Monitoring bladder function after severe contusion spinal cord injury in awake rats

Michael Kleindorfer[1,2], Karin Roider[1], Evelyn Beyerer[1], Sophina Bauer[1,2], Patrick Heimel[3,4,5], David Hercher[4,5], Martha Georgina Brandtner[6], Lukas Lusuardi[2], Ludwig Aigner [1] and Elena Esra Keller[1]

[1] Institute of Molecular Regenerative Medicine, Paracelsus Medical University, Salzburg, Austria
[2] Department of Urology and Andrology, Landeskrankenhaus – University Clinic, Paracelsus Medical University, Salzburg, Austria
[3] Core Facility Hard Tissue and Biomaterial Research, Karl Donath Laboratory, University Clinic of Dentistry, Medical University Vienna, Vienna, Austria
[4] Ludwig Boltzmann Institute for Traumatology, The Research Center in Cooperation with AUVA, Vienna, Austria
[5] Austrian Cluster for Tissue Regeneration, Vienna, Austria
[6] Department of Pediatric and Adolescent Surgery, Landeskrankenhaus—University Clinic, Paracelsus Medical University, Salzburg, Austria

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Background

Spinal cord injury (SCI) is a complex clinical condition with a wide range of permanent functional and neurological consequences. A prime factor limiting the patient's quality of life (QoL) is difficulties in bladder function. Chronic animal models that help to develop novel therapeutic strategies are highly demanded, but their availability is scarce and frequently accompanied by substantial limitations.

Animal Model

We want to provide our detailed protocols that allow full reproducibility of a novel model for investigating both the acute and chronic condition and give transparency regarding challenges. The preclinical animal model of female rats with mid-thoracic SCI contusion and a permanently implanted urinary catheter allowed the measuring of bladder function repetitively. Over a period of six months, data were collected weekly from the same, conscious individuals.

Study Aim

The ability to generate a complete data set from one single individual, rather than requiring multiple subjects, has the potential to markedly reduce the number of experimental animals, eliminate group differences, and give more flexibility for therapeutic intervention. Future projects could also benefit from the described optimizations in animal care.

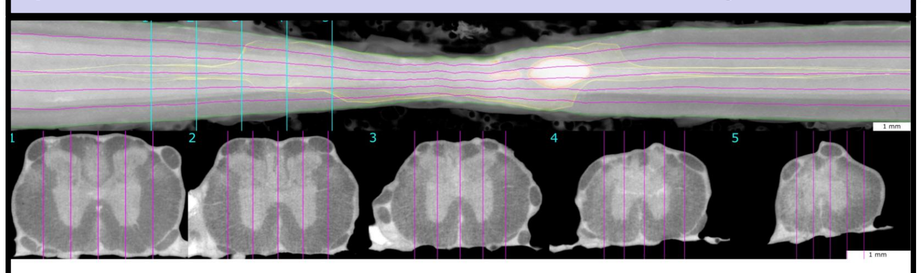
To our knowledge, this is the first study that obtained a clinically relevant urodynamic dataset seamlessly from the acute to the late chronic phase in rats with SCI

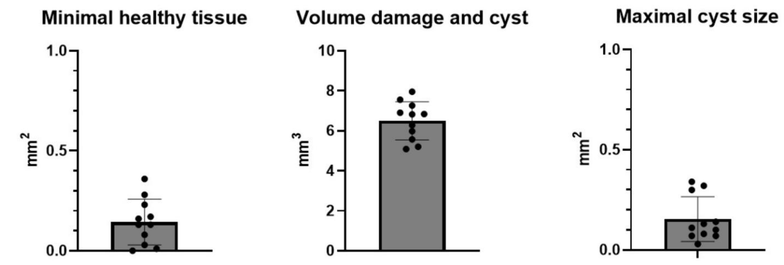
Permanently Implanted Urinary Catheter

+ **infusion harness** to hold catheter end in place an inaccessible for the animal`s manipulation
+ **screw-off lid** for fast and easy access
+ antibiotic **Beneocin powder** to avoid abrasion wounds caused by silicon straps of the harness
+ **tailored flushing protocol** using 3.23% citric acid to assure patency of the catheter lumen and avoid clogging caused by accumulation of minerals or formation of a biofilm



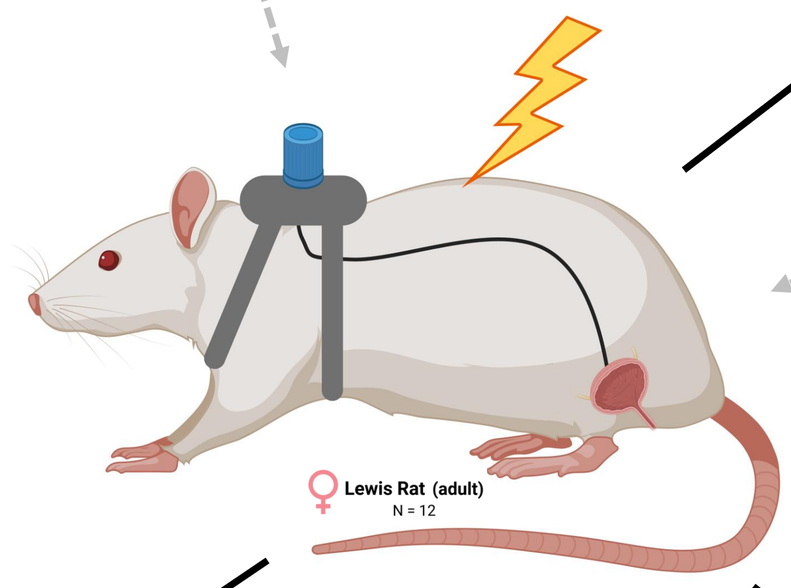
µCT-scans Confirmed Consistent Contusion SCI Severity at Th8/Th9





