Presentation number: PSTR164

Use of a Porcine Model for Studying Spinal Cord Injury: A Translational Approach

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INTRODUCTION

Rodent models for spinal cord injury (SCI) are well documented for early studies of regenerative abilities of implants and treatments for SCI. However, there are limitations to the ability to translate the information to humans. Anatomically and physiologically, the spinal cord of rats is significantly different from humans:

- The rat corticospinal tract is primarily dorsal
- Distinct tract organization differs from humans
- Significant differences in spinal cord diameter
- Distance between the cell bodies of injured axon and the injury site
- Relative dedication of the cord to specific ascending and descending pathways
- Degree of vascularization, size of the sensory and motor neuron populations, and white/gray matter composition
- Different metabolic rates, immune responses, and regenerative capacity that may not translate to human outcomes (i.e., rats heal substantially faster than humans)

However, a **porcine SCI model** is more adequate for the following reasons:

- Anatomical similarity: Porcine spinal cord anatomy, including white matter distribution and tract organization, more closely resembles human anatomy compared to canine models
- Physiological relevance: Similar cardiovascular and respiratory responses to SCI, making them better models for studying secondary injury mechanisms and therapeutic interventions
- Ethical considerations: Fewer ethical concerns and regulatory hurdles associated with using pigs compared to dogs in research settings
- Standardization: Pig models offer better standardization opportunities due to more controlled breeding and genetic backgrounds

CONCLUSIONS

- This study introduces a porcine spinal cord injury model that integrates conventional outcome metrics, including body weight and motor function scores, with translational endpoints such as electrophysiological assessments and automated gait analysis.
- The experimental findings indicate that the magnitude of the dropped weight influences injury severity. The data show that a 15 cm drop height was associated with more pronounced neurological deficits when compared to a 10 cm drop.
- Analogous to clinical scenarios in humans, early post-injury electrophysiological measurements reliably forecast functional outcomes, facilitating effective stratification and group allocation of experimental animals for therapeutic interventions, which is crucial for minimizing experimental variability.

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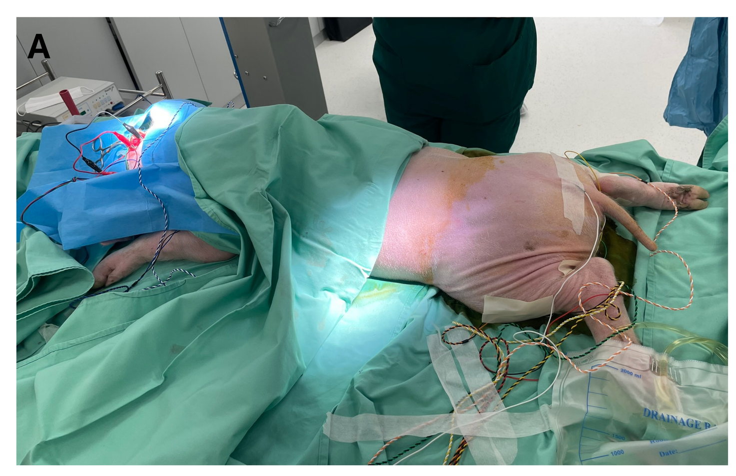
METHODS



