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Review Article

High resolution small animals dedicated magnetic resonance scanners as a tool for laboratory rodents central nervous system imaging

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ABSTRACT

Introduction: Magnetic resonance imaging (MRI) is a noninvasive technique applied in medical diagnosis and for studying animal models of human diseases. MRI offers longitudinal *in vivo* studies without the need to sacrifice animals, thus making data easier to compare. The number of required animals can be limited.

Aim: The aim of this article was to present the role of dedicated small animal MRI scanners in the management of central nervous system visualization and injury in rodents on the basis of the current literature.

Material and methods: Highly specialized animal MRI scanners with a high magnetic field and small bores are used for imaging the nervous system of rodents *in vivo*. Compared to clinical scanners currently operating at magnetic field strengths of up to 3.0 T, dedicated animal MRI scanners operate at higher field strengths between 4.7 T and 14.1 T.

Results and discussion: Small animal imaging results in the reduction of image quality. It is caused by a small signal-to-noise ratio (SNR). The way to increase the SNR is to apply a high magnetic field. Animal MRI scanners operating at higher field strengths between 4.7 T and 14.1 T allow researchers to obtain images with high resolution, and with clearly visible structures of rodent neuroanatomy. Although MRI diagnostics is very useful in neurobiological experiments, the major drawback of dedicated animal MRI scanners is their high cost.

Conclusions: High resolution dedicated small animal scanners of up to 14.1 T are best suited for rodent neuroanatomy imaging as well as for neurobiological experiments and their results.

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1. Introduction

Magnetic resonance imaging (MRI) is the widely used method for imaging whole body structures. The quality of obtained images is enhanced by an increase in magnetic field strength. It provides the possibility of imaging smaller structures.

MRI provides an opportunity to monitor lesions *in vivo* in experimental therapies, with the use of animal models, such as rats and mice, in order to transpose results for the planning of clinical examinations. This method contributes to reducing both costs and the number of animals needed.

Using clinical MRI scanners is connected with the problem of small object volume. It is important to increase the signal-to-noise-ratio (SNR). The way to increase the SNR is to use a high magnetic field. Thus, high resolution dedicated animal scanners have been used for small animal imaging.[17] These scanners are characterized by a high magnetic field strength between 4.7 T and 14.1 T. Dedicated animal scanners allow for an improved SNR, reduce the time of examination, improve resolution, and reflect cortex oxygenation better.[18] The main disadvantage is the high cost of the apparatus, as compared to clinical scanners.

2. Aim

The aim of this paper is to present the role of the dedicated small animal MRI with respect to the management of the central nervous system (CNS) anatomy and injury in rodents on the basis of the current literature.

3. Material and methods

Highly specialized animal MRI scanners with a high magnetic field and small bores are used for imaging the nervous system of rodents *in vivo*. Compared to clinical scanners currently operating at magnetic field strengths of up to 3.0 T, dedicated animal MRI scanners operate at higher field strengths between 4.7 T and 14.1 T.

4. Results

4.1. *Scanners with a magnetic field strength of 4.7 T*

A dedicated animal Varian scanner (Oxford Systems) and transmit/receive coil with an inner diameter of 63 mm was used by Modo et al.[16] The experiments were performed on Sprague-Dawley rats weighing 280–330 g. In part of the group ischemic damage was induced by provoking a middle cerebral artery occlusion (MCAo, rat model of stroke). Then, 3 months following the induction of MCAo, neural stem cells (NSCs) were transplanted into the contralateral hemisphere. NSCs were labeled by gadolinium rhodamine dextran (GRID). Animals were anesthetized with isoflurane in a mixture of 30% O_2 and 70% N_2O. It was discovered that NSCs migrated from the injection site via the corpus callosum into the lesioned area. On T1-weighted images an insignificant number of cells were detected; however, on T2-weighted images cells were easily identified from host cells. Proton density-weighted images also visualized the injected cells, but not as clearly as T2-weighted ones. In the control group (without stroke) cell migration was observed only around the injection area. Histological analysis with a fluorescent microscope confirmed the observations obtained through MRI. Immunohistochemical analysis with fluorescent labeled antibodies for the identification of astrocytes and neurons, allowed for distinguishing of astrocytes and neurons differentiated from the injected stem cells. Imaging parameters are presented in Table 1.

A dedicated animal Varian scanner (Varian Inc., Paolo Alto, CA, USA) with a magnetic field strength of 4.7 T was used in experiments with stem cells.[14] Adult female C3H mice weighing 25-35 g, and neonatal C3H/SCID mice were used. Adult mice were anesthetized with 5 mg/kg xylazine and 100 mg/kg ketamine, then SPIO-labeled C17.2 NSCs were injected into the cortex and hippocampus. Labeled cells were injected into the right hemisphere, and unlabeled ones into the right hemisphere as a control. Neonatal mice were cryo-anesthetized and labeled cells were injected into the cerebral ventricles. Neonatal mice with unlabeled NSCs or *phosphate-buffered saline* (PBS) injected into the cerebral ventricles were used as the control group for the second group. *In vivo* MR imaging was performed 4 weeks following the injections in adult mice, and 7 weeks following the injections in neonatal mice. Next, *ex vivo* imaging was performed on the 9.4 T vertical bore magnet. In adult mice until the 32nd day after the transplantation, labeled cells were detectable in the hypointense area near the injection site. During the *in vivo* experiment on neonatal rats, labeled cells were not detectable. The presence of labeled cells was found out in *ex vivo* studies as a hypointense area, especially in the olfactory bulb, cortex, hippocampus and the cerebellum. In the control group no hypointense areas were visualized. After MR imaging, histological tests were conducted, and the results were consistent with MRI scans. Imaging parameters are presented in Table 1.

A Bruker Biospec Avance 47/40 scanner (Bruker, Karlsruhe, Germany) with surface coil was used to visualize spinal cord injury in rats.[9] Female Sprague-Dawley rats, weighing 250–300 g, were used in the experiment. The rats' spinal cords were transected at the midthoracic level; rats with unlesioned spinal cords served as control groups. Groups of rats 2–3, 4 and 6 months after the transection and control groups were submitted to MR imaging *in vivo*. Animals were anesthetized with halothane. In the unlesioned spinal cords white and gray matter were easily identified on T1-, T2- and PD-weighted images. However, gray and white matter lesions in spinal cord injury were visible near the cut, up to 10 mm rostrally and caudally. Additionally, co-occurring pathologies were observed, e.g. vertebral dislocation, intramedullary microcysts, and dorsal spinal cord compression. The Omniscan (contrast agent) injection caused a sudden signal intensity, and then filled in the vessels, which testified to the development of scars with a strong vascularization. Histological analysis confirmed the observations obtained through MRI. Imaging parameters are presented in Table 1.

A Bruker Biospec Avance 47/40 scanner with surface coil was also used for *in vivo* imaging of animals implanted with