Physiological Monitoring for Pre-clinical Magnetic Resonance Imaging

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Abstract.

Imaging small animal is used widely as preclinical experimental instrument in modelling both animal and human diseases, as well as cancer studies, cardiovascular and musculoskeletal disorder. Their

Application signified the most important influence on the improvement in studying animal model in vivo. The basic objective of this work is the designing of MRI compatible circuit, suitable enough in physiological monitoring for preclinical MRI, for the purpose of monitoring temperature, respiration (pressure) of anaesthetized small animal such as rats and mice in a high field 4.7T MRI scanner. The circuit were selected and signal processing circuits were developed to record physiological temperature, respiration. These were tested on the bench and also in a 4.7T preclinical MRI system. Sensor were not affected by the Bo field but the waveforms showed artefacts in response to RF and gradient pulses. The circuit compatibility with MRI shows the behaviour of RF field and the gradient field which changes with time. Measurement were carried out to test the 4.7T MRI scanner's interactions with RF pulse, gradient pulse, and the physiological sensors. Measurement of the parameters shows that, temperature, pressure, and battery voltage were not affected by the gradient pulse sequence, but, the RF pulse sequence has effect on all the parameters.

Keywords: MRI, Compatible Circuit, Physiological Monitoring, Temperature, and Respiration, pre-clinical, magnetic field

INTRODUCTION

Physiological monitoring for preclinical magnetic resonant imaging (MRI), are designed to mainly meet the physiological monitoring and gating requirement for anaesthetize small rodents such as rats and mice, even larger animals in an MRI setting. Small animals such as rats and mice are among the animal's species widely used in cardiovascular disease studies. Gene-knockout and transgenic skill have allowed scientist to investigate the outcome of specific or collections of genes [1], of many cardiovascular diseases. Also, the development of surgical models of the animals that matches the

disease of human. Treatments modalities have been established base on hereditary variation studies and verified on these animals to evaluate the effectiveness of the treatment. Non-invasive, exact dimensions of cardiovascular keys for instance, ventricular volumes, ejection fraction mass etc are necessary for phenotyping and numerically assessing the animals. The major benefits of the MRI is an excellent in soft tissue contrast, and also has the ability to image 3-D structure and function in high inter-session replicate [1]. Biomedical research has increased significantly through the use of non-invasive imaging technologies in the study of biological and biochemical processes within living animals and humans. Certainly, imaging small animal is used widely as preclinical experimental instrument in modelling both animal and human diseases as well as cancer studies, musculoskeletal disorder, cardiovascular, and neurodegenerative. Their application signified, the most important influence on the improvement in studying animal model in vivo. Using longitudinal monitoring from the beginning and the development of disease around similar animals, and studying the effectiveness of biological drug therapy. This provide a fast