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DUAL RESERVOIR NERVE GUIDE CONDUIT WITH FK506 AND GDNF AS A NOVEL APPROACH FOR PERIPHERAL NERVE REGENERATION

Ria Sandhu[1] (Jill Shea, PhD[2])
1-Department of Bioengineering
2-Department of Surgery

Roughly 30% of limb injuries from combat consist of nerve damage, and over 200,000 nerve repair surgeries are conducted every year, costing an estimated $150 billion within the United States. Since nerve damage can result in serious disability and loss of function, multiple strategies have been developed to regenerate peripheral nerves. Currently, for smaller nerve gap injuries that are less than 5 mm in length, the most common method for repair is neurorrhaphy, a technique that involves directly combining the severed ends of the nerve with a suture. However, there is a need to develop a more efficient method to repair large nerve gaps (>5mm) other than autologous nerve grafts. As an alternative, artificial nerve guide conduits have been developed to combat donor site morbidity and provide structural support for large nerve gaps. Along with conduits, neurotrophic factors, such as FK506 and glial cell line derived neurotrophic factor (GDNF), have been shown to enhance nerve regeneration. Hence, the design aim of the project was to develop and analyze the release kinetics of a dual reservoir-based nerve conduit made of Poly-L-lactic acid, a biodegradable polymer, as means of locally delivering FK506 and GDNF at therapeutic levels (~1-10 ng/ml/day). The nerve guide conduit consists of two concentric tubes that comprise a dual reservoir system (Fig. 1). Drug release kinetics of the device were tested with a 15-day dextran release test and a 30-day FK506-GDNF release test. Both release tests confirmed non-therapeutic release from the devices. However, with design improvement and further research, the potential success of our artificial nerve guide conduit could influence future nerve repair strategies.

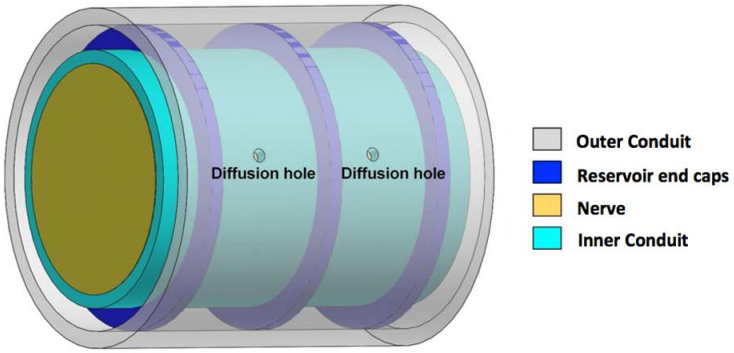

Figure 1: Dual Reservoir Device Schematic. Outer (grey) and inner (light blue) tubes combined with three rings (dark blue) comprise the conduit. The holes on the inner tube control the diffusion rate of drug placed within the dual reservoir chambers.