Introduction

When a nerve is cut, nerve axons regenerate from their base cell and propagate toward the distal site they formerly occupied. Upon encountering a gap, nerve cells are prone to dendritic growth, causing a painful and permanent neuroma. If axon growth is guided, the patient has an improved chance of recovery. Nerve conduits are manufactured devices that bridge gaps in peripheral tissue to assist with effective nerve growth.

Problem Statement

The goal of this project is the creation of a customizable leak proof nerve regeneration conduit that reliably stores and diffuses a volume of drug at a controlled rate, utilizing commonly available additive manufacturing methods. A manufactured device can aid in nerve regeneration following a nerve injury by guiding regrowth into extant nerve architecture.

Materials

PLA vs. PLA/PHA

Biopolymers are materials which are not petroleum based, made instead from renewable biomass sources. These materials are often biocompatible and bioresorbable in the body. PLA is one such material, commonly available as a 3D printing filament. Some surgical aids are currently produced from PLA designed to be absorbed by the body rather than removed. Polyhydroxyalkanoate (PHA) is another nontoxic bioplastic and is absorbed by the body more quickly than PLA. A 3D printing filament composed of a mixture of PLA and PHA was selected as the subject of research for the design of this project.

Methods

Geometric Testing

Because of the small scale of these nerve conduits, we needed to verify that the prints matched the CAD model. The following geometries were measured:

- Outer Dimensions
- Inner Chamber Dimensions
- Channel Dimensions
- Diffusion Hole

Degradation Testing

An important aspect of the nerve conduit is to bio absorb into the body, eliminating the need for post-op procedures after healing. To compare two plastics that have been used in similar medical applications, we conducted a degradation test. The two tested plastics were PLA and PLA/PHA.

- Submerged in PBS to mimic the body
- Elevated temperature to shorten testing time
- 5 samples of each plastic were weighed over thirteen days

Diffusion Testing

Nerve regeneration can be greatly aided with the medication Tacrolimus (FK506). We designed a surrounding chamber that could slowly administer this drug over time through a diffusion hole. To test the diffusion rate, we used Dextran in place of FK506. Dextran has a similar viscosity to FK506 but can be detected by fluorescence.

- Drug chamber filled with Dextran
- Conduct submerged in PBS
- Concentration of Dextran in the PBS solution was tested everyday for five days

Electro Spun Scaffolding

High voltage electrospinning was conducted using PLA/PHA polymer in solution. Electrospinning produces a porous polymer sheet composed of porous nanofibers, much thinner than is possible with a 3D print. The DEX solution was deposited at a rate of 5mL/min on a metal sheet, driven by the voltage difference.

Results

Geometric Test Results

The average diffusion hole area was 0.020 mm² and the average exterior print tolerance measured was ±0.8 mm. Given the measured geometry and the expected geometry from the CAD model, the error between the two values was calculated.

- PLA average error of roughly 11%
- PLA/PHA average error of roughly 7%

Establishing that PLA/PHA provides more precisely printed conduits.

Degradation Test Results

After collecting the weight loss of each sample over the time period, the half-life was calculated for each PLA and PLA/PHA sample. A target half-life of 30 weeks ± 15 weeks was desired.

- PLA average half-life of 47.75 weeks
- PLA/PHA average half-life of 41.4 weeks

Establishing that PLA/PHA degrades at a slightly faster rate than the standard PLA, meaning it doesn’t persist in the body longer than necessary.

Diffusion Test Results

Collected data from the diffusion of Dextran over each day can be visualized in the adjacent plot. The average diffusion rate for each material was then calculated. The target diffusion rate for the conduits was 12.45 ng/day ± 4.65 ng/day.

- PLA average diffusion rate of 16.1 ng/day
- PLA/PHA average diffusion rate of 12.1 ng/day
- Average standard deviation of 2.5 ng/day
- PLA/PHA average standard deviation of 12.3 ng/day

Although both materials exceeded the target value, the PLA/PHA prints had better precision due to lower standard deviations within the data. However, from previous research on this subject, it is more desirable to error over the target diffusion rate than under.

Electro Spun Scaffolding Results

Electro spin scaffolding proved to be a viable addition to the project, providing a permeable scaffolding that allows medication to reach the regenerative nerve site while providing a structure to guide the nerve. The scaffolding will degrade at a faster rate than the other features of the conduit, ensuring that it will not inhibit the growth of the nerve.

Conclusion

1. Created a functioning 3D printed nerve regenerative conduit with a PLA/PHA filament that included interior features to help nerve growth. Metrics analyzed for the conduit included exterior print features, diffusion hole area, half-life, and diffusion rate.
2. PLA/PHA filament offered advantages against the previously used PLA filament through more precise geometric dimensions, better controlled diffusion rates, faster degradation rates, and creation of electro spin interior structures.
3. The new material provides an improved method of the creation of 3D printed conduits to diffuse a more controlled amount of drug to help the nerve grow, along with providing the nerve with interior features to help promote quicker growth. It also showed trending results of the ability to adjust the material properties to decrease the time for the conduit to linger in the body.

Future work could include more analysis on the impacts of changing the amount of PHA included in the PLA/PHA filament. Along with this, the method of creating the diffusion hole, rather than having it be included in the 3D printing process, should be altered to create a more consistent and desired diffusion rate.