

MRI Depiction of Blood-Spinal-Cord-Barrier Permeability after Spinal Cord Contusion Injury in Animal Model – in Vitro Study

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Abstract. *The blood-spinal cord barrier (BSCB) controls the exchange of substances between the blood and the central nervous system. Spinal cord injury (SCI) causes a BSCB breakdown, which results in increased capillary-permeability for plasma molecules that increase neuronal damage. Contrast enhanced MRI is a technique to determine evolution and duration of BSCB-breakdown after standardized SCI and define the “therapeutic window” for this injury model.*

Keywords: MRI, blood-spinal cord barrier, “therapeutic window” after spinal cord injury

1. Introduction

The Blood-Spinal-Cord-Barrier represents a selective physiologic barrier that provides a stable microenvironment within the neuronal tissue. It was shown that blood–spinal cord barrier permeability can be measured using quantitative autoradiography following contusion injury to the rat spinal cord [1]. MR technique was used with advantage for high resolution in-vivo mouse models [2]. Here we used contrast enhanced MRI to determine evolution and duration of BSCB-breakdown after standardized SCI and define the “therapeutic window” for this injury model.

2. Subject and Methods

In male Sprague-Dawley rats, a laminectomy was carried out at TH11 and a contusion injury was inflicted, using the IH® Impactor with a force of 150kdyn. Rats were divided into groups with different observation times: 0h (n=8); 24h, 72h, 4d, 5d, 6d, 10d (n=5 each).

At the end of the observation time each rat received an i.v. injection of 0.8ml/kg gadopentetate dimeglumine (Magnevist®, Bayer HealthCare). For definition of MRI timepoint, three rats were euthanized 10 minutes (0h group) after contrast agent (CA) administration and dynamic MRI measurement of excised spines was performed every 2 hours up to 18 hours. All other rats were euthanized 1 hour after CA administration, for evaluation of BSCB permeability. Subsequently, imaging was performed on the 3T MEDSPEC whole body scanner (Bruker, Ettlingen, Germany) equipped with a 200 mT/m microimaging gradient system and a 35 mm inner diameter micro-imaging coil. T1 weighted multislice SE sequence with the setup: FOV = 6 cm, slice thickness = 1,5 mm, matrix dimensions = {256, 256}, TR = 850 ms, TE = 17,6 ms. In case of high resolution sagittally oriented measurements (as shown on Figure 1.), matrix dimensions = {512, 512}.



Figure 1. High resolution sagittally oriented MR image of a rat spinal cord – in vitro, after the spinal cord contusion injury.

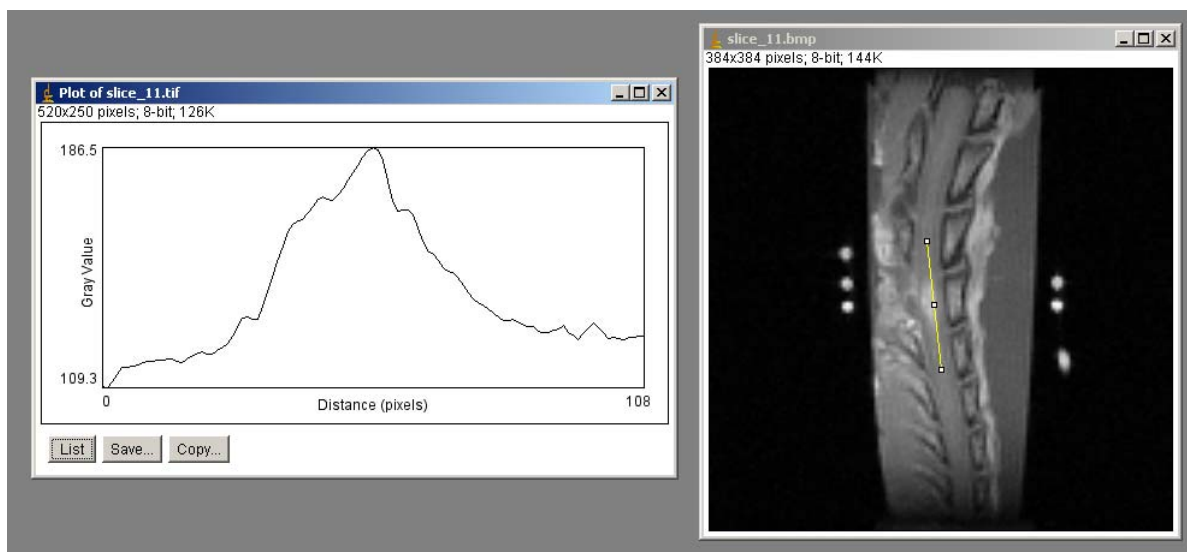


Figure 2: image intensity profile drawn along the spinal cord in the lesion site.



