg)	Genipin Diffusing From the Model (mg)
.02000	.019907	.00009219
.04000	.039999	.000001

ImageJ Analysis



- Known amounts of genipin were analyzed in ImageJ to create a calibration curve to correlate mass and blue color
- Ran water through clots for 24 hours and analyzed what percentage of initial genipin remained

Initial Genipin (µg)	Av. Percent Lost
25	11.3%
40	19.8%

Production Cost Estimation

Component	Size	Price
Genipin	25 mg	\$24.50
Coils with Catheter	1 coil	\$1000
Coating by Technician	1 coating	\$6.50 (0.5hr @ \$13/hr)
		Total: \$1031

- Our unit cost is approximately \$1031 per procedure, assuming one coil is used.
- Only a 3% increase per-unit, but ultimately will decrease total patient costs by reducing the number of follow-up procedures required.

FDA Regulatory Pathway

Our supervisor, Dr. Chris Bettinger, already has a patent entitled "Coated Vaso-Occlusive Device for Treatment of Aneurysms". This accounts for the genipin coating for the coils aspect of our project. The patent specifically talks about coating platinum coils with genipin to increase the efficacy of the clot created to treat intracranial aneurysms.

Future Work

In the future, our project aims include:

- Develop and optimizing the genipin spray coating method for mass production
- Gaining FDA approval for clinical trial testing
- Conducting hospital testing

Acknowledgments

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