Biomaterials and Stem Cells – Combined Therapy for Spinal Cord Injury Treatment
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Introduction
Spinal cord injury (SCI) is characterized by tissue loss and a stable functional deficit. While several experimental therapies have proven to be partly successful in the treatment of acute SCI, treatment of chronic SCI is still challenging. We studied whether we can bridge both acute and chronic spinal cord lesions by the implantation of hydrogels, either alone or seeded with mesenchymal stem cells (MSCs) or spinal cord precursor cells (SPCs), and whether this treatment leads to functional improvement in chronic SCI.

Materials and Methods
A hemisection (HS) or balloon-induced compression lesion (BCL) was performed in adult 2-month-old male Wistar rats. HPMA-RGD hydrogels [N-(2-hydroxypropyl)methacrylamide with attached amino acid sequences – Arg-Gly-Asp] were implanted into the lesion, with or without seeded stem cells, either immediately (HS) or five weeks after injury (BCL). The animals with BCL were behaviorally tested using the BBB (motor) and plantar (sensory) tests once a week for 6 months. Staining for axons (NF160), Schwann cells (p75), blood vessels (RECA 1), astrocytes (GFAP) and connective tissue (hematoxylin-eosin) was performed one or six months after injury.

Results
In both types of lesion, HS and BCL, the hydrogel implants adhered well to the spinal cord tissue. Histological evaluation showed the ingrowth of connective tissue elements, blood vessels, neurofilaments and Schwann cells into the hydrogels. Astrocytes were observed in the hydrogel implants only 6 months after SCI. One month after HS, both SPCs and MSCs survived well, and SPCs migrated outside the hydrogel and penetrated the host tissue. MSCs were also present in the hydrogels 5 months after implantation. Combined therapy also prevented tissue atrophy in chronic SCI, and behavioral analysis showed a statistically significant improvement in rats with combined treatment, compared with the control group.

Discussion and Conclusions
We conclude that HPMA-RGD hydrogels can successfully bridge acute as well as chronic spinal cord injuries and provide a scaffold for the ingrowth of blood vessels, neurofilaments and Schwann cells. They can serve as stem cell carriers, and the presence of MSCs leads to functional improvement even at 6 months after spinal cord injury.

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Disclosures
The authors report no conflicts of interest.