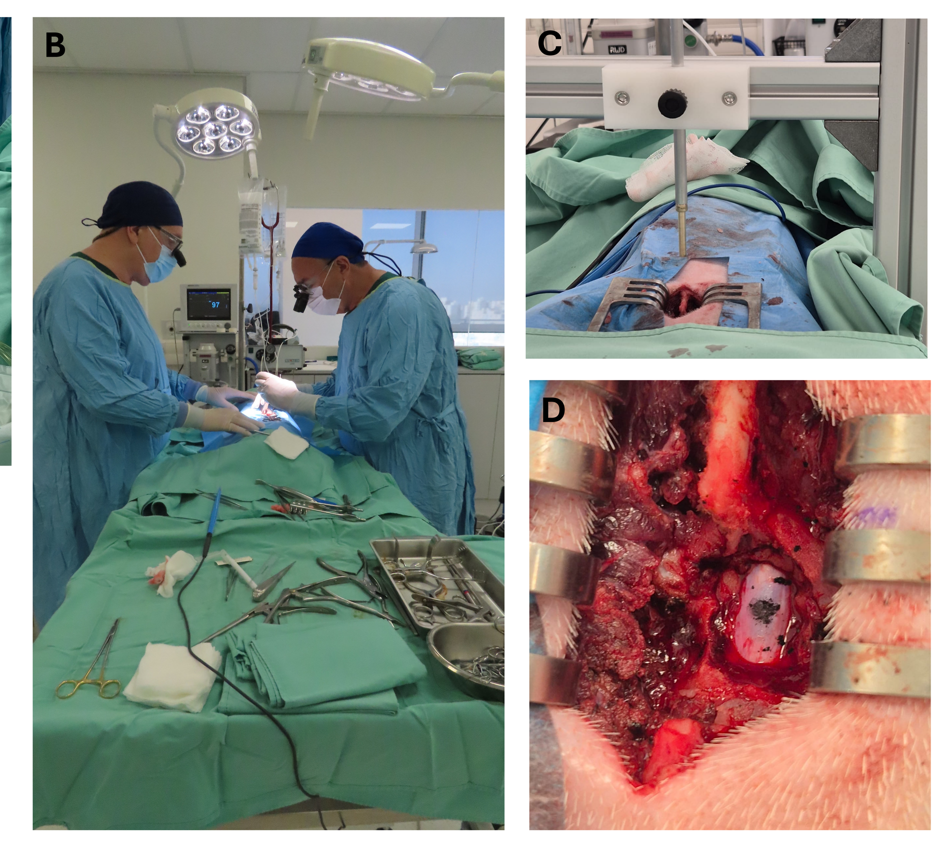


Figure 1: SCI Induction. (A) Electrophysiology setting: the animals are connected to cranial electrodes using screws, gastrocnemius muscle electrodes (needles), and posterior tibial nerve electrodes (needles). (B) The operation setting. (C) Swine spinal cord contusion weight drop apparatus. (D) The location of the injury marked in black using chalk powder.

Two injury severities were tested: a 50g weight dropped from 10 cm and 15 cm heights.

Group No.	Weight Height	Application Time
G1	50-gram weight from 10 cm	5 minutes
G2	50-gram weight from 15 cm	5 minutes

SCI outcome measures:

- Body weight
- Motor function score
- Electrophysiology
- Computerized gait analysis

RESULTS

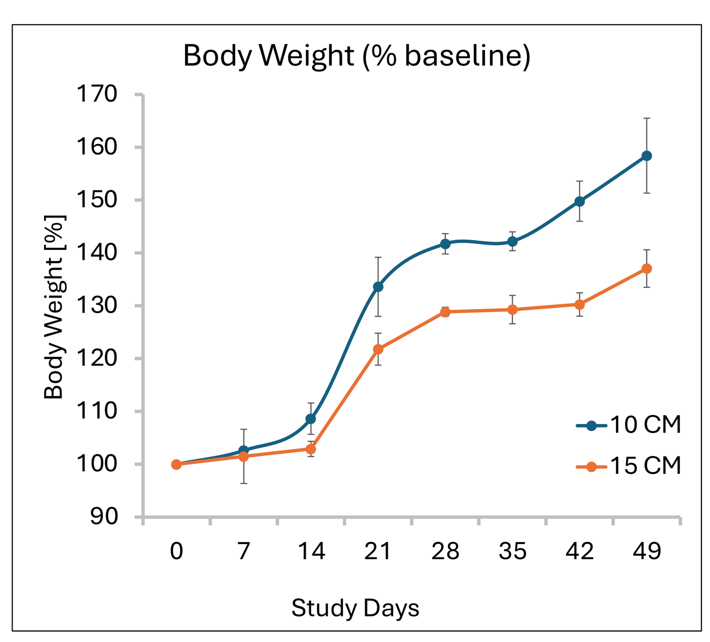


Figure 2: Changes in body weight. All animals gained weight; however, animals with a weight drop from 15 cm gained less weight than animals that experienced a weight drop from 10 cm.

