MRI compatible small animal monitoring and trigger system for whole body scanners

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Abstract

Performing magnetic resonance imaging (MRI) experiments with small animals requires continuous monitoring of vital parameters, especially the respiration rate. Clinical whole-body MR scanners represent an attractive option for preclinical imaging as dedicated animal scanners are cost-intensive in both investment and maintenance, thus limiting their availability. Even though impressive image quality is achievable with clinical MR systems in combination with special coils, their built-in physiologic monitoring and triggering units are often not suited for small animal imaging. In this work, we present a simple, MRI compatible low cost solution to monitor the respiration and heart rate of small animals in a clinical whole-body MR scanner. The recording and processing of the biosignals as well as the optimisation of the respiratory trigger generation is decribed. Additionally rat and mouse in-vivo MRI experiments are presented to illustrate the effectiveness of the monitoring and respiratory trigger system in suppressing motion artifacts.

Keywords: Small animal imaging, physiological monitoring, MRI, respiratory trigger, motion suppression

MRT-kompatibles Kleintier-Überwachungs- und Triggersystem für Ganzkörper-Scanner

Zusammenfassung

Die Durchführung von Experimenten mit Kleintieren mittels MRT erfordert eine kontinuierliche Überwachung lebenswichtiger Parameter, insbesondere der Atemfrequenz. Klinische Ganzkörper-MR-Scanner stellen eine attraktive Option für die präklinische Bildgebung dar, da dedizierte Kleintierscanner kostenintensiv in der Anschaffung und im Unterhalt sind, was die Verfügbarkeit einschränkt. Obwohl eine beeindruckende Bildqualität mit klinischen Ganzkörper-MRT-Systemen in Kombination mit speziellen Spulen erzielt werden kann, sind deren eingebaute physiologische Überwachungs- und Ansteuerungseinheiten oft nicht geeignet für die Kleintierbildgebung. In der vorliegenden Arbeit präsentieren wir eine einfache, MRI-kompatible, kostengünstige Lösung zur Überwachung der Atmung und Herzfrequenz von Kleintieren in einem klinischen Ganzkörper-MR-Scanner. Neben der Beschreibung der Aufnahme und Verarbeitung der Biosignale sowie der Optimierung der generierten Triggersignale werden In-vivo-MRT-Messungen an Ratten und Mäusen präsentiert, die die Unterdrückung respiratorisch induzierter Bewegungsartefakte demonstrieren.

Schlüsselwörter: Kleintierbildgebung, physiologische Überwachung, MRT, Atemtriggerung, Bewegungsunterdrückung

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1 Introduction

Magnetic Resonance Imaging (MRI) of small rodents gains increasing importance in preclinical medical research as MRI provides a powerful diagnostic tool to non-invasively assess the three-dimensional anatomy with high spatial resolution and excellent soft tissue contrast. In particular, the non-invasiveness of MRI allows to perform longitudinal studies on small groups of animals *without* the need to sacrifice simlilarly sized groups of animals at each timepoint during the study, as is necessary with, e.g., histological methods. Ideally, preclinical small animal MRI is performed on dedicated high field MR scanners [1,2]. However, many research groups have no or only limited access to dedicated animal scanners whereas clinical MRI scanners are more widely available [3–9]. Apart from intrinsic gradient limitations [3,5,10] one problem is that clinical scanners usually do not provide physiological monitoring and trigger units that are sufficiently sensitive for rats or mice [11]. Since small rodents are usually anaesthetized during a considerable time period (sometimes up to 2h or even longer), body temperature and other important vital parameters, such as the respiration and heart rate, have to be monitored during scanning.

Although several commercial MRI compatible physiology monitoring systems are available on the market for preclinical imaging (e.g., Biopac Systems Inc., 45145 Essen, Germany; Small Animal Instruments, Inc., Stony Brook, NY 11790, USA), these systems are often scanner specific and constitute a considerable addititonal investment. Consequently, for occassional small animal imaging on clinical scanners a low cost monitoring device with broad applicability would be beneficial.

To sense small motions of an animal, a variety of physical principles can be employed. Optical sensors are well suited to work in the presence of (electro)magnetic fields [12,11]. However, the design of SNR efficient small animal coils tends towards tight fitting coils which restrict access to the animal, like for example the Litz coil (Doty Scientific Inc., Columbia, SC, USA) with shielding tube [13,5]. Placement of the optical sensor in close proximity to an animal part which provides respiratory motion can get tricky in tight coils and the necessary adjustment to align the optical fibres and the reflecting surface need manual access as well. Another disadvantage of the optical sensor described in [11], as well as other approaches as plethysmographs [14] or small pick-up coils [15], is the inability to monitor the heart beat. Sato et al. [16] recently published a system capable to simultaneously monitor respiratory and cardiac motion which is based on a piezoelectric sensor in direct contact with the animal. This design, however, is not MRI compatible and cannot easily be modified due to the electronic pressure pickup. Other MR compatible respiratory monitoring systems [17] use small PVC pads filled with foam rubber, which are placed under the animal's chest or abdomen as pressure sensor.

The current work describes and evaluates an MR compatible monitoring and trigger system that combines a mechanical PVC pressure pad in the scanner with electronic signal post-processing taking place outside the rf cabin. Our design focuses on a fast cost-effective setup providing easy handling even in restricted spaces and allowing quick animal exchange for high throughput.

2 Material and Methods

2.1 Pressure sensor and signal processing

For monitoring the vital signs a small clinical pressure pad of 2 cm diameter (Graseby Medical Limited, Watford, UK) was placed underneath the animal. The original connection line of the MR-safe pressure pad was extended to a total length of 7 m stretching as far as the outside of the RF cabin by using standard Luer-Lock infusion extensions (Perfusor®-connection, B. Braun Melsungen AG, Melsungen) (see Fig. 1).

The mechanical pressure signal is converted outside the RF cabin into an electrical signal by the piezoresistive differential pressure sensor (MPX 2010, Motorola Solutions Inc., Schaumburg, USA). The sensor has two inputs one of which was left open serving as a reference (ambient pressure), whereas the other was connected to the pressure pad. The selected sensor type is sensitive in the range of 0-10 kPa while the burst pressure of 75 kPa is sufficiently high to avoid accidential damage to the sensor. The sensor provides two symmetric outputs, which are proportional to the pressure difference. The symmetric electrical signal is amplified by a difference amplifier (see Fig. 1, pre-amplifier) using an integrated instrumentation amplifier (INA118P) with excellent common mode rejection (CMR $\approx$125 dB). This setup yields signal amplification of approximately 60 dB and, at the same time, suppresses the common mode noise from the pressure sensor.

To remove DC offsets or any constant bias caused by, e.g., the weight of the animal on the pressure pad, AC coupling was used with the pre-amplifier. AC coupling was accomplished with the common UA 741 integrated operational amplifier (op-amp), which constitutes an active first-order low-pass filter. The output of the low-pass filter was coupled back to the reference point of the instrumentation amplifier (see Fig. 1). This negative feedback suppresses all signal components below 1.6 Hz in the pre-amplifier. To further improve the signal-to-noise ratio an additional second-order Sallen-Key low-pass filter attenuated all frequencies above 7 Hz. In particular, the ubiquitous 50 Hz noise was attenuated by $\approx$ 28 dB.

The final output amplification with a total gain of 33-60 dB was realized by an adjustable two-stage amplifier, employing two UA 741 op-amps. The total gain of the pressure sensor signal was thus in the range of 93-120 dB. As power supply for the pressure sensor and all op-amps an iron free, symmetric 12 V commercial power supply was used (Conrad Electronic