Medication & Supplementation Post SCI

+ **Meloxicam** (2 mg/kg) and **Enrofloxacin** (5 mg/kg) for analgesic and antibiotic coverage the first five days post injury and upon requirement afterwards
+ **Montelukast** (10 mg/kg) for anti-inflammatory purposes after injury
+ **Nutri-Cal** (500µL) as high-caloric food supplement for the first five days post injury to assure a minimum nutritional uptake
+ **Saline solution** (0-3mL) injections in case of suspected dehydration or insufficient water uptake

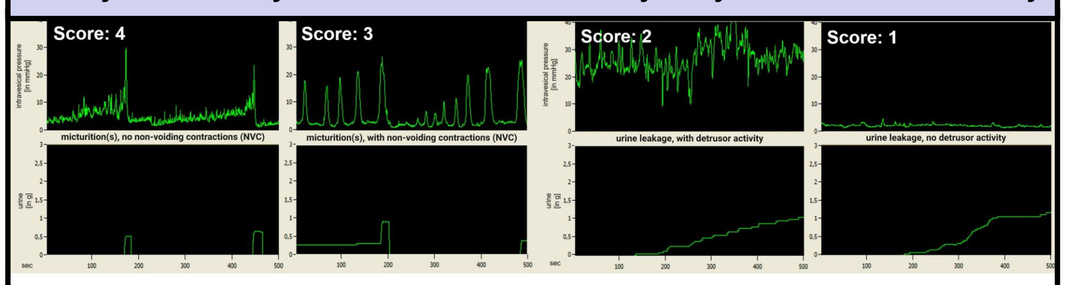


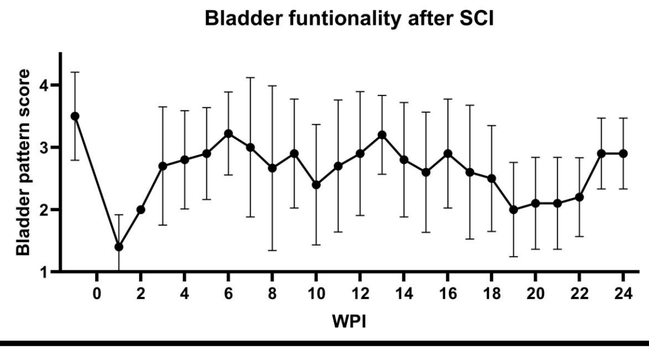
Extensive Skin Care

+ **regular washing** to remove spilled urine and avoid skin irritation
+ **Pantothen cream** to maintain a good skin barrier preventing the early onset of decubitus formation
+ **Cavillon Advanced**, originally designed for treatment of incontinence associated dermatitis, to create a stretchable and water-repellent protective coating to stop progressing decubitus

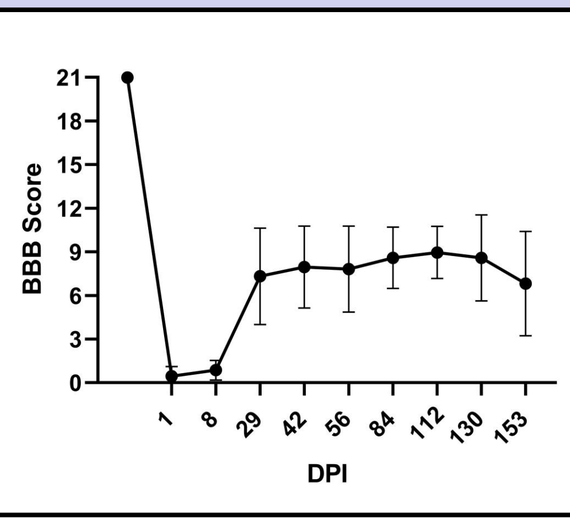
★ Primary Outcome

Weekly Awake Urodynamic Measurements & Analysis by Patterns of Functionality





Hind Limb Function Reflected Injury Severity Post SCI



Conclusions & Outlook

The combination of an SCI animal model with an implanted urinary catheter for repetitive measurements and a customized flushing protocol created a versatile model for therapeutic applications. Bladder function could be monitored for the first time through all stages of the pathology after SCI in a single rat, which would otherwise require the use of several individuals. With additional improvements in practice and care, this can lead to a markedly reduced number of experimental animals and improved animal welfare. We expect all these aspects to be valuable contributions to the 3R principle.

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MICHAEL KLEINDORFER, MSc
PhD Student
Institute of Molecular Regenerative Medicine
Paracelsus Medical University

michael.kleindorfer@pmu.ac.at

termis EUROPE