A Multiple Mouse Biological Loading and Monitoring System for MRI

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Introduction

Recently, murine MRI studies have become significant in facilitating research on human disease models due to their genetic homology. Three-dimensional, high-resolution images of mice *in vivo* have also allowed for further insight into anatomy and function. However, with imaging times on the order of hours, high throughput of specimens has been problematic.

Multiple mouse imaging is an innovative concept in increasing throughput of an MRI study by imaging mice concurrently in shielded transmit/receive radiofrequency (RF) coils in a common magnet [1]. We have designed a system to allow rapid reproducible loading of multiple mice into an MRI, while maintaining biological stability throughout the imaging session.

The process of loading living specimens into the MRI can be broken down into three phases: preparation, loading and maintenance. The preparation phase includes the induction of the anesthetic and the application of the monitoring leads before the mice are inserted into the MRI scanner. During the loading phase, the mice are positioned inside the magnet bore and are connected to the monitoring and anesthetic systems. Lastly, the maintenance phase monitors the physiology of the mice and preserves their body temperature throughout the imaging process.

Methods

Seven mice were initially induced with isoflurane in a large, heated induction chamber fitted with self-closing iris ports to allow for convenient access. Once the mice were anesthetized, hair was removed from their chests for the application of ECG and temperature monitoring leads. In lieu of conventional pad/cuff electrodes and rectal temperature probes, we devised a custom form-fitted polypropylene platform with embedded ECG and temperature probes called the 'sled' (Fig. 1) (patent pending).

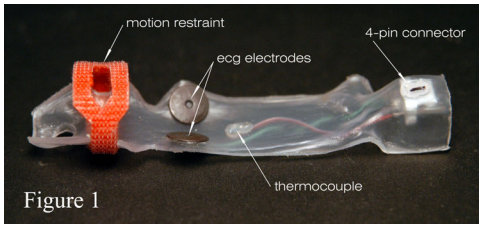

Figure 1

The sled was constructed by generating a precise physiological plaster facsimile of a representative specimen in the favorable position. A polypropylene sheet was then vacuum formed and cut around the plaster facsimile to create a thin, lightweight, autoclavable platform. For our purpose, neonatal/pediatric ECG electrodes were embedded into the sled to contact the chest, and a thermocouple was mounted in a similar fashion to measure skin temperature at the abdomen. Motion restraints made from hook and loop fasteners were used to limit movement of the head. Once positioned on the sled, the mice were loaded into 50mL centrifugal tubes and mounted on the mouse loading system.

The mouse loading system consists of two major parts: the 'coil cradle' and the 'mouse hive' (Fig. 2). The coil cradle's main function is to position up to 19 'Millipede' coils (Varian NMR Systems, Palo Alto, CA) in a hexagonal array inside the magnet, and the mouse hive is designed to hold the multiple specimens housed in the modified 50 mL centrifugal tubes. These two parts are positioned along a common rail system, allowing integration within the bore of a 7-Tesla MRI scanner (Varian).

Isoflurane mixed with humidified oxygen (Fisher & Paykel, Auckland, NZ) was supplied from the coil cradle end to the specimen through a tube along the axis of each individual coil. With the mouse hive fully inserted into the magnet, the tips of the modified centrifuge tubes create air tight seals with the anesthetic delivery system (Fig. 3). This anesthesia gas mixture flows into the tubes, past the mice and is collected by a scavenging unit attached to the back of the mouse hive. Using a 4-pin connector, the monitoring leads from the sled are electrically connected to wires that run co-axially with the scavenging tubing, which are ultimately connected to their respective monitoring devices using a single, multiple-pin CPC connector (Electrosonic, Toronto, Canada).

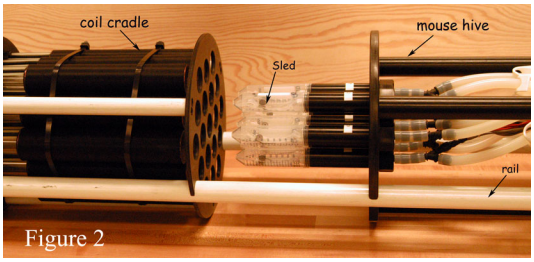

Figure 2

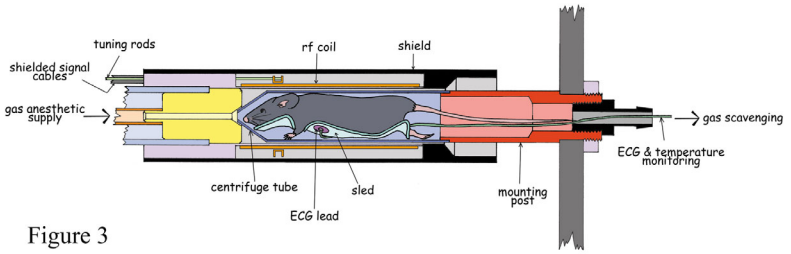

Figure 3

T-type thermocouples affixed to the sled were connected to a 16 channel temperature monitor/data logger (Topac, Hingham, MA). A variable temperature, industrial-strength dryer (Edemco, Colorado Springs, CO) was used to supply the warm air delivered to the coil array and dispersed using a custom made polycarbonate manifold. The mice's body temperatures were maintained at 34~37 ºC throughout the imaging process. The ECG signal from each mouse was monitored using an ECG trigger unit (Rapid Biomedical, Wurzberg, Germany) and oscilloscope (Agilent, Palo Alto, CA).

A Two-dimensional spin-echo sequence was used to acquire 7 slices per specimen in parallel (TR 2200ms, TE 15ms, 1mm slice thickness, 110µm x 110µm, NEX 4, 256 x 146 Matrix).

Results & Discussion

The preparation and loading phases of 7 live mice took approximately 24 minutes in total, resulting in a time of about 3.5 minutes per mouse. Figure 4 shows one of the seven slices taken from each mouse and are displayed in a similar configuration to our array. After imaging, all mice recovered well.

In addition to facilitate rapid loading, the polypropylene sled can also be used in reproducing standardized body positions, since further extension of small animal imaging is the use of comparative and computer-aided image processing algorithms.

We are currently in the process of optimizing the tuning and shimming process, which are the current rate limiting steps.

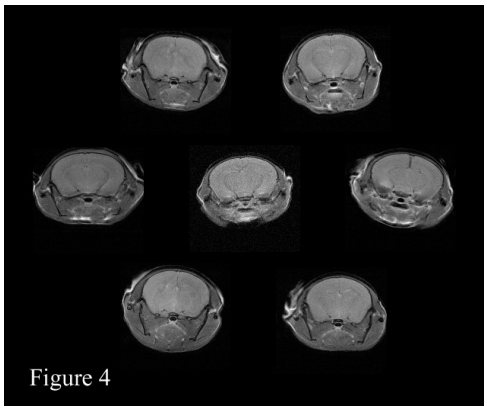
Figure 4

Reference

[1] Bock, NA *et al.* Magn Reson Med 49, 158-167 (2003).