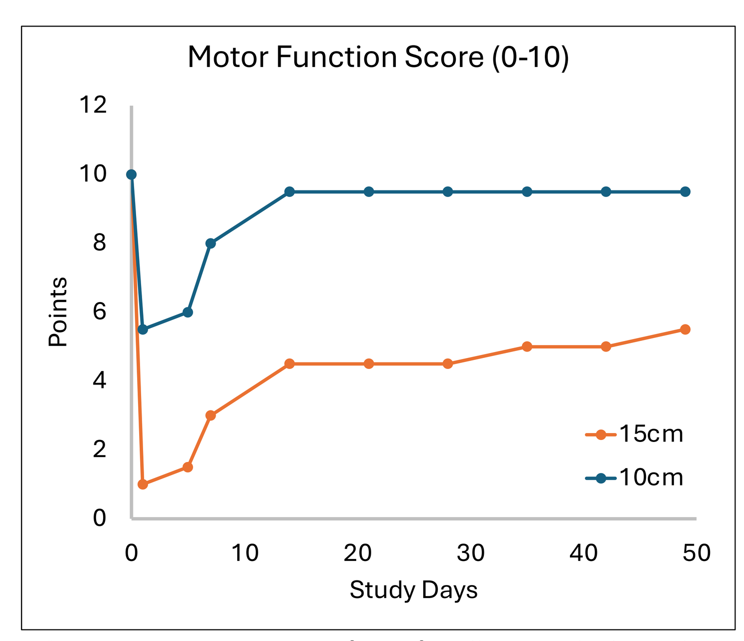


Figure 3: Motor score (0–10). All animals lost their motor function after the SCI procedure. Animals that experienced a weight drop from 10 cm recovered, while animals that experienced a weight drop from 15 cm did not completely recover.

Stages of hindlimb function	Score	Description of Motor Function Assessment
Dragging	1	No active hindlimb movements, with rump and knees on the ground.
	2	Active hindlimb movements, with rump and knees on the ground.
	3	Active hindlimb movements, with ''weight-bearing extensions'' that lift the rump and knees transiently off the ground.
Stepping	4	Active rhythmic hindlimb crawling with at least three reciprocating gait cycles.
	5	The animal can take between two and six steps with the rump and knees constantly off the ground during steps. Knees do not fully extend. Dorsal and plantar hoof placement. Impaired balance.
	6	The animal can take more than six steps with the rump and knees constantly off the ground. Knees do not fully extend. Dorsal and plantar hoof placement. Impaired balance.
Walking behavior	7	The animal can take two to six steps with the knees fully extended. Dorsal and plantar hoof placement. Impaired balance.
	8	The animal can take more than six steps with the knees fully extended. Dorsal and plantar hoof placement. Impaired balance.
	9	The animal can take more than six steps with the knees fully extended. Plantar hoof placement. Imbalanced trunk.
	10	The animal demonstrates normal ambulation with normal balance.