Figure 3. Series of time dependent MR images of the contrast enhancement rat spinal cord, after the injury – in vitro study 0, 1, 4 and 6 days after CSI

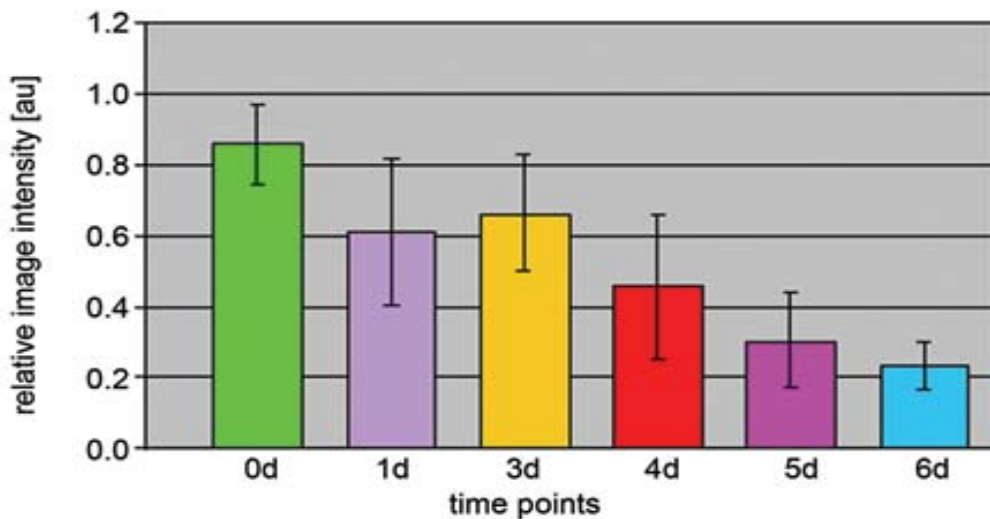


Figure 4: Extent of BSCB permeability up to 6 days

3. Results

Figure 1 shows high-resolution MR image of a rat spinal cord without CA application. Lesion site is apparent due to tissue damage on the right side. Without CA application lesion site has only limited contrast in comparison to the healthy tissue.

Figure 2 shows intensity profile drawn along the spinal cord. Line shows the profile trajectory. Line plot on figure 3 shows image intensity along the profile.

Definition of MRI timepoint

When euthanization and MRI were performed 10 minutes after CA application, signal increase was mainly detectable in the spinal cord arteries, the dynamic post-mortem measurement over 18h yielded increasing enhancement of the injury site over time. Adequate distribution of the CA within the neuronal tissue could be observed when euthanization and MRI were performed 1h after CA application.

Evaluation of BSCB permeability

Signal enhancement at the injury epicenter was measured after observation periods up to 6 days, gradually decreasing with time as well as with distance from the injury site. (Fig.3.) After 6 days or later, little or no signal enhancement was visible. Figure 4 shows decrease of the relative contrast intensity in image.

4. Discussion and conclusion

The BSCB controls the exchange of substances between the blood and the central nervous system. These barriers, formed by cells lining the blood vessels in the brain and the spinal cord, protect nerve cells by restricting entry of potentially harmful substances and cells of the immune system. Impairment in cellular machinery of the BSCB may lead to a barrier breakdown in many brain and spinal cord diseases or injuries.

Our study shows that the inflicted SCI distinctly increases BSCB permeability for 5 days. Delayed dispersion of the contrast agent within the neuronal tissue has to be considered. We show on the animal model, that BSCB is open for 5 days after the injury. These 5 days could be used for diagnostics and treatment as well. This is critical period, during which neuroregenerative medication can be applied and efficiently used. After this period, further treatment has only a limited efficiency, due to re-organized BSCB, which protects spinal cord from all kind of metabolites transported to the lesion site after intravenous treatment administration.

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References

- [1] P.G. Popovich et al. *Experimental Neurology* 142: 258-275, 1996
- [2] M. Bilgen et al. *Magn. Reson. Imaging* 20(4): 337-41, 2002