Benefits of Surgical Implantation of an Investigational Biodegradable Neuro-Spinal Scaffold in Various Animal Models of Acute Spinal Cord Contusion Injury: Clinical Translation

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The pathophysiological sequelae of the primary spinal cord injury (SCI) include edema, spinal cord swelling, reduced blood flow, and local tissue ischemia resulting in further cellular necrosis culminating in the appearance of a tissue void (cavity). Biodegradable scaffolds can be implanted within the necrotic lesion to fill this void and provide structural support to the surrounding viable tissue while serving as a locus for appositional healing.[1,2] This work focuses on translational animal studies using clinically-relevant contusion injuries in both rats and pigs to support current clinical investigation.

A spinal T10 contusion injury was created in Sprague-Dawley rats and cylindrical scaffolds (1.0 mm diameter, 2.0 mm length) were surgically implanted at the lesion site between 24 and 72 hours later. Histological analysis at 12 weeks revealed that rats in the non-treated control group developed large cavities surrounded by a thin rim of spared tissue. In contrast, in rats implanted with scaffolds, cavity volume decreased by 86% and spared tissue width increased by 44%. Although scaffolds were fully resorbed by 12 weeks after implantation, the amount of remodeled tissue at the site of implantation in the lesion epicenter increased by 111%. These results demonstrate that biodegradable scaffold implantation in the acutely injured spinal cord can reduce cavitation and promote tissue sparing and remodeling.

To translate the use of biomaterial scaffolds for acute SCI treatment, evaluating the neurosurgical techniques used for implanting a device into the recently injured spinal cord in a clinically relevant, large animal model is needed. Four Gottigen pigs were contused at T10 with a 50g weight dropped from 40cm, followed by a 100g compression for 5 minutes as described previously[3]. At 4, 6 and 24 hours following injury, the necrotic injury center was gently debrided following internal decompression via myelotomy and a scaffold was implanted. Further, at 24 hrs post-injury (n=2) intraparenchymal pressures were measured using a 1F pressure catheter. In each animal, the intraparenchymal cavity accommodated a cylindrical scaffold of at least 2mm diameter and 7mm length. In addition, the surgical technique provided the added benefit of reducing intraparenchymal pressures below pre-surgery levels. Our findings demonstrate the feasibility of biodegradable scaffold implantation within 4 to 24 hours in a clinically relevant large animal model of acute SCI.

Multimodal therapeutic interventions are needed to provide next generation spinal cord injury treatments. Acute parenchymal surgical decompression and scaffold implantation to provide structural support to residual tissue and serve as a permissive environment for appositional healing is currently under clinical investigation. In an ongoing pilot clinical trial, 3 subjects have been enrolled to date. Two of the three subjects converted from complete (AIS A) to incomplete injuries (1 subject to AIS B and 1 subject to AIS C) at 1 month post-implant.

References

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