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

Prototype Design
- Genipin, a natural, biocompatible, crosslinker, was tested to be used as a crosslinking agent to stabilize the clotting of the ICA.
- The amount of genipin is correlated with the intensity of the blue color.
- A colorimetric assay is utilized to determine relative genipin concentration a different times, which is used as a metric for clot degradation.

Design Description
- 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.
- 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 ICA
\[
\frac{d[G]}{dt} = 3.10 \times 10^{-3}[G][T]^{1.4}
\]

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.
- In the future, our project aims to include:
  - Develop and optimizing the genipin spray coating method for mass production.
  - Gaining FDA approval for clinical trial testing.
  - Conducting hospital testing.

Production Cost Estimation

<table>
<thead>
<tr>
<th>Component</th>
<th>Size</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genipin</td>
<td>25 mg</td>
<td>$24.50</td>
</tr>
<tr>
<td>Coils with Catheter</td>
<td>1</td>
<td>$1000</td>
</tr>
<tr>
<td>Coating by Technician</td>
<td>1 coating</td>
<td>$6.50 (0.5 hr @ $13/hr)</td>
</tr>
</tbody>
</table>

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

Acknowledgments
We would like to thank Dr. Bettinger for his guidance as our advisor for this project, Dr. Zapanta and Angela La for their advice, and Heather Bowman for lab assistance. We would also like the thank the URO for funding our project.

References

Table 1: Summary of Prototype Dimensions

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Width</td>
<td>75 mm</td>
</tr>
<tr>
<td>Total Length</td>
<td>75 mm</td>
</tr>
<tr>
<td>Aneurysm Space Diameter</td>
<td>9.9 mm</td>
</tr>
<tr>
<td>Vessel Diameter</td>
<td>6.25 mm</td>
</tr>
</tbody>
</table>

Table 2: Summary of Production Cost

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity</th>
<th>Cost</th>
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