

Collagen Conduits for Neural Repair

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INTRODUCTION:

In peripheral nerve damage, the nerve distal to injury quickly degenerates. While it is easy to suture together two ends of nerve where a short gap exists *in vivo*, for longer gaps conduits or autologous nerve grafts are used to plug the gap. We have developed a form of nerve regeneration conduit based on high density, plastic-compressed collagen/fibronectin, as the basis of next generation biomimetic constructs.

METHODS:

Acellular, type I collagen gels were made, as previously described¹, and routinely compacted by a combination of compression and blotting. These compressed sheets were rolled to form spiral constructs approximately 10mm long by 4mm diameter. Four types of conduit were made. (i) Tight spiral collagen rod, (ii) collagen rod with central hollow core of 350 microns, (iii) collagen rod with 20% strain applied parallel to its long axis (iv) composite of collagen and orientated fibronectin, spirally wound together to give a collagen sheath and fibronectin core. Each conduit was implanted into a standardised 0.5cm nerve gap formed by sectioning the rat sciatic nerve. Constructs were recovered after 4 weeks and regeneration monitored histologically along the construct length.

RESULTS:

Conduits from each group integrated well with proximal and distal ends of the nerve injury. The plain collagen conduits seemed to integrate better on a gross level compared to the composite conduits. Schwann cell migration was seen throughout the construct. From the proximal end, this was present as part of a growth cone of new tissue from the proximal stump. The appearance of a schwann cell growth cone only at the proximal end seems to indicate the importance of neurite outgrowth for this formation.

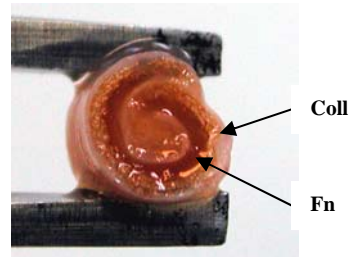


Figure 1. Two component spiral assembly construct of co-compressed collagen and fibronectin material sheets. Figure shows the gross, spiral structure (transverse, between forceps) formed by off-setting the two sheets prior to spiral assembly, to give a fibronectin (Fn) core and collagen (Coll) sheath.

DISCUSSION & CONCLUSIONS:

Nerve regeneration constructs fabricated by Plastic compression of collagen and fibronectin were made rapidly, were robust and simple to suture in to place, easy to prepare with meso-structure built in. These included heterogenous layers, zones and channels. The integration *in vivo* and in-growth of neural cell regenerate across the constructs indicates that they will be effective guides for repair. Their great strength lies in their ease of fabrication and ability to introduce biomimetic zones and structural features, at the cell scale (i.e. meso-level). We conclude that this approach to native protein conduits is a good basis for fabricating multi-functional implants.

REFERENCES:

1. Prajapati RT, Chavally-Mis B, Herbage D, Eastwood M, Brown RA. 2000. 'Mechanical loading regulates protease production by fibroblasts in three-dimensional collagen substrates.' *Wound Repair Regen.* 8(3): 226-37

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