Project Details
Group Design Project

• Groups (5-6 students) will select a topic from the list given and write a 8-10 page paper that designs a tissue engineering approach and experiments to test the approach.

• Presentation of approach in class (10%)

• Written paper (13%) will include the following 3 sections (2.7-3.3 page each, 1.5 line spacing, 1 in margins):
  Background & Significance
  Innovation
  Experimental Design
  + References (not counted in 8-10 pages)
  + Description of group member contributions
Paper- Group Member Contributions

- Discussion and planning of approach:
- Background section:
- Innovation section:
- Experimental section:
- References and editing:
- Presentation slides:

- Additional or *slightly* modified categories ok as well
Dates

• Project Presentations (12/5, 12/7, 12/12- in class)
  Order picked randomly
  Peer feedback
  **Presentation slides emailed to Prof. Underhill by 8am- day of presentation**

• Paper Due (12/20, 5pm)
Background & Significance

Provide background on the problem that you have chosen to address

• Why is this an important problem to work on? Describe the clinical context, including the numbers of patients affected and the consequences of this problem.

• If you are addressing a basic science question, try to make the connection between the question that you are trying to answer and human disease.
Innovation

Review the current state-of-the-art techniques on your topic and describe the approach that you will be experimenting with as a solution to current limitations.

• What is the current state-of-the art?
• What new methods have been demonstrated in research labs?
• What can currently be accomplished, and most importantly, what is the limitation that you wish to address, and why?
• Why is your approach different and innovative in comparison to previous attempts?
• What is it about your approach that makes you believe that you might succeed where others have not?
Experimental Design

Describe the exact experiments that you plan to perform in order to establish whether your proposal works or does not work. It might make sense to make a table of the different experimental conditions that you plan to try.

- Make proper use of experimental controls, and make sure that you can isolate the effect of one single experimental variable by using enough different conditions.
- Consider the possible results that you might measure, and describe how different results would be interpreted.
- Describe the number of replicates and repeats that you think are necessary to establish statistical significance.
Presentations

• ~11 min presentation (~7-9 slides)
  – Contribution from each group member
  – 3 min questions/discussion
  – Powerpoint format

  – Title Slide
  – Background and Significance (2 slides)
  – Innovation (2 slides)
  – Experimental Design (2 slides)
  – Summary and Conclusion (1 slide)
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• Attendance and completed peer-feedback form considered in presentation grade
Peer-Feedback

My name:

Group: ________________________________

Sufficient Background Information:  5  4  3  2  1
Presented Clear Experimental Approach:  5  4  3  2  1
Cited Related Literature:  5  4  3  2  1
Entire Group Interactive & Knowledgeable:  5  4  3  2  1

Feedback:
Sample Presentation
(subsequent slides)
Biodegradable Multidrug Polymer Scaffold for Post-Subdural Hematoma Extraction

BIOE 476 Final Project
Background

What is it?
- Blood build up in outermost meningeal layer
- Causes increased intracranial pressure and brain tissue damage

How do you diagnose it?
- CT Scan
- MRI

What are treatment options?
- Craniotomy
- Trephination (Burr holes)³
Significance

500,000 cases per year\(^1\)

Can result in permanent brain damage and high frequency seizures

Most common form of Traumatic Brain Injury\(^2\)

Mortality Rate\(^2\)
- <40 yrs: 20%
- 40-80 yrs: 65%
- >80 yrs: 88%

[3]
Innovation: Current Approach

**Burr Holes**

- Drill Burr hole to pierce and drain hematoma\(^6,7\)
- Evacuate using suction and irrigation
- Install drain, cover and close

**Drugs Involved**

- General anesthetic during surgery\(^7\)
- Diuretics and corticosteroids\(^8\)
- Phheytoin\(^8\)
Innovation: Biodegradable Polymer Burr Hole Cap

Memantine in Matrix
- Reduces hematoma expansion\textsuperscript{16}
- Lowers brain tissue loss\textsuperscript{17}

Bone growth factor in PLGA microspheres
- BMP-2\textsuperscript{9}
- Enhance skull repair\textsuperscript{10}

PLL\textsubscript{A}/PLGA Porous Matrix\textsuperscript{11}: Biocompatible & Biodegradable\textsuperscript{12}
## Methods: Biomaterial Composition

<table>
<thead>
<tr>
<th>PLLA/PLGA</th>
<th>Memantine</th>
<th>Bone Morphogenetic Protein -2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PLGA Microspheres with BMP-2\textsuperscript{13,14,15} &lt;br&gt; 100 µm diameter &lt;br&gt; 50:50 lactic to glycolic acid ratio &lt;br&gt; PLLA/PLGA Scaffold &lt;br&gt; Pore diameter: 250-500 µm\textsuperscript{11} &lt;br&gt; 50:50 PLLA to PLGA ratio</td>
<td>• Selectively blocks excessive extrasynaptic NMDA receptors\textsuperscript{18} &lt;br&gt; • Blocks tissue plasminogen activator\textsuperscript{16} &lt;br&gt; <strong>Dose</strong>: 1-10 micromolar lasting 3-14 days\textsuperscript{16}</td>
<td>• Strong osteogenic inducer of bone formation\textsuperscript{19} &lt;br&gt; • Induced skull bone repair in nonhuman primates\textsuperscript{19} &lt;br&gt; <strong>Dose</strong>: 100ng/mL slowly released mimicking natural BMP release\textsuperscript{19,20}</td>
</tr>
</tbody>
</table>

[A] PLLA

[B] Memantine

[C] Bone Morphogenetic Protein -2

\[21\] [22] [23]
Methods: Procedure

1. CT Scan
2. Burr Holes & Scaffold Creation
3. Hematoma Evacuation and Scaffold Insertion

[24]
[5]
Experimental Methods: Models

**In Vitro**
- Culture 3D Rat bone cells
- Expose to differing BMP-2 concentrations\(^{25}\)

**In Vivo: Monkey Model**
- Induce Subdural Hematoma (SDH) in monkey using CSF and blood to form a clot
- Model resembles human SDH both morphologically and neurologically\(^{26}\)
Experimental Methods: Studies

- Study biodegradation kinetics of spheres and scaffold
- Radiolabel PLGA/PLLA via solvent evaporation process
- Observe effects of BMP-2 concentrations
- microCT Scans
- Observe using CT Scans and visual inspections
- Vary drug conc. in scaffold
- Observe diffusion kinetics and cell uptake
- Fluorescently tag Memantine
Summary

• Treatments focused on hematoma extraction

Present Day

Our Proposal

• Biodegradable scaffold with microspheres to deliver bone growth factors and Memantine

Benefits

• Minimizes surgery invasiveness
• Reduces tissue loss
• Enhances bone regrowth
References


References


