A Braided Double Layer Nerve Conduit for Peripheral Nerve Regeneration

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Background

Several hundred thousand people are affected by peripheral nerve defects every year, and many patients remain disabled for the rest of their lives. Nerve injuries could be caused by mechanical, thermal, chemical or other factors, which result in the disruption of the communications between nerves and their supporting cells. However, nerves have self-regenerating ability. Hence, artificial nerve conduits were introduced as a promising way to stimulate and enhance the regeneration process.

A nerve conduit (NC) is a kind of nerve guidance channel (see Fig. 1), which is fabricated into tubular shape by using degradable or non-degradable materials. When a NC is implanted into the body, it will be extended, compressed and rotated by the various movements of the patient. So, flexibility and an ability to maintain dimensional stability during the regeneration process is highly desirable. It should also provide directional guidance so the new nerve grows to reunite the severed stumps; meanwhile it would prevent the formation of scar tissue and retain growth factors secreted by the damaged nerve ends.

Methods

1. To design and fabricate a double layer braided structure to enhance mechanical performance and dimensional stability for peripheral nerve regeneration.
2. To incorporate grooved fibers (4DG) so as to increase the surface area for Schwann cells attachment and to provide grooves to guide the direction of cells migration.

1. To prepare a double layer nerve conduit by braiding two layers by a 16-spindle braiding machine.
2. First braid 170-denier yarns around both one layer of PL4D and 10 monofilament sutures (O.D. 1.5 mm) to fabricate the inner core layer. Then braid an outer layer around the braided inner layer with 5 additional parallel sutures, to get a double layer NC (d=2mm).
3. Heat set the NCs in an oven at 65°C for 15 minutes to stabilize the structure.
4. Remove all the sutures from the NCs, forming a double layer tubular nerve conduit with 4DG round fibers aligned inside the conduit (4DG-2NC) or round-2NC).
5. Round-2NC was served as the control sample.
6. Remove all the sutures and the inner layer to get a hollow one layer NC (1-layer NC), which served as the control sample.

Results

Table 1. Basic Properties of Nerve Conduits

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|---|---|---|---|
| Diameter/mm | Pore Size/μm | Pore Size/μm |
| 4DG-2 NC | 2.00 | 75.19 | Outer layer: 30*50 |
| 1-layer NC | 2.00 | 91.15 | Inner layer: 30*100 |
| Outer layer: 105 |
| Inner layer: 75 |

Advantage 1: Double layer structure significantly enhanced mechanical performance and dimensional stability

Fig 5. Tensile Strength of 2-layer NC and 1-layer NC.

Advantage 2: Incorporation of 4DG fibers improved cell attachment and proliferation.

Table 2. Basic Properties of Seeding Fibers

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|---|---|---|---|
| Cross section | Total Channel Area % | Surface Area | Major Channel Area (width * length) |
| PLA-4DG | Diced | 40 | 20μm * 34μm | NA |
| PLA Round | Round | NA | 20μm | NA |

Future Work

1. Apply laminin coating to NCs to improve cell attachment.
2. Incorporation of 4DG fibers greatly increased the surface area for enhanced cell attachment in peripheral nerve regeneration.
3. The deep grooves of 4DG fibers improved cell migration between two nerve stumps.

Conclusions

1. The double layer structure significantly enhanced mechanical strength, surface attachment strength, and compression resistance for peripheral nerve guide.
2. Incorporation of 4DG fibers greatly increased the surface area for enhanced cell attachment in peripheral nerve regeneration.
3. The deep grooves of 4DG fibers improved cell migration between two nerve stumps.

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Fig. 1. A Commercial Collagen Nerve Conduit
Fig. 2. Properties of An Ideal Nerve Conduit
Fig 4. Representative micrographs of a 4DG-2 NC taken by a scanning electron microscope. (a) displays the transverse direction. (b) displays the longitudinal direction. Scale bars = 400μm.
Fig 5. Tensile Strength of 2-layer NC and 1-layer NC.
Fig 6. Suture Retention Strength of 2-layer NC and 1-layer NC.
Fig 7. Compression Resistant Ability of 2-layer NC and 1-layer NC.
Fig 8. Cross sections of 4DG (a) and Round (b) fibers. Scale: 10μm.
Fig 9. Schwann Cell Proliferation by MTT Assay
Fig 10. Cell attachment at day 7 to 4DG fibers identified by DAPI stain (a); Cell attachment at day 7 to 4DG-2NC under SEM (b); Cell attachment at day 7 to round-2NC (c & d).

References