Electrophysiology

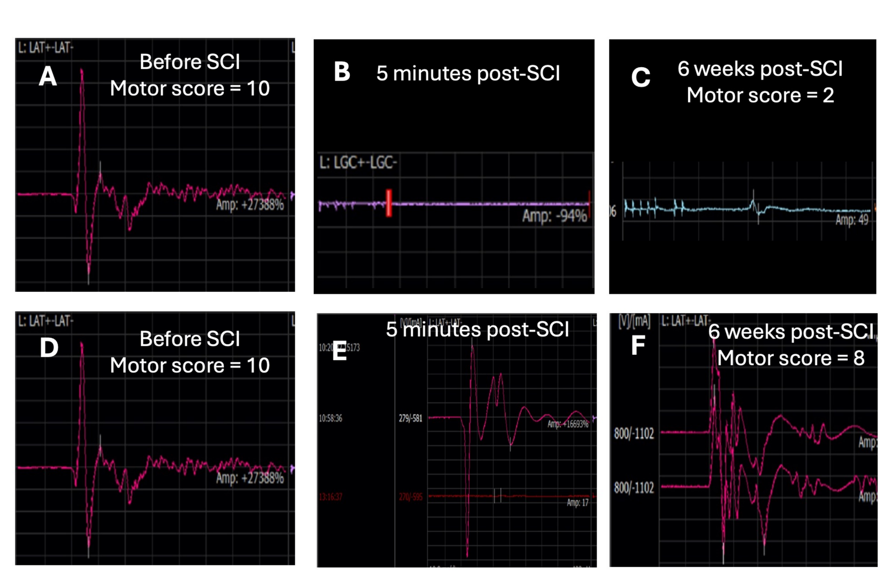


Figure 4: Representative examples of MEP waves in the SCI pig model. (A) Before SCI, a typical large MEP wave. (B) Recording 5 minutes after SCI shows no signal - no signal was generated following the stimulation. (C) Six weeks post-SCI, the animal that did not generate any signal 5 minutes post-injury showed a small signal at 6 weeks post-injury. (D) MEP recording at baseline before injury. (E) Immediately after a weight drop from 10 cm, the animal showed a smaller yet well-present MEP signal. (F) Six weeks post-injury, the animals that generated a well-defined MEP signal post-SCI showed a well-defined MEP signal also after 6 weeks. In general, as in humans, monitoring electrophysiology (MEP) immediately after injury is a good predictor of recovery.

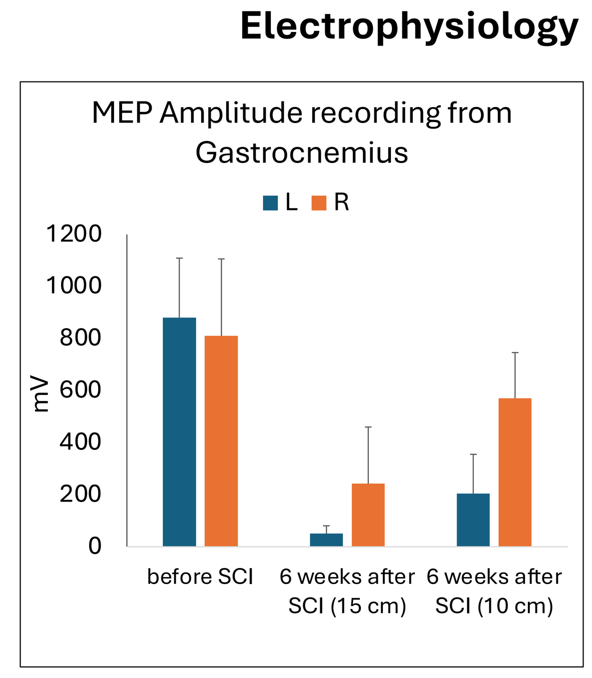


Figure 5: MEP recording from the gastrocnemius muscle. After SCI, there was a reduction in the amplitude of the MEP. This reduction was more pronounced in animals exposed to a weight drop from 15 cm than in animals exposed to a weight drop from 10 cm.

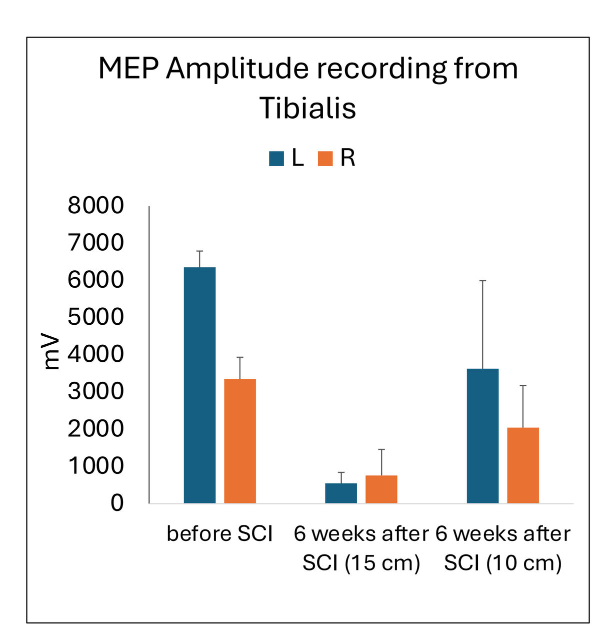


Figure 6: MEP recording from the tibialis muscle. After the SCI, there was a reduction in the amplitude of the MEP. This reduction was more pronounced in animals exposed to a weight drop from 15 cm than in animals exposed to a weight drop from 10 cm.

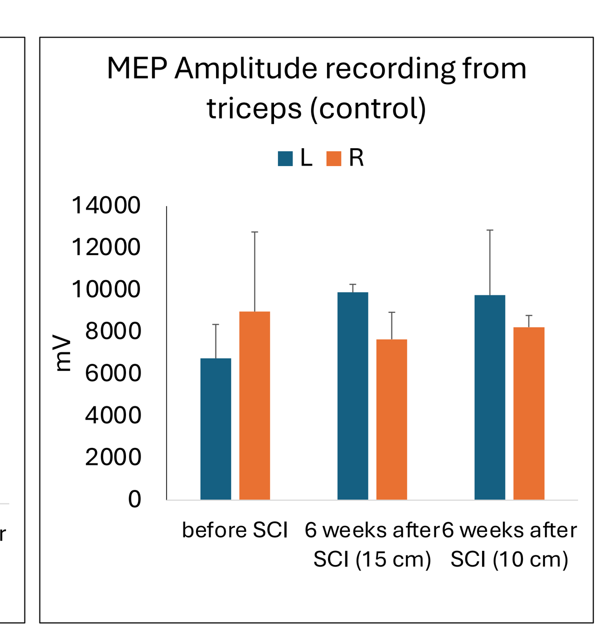


Figure 7: MEP recording from the triceps muscle. This recording served as a control for the recording method. As these muscles are located in the front legs, there should be no difference between the measurements. Indeed, no differences between the measurements were found.

Computerized gait analysis

Before SCI, Motor score: 0 | **Score: 5** | **Score: 8**

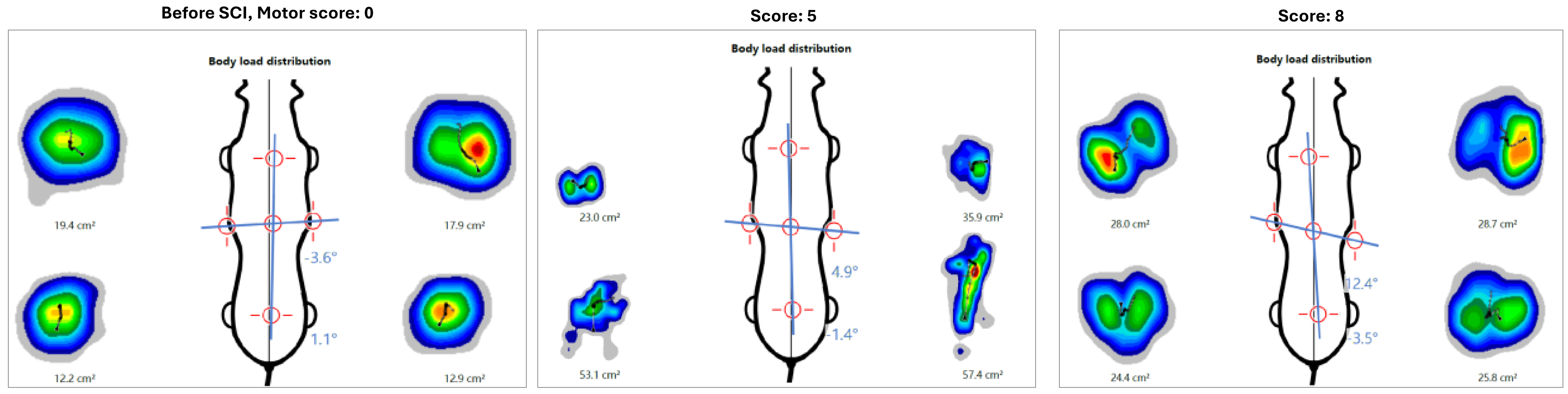


Figure 8: Computerized gait analysis. On the left (motor function score of 0), there is similar weight distribution and a well-organized posture in the hoof heat map. In the middle (score of 5), although the animal can stand, the left and right legs are disoriented, and the animal drags its leg on the platform. On the right (score of 8), the animal taps with its legs but can carry weight and walk.