In the event of peripheral nerve injury, loss of function may occur as the result of a severed nerve. Hollow nerve gap conduits are used to provide a protected environment for nerves to reconnect and regain function, although therapies for nerve gaps larger than 3 cm lack a stable environment for nerves to reconnect. Development of a nerve guide conduit filler has been proposed to mimic the cell’s microenvironment. This would lead to increased functional regeneration.

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Related Work and State of Practice
A wide range of biomaterials are used in tissue engineering.1 Environmental cues have been shown to alter cell behavior.2 This research provides topographical, mechanical, and electrical cues through hyaluronic acid (HA) and HA nanofibers containing multiwalled carbon nanotube (MWCNTs) further referred to as HA-CNT. Similar research techniques used in our lab provide chemical cues. HA and HA-CNT fibers are fabricated through a process called electrospinning and allows for biomaterial deposition on a surface.

Opportunity and Significance
In the event of peripheral nerve injury, loss of function may occur as the result of a severed nerve. Hollow nerve gap conduits are used to provide a protected environment for nerves to reconnect and regain function, although therapies for nerve gaps larger than 3 cm lack a stable environment for nerves to reconnect. Development of a nerve guide conduit filler has been proposed to mimic the cell’s microenvironment. This would lead to increased functional regeneration.

Technical Objectives
We are aiming to create a biomaterial to act as a filler for the hollow nerve gap conduits to promote functional regeneration of the severed nerves. We have hypothesized that cell behavior can be altered by providing electrical stimulation through electroactive nanofibers. Objectives include:

- Material characterization, including contact angle goniometry
- Fiber roughness characterization
- Cellular attachment assays

Technical Approach, Accomplishments and Results
Electrospinning is used for nanofiber fabrication. In the electrospinning process, a positive voltage is applied to a polymer solution being pumped using a syringe pump. A rotating mandrel collects the nanofibers, with alignment depending on the speed of mandrel rotation.

CNT is electrospun within Hyaluronic nanofibers to make composite fibers that mimic cellular microenvironment.

Objective 1: Material Characterization - Contact Angle Analysis
Contact goniometry images of HA Parallel fibers (bottom left) and HA-CNT Parallel fibers (bottom right). Scalebar for SEM at 1 μm.

Objective 2: Surface Roughness Analysis
Contact angle goniometry results for 3 μL water droplet on surface of respective nanofibers. Droplet analyzed on three different orientations, including image taken parallel to aligned fiber direction (Pa) image taken perpendicular to aligned fiber direction (Pe) and image taken of droplet on random fiber surface (R).

Objective 3: Attachment Assays (In Progress)
Attachment occurred over a 24-hour period, after which the cells were fixed and stained. FITC was used for imaging cell bodies, and DAPI stain was used for cell nucleus identification. Data currently in collection.

Next Steps for Development and Testing
Preclinical trials need to be completed. Additional testing includes molecular mechanism analysis to further validate in vitro studies, followed by in vivo tests using sciatic nerve rat models.

Commercialization Plan & Partners
This work was completed with Elisabeth Steel under the guidance of Dr. Harini G. Sundararaghavan. Formulation and process intellectual property has been filed with the Technology Commercialization Office with intent to pursue patent protection. The main hurdles to commercialization is the cost of in vivo validation tests.

References