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Title: Biodegradable Neuro-Spinal Scaffold Promotes Neuropermissive Remodeled Tissue Following Spinal Contusion Injury in Rats

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Biodegradable Neuro-Spinal Scaffold Promotes Neuropermissive Tissue Remodeling Following Spinal Contusion Injury in Rats

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Contusive spinal cord injury (SCI) produces cellular necrosis and secondary tissue loss culminating in a fluid-filled cystic cavity. Limited endogenous repair results in focal cellular trabeculae composed of Schwann cells, fibroblasts, astrocytes, pericytes, macrophages, collagen, and sprouting axons. We hypothesized that implantation of a biodegradable, biomaterial scaffold into the injured spinal cord could serve as a locus for appositional healing and tissue remodeling that would enhance endogenous repair. We evaluated the effect of implantation of scaffolds composed of the block copolymer poly(lactic-co-glycolic acid)-poly(L-lysine) (PLGA-PLL) on tissue remodeling in a contusion model of SCI. A T10 contusion injury was created in female Sprague-Dawley rats (IH Impactor 220 kDyn). Cylindrical scaffolds (1.0 mm diameter, 2.0 mm length) were surgically implanted at the lesion site 24 to 72 hours later. Remodeled tissue at the injury epicenter was evaluated at 12 weeks by histology and immunolabeling of paraformaldehyde-fixed frozen sections. Rats in the non-treated control group developed large cavities surrounded by a rim of spared tissue. In contrast, in rats treated with scaffold implantation, cavity volume decreased by 86%, and spared white matter width increased by 44%. Although scaffolds were fully resorbed by 12 weeks after implantation, the amount of remodeled tissue at the implantation site in the lesion epicenter increased by 111%. Remodeled tissue contained laminin and sparse collagen. Schwann cells (myelin protein zero positive) were present in significant numbers in the remodeled tissue of the lesion epicenter and the perilesional white matter. Sprouting axons (β 3-tubulin and neurofilament positive fibers) indicated neural regeneration within the remodeled tissue. These results demonstrate that PLGA-PLL scaffold implantation in the acutely injured spinal cord can act through appositional healing to reduce cavitation, promote tissue sparing, and support neural regeneration. Schwann cells may contribute to both neural regeneration and remyelination of focally demyelinated white matter axons. Scaffold implantation may augment endogenous cellular recovery processes to contribute to functional neurological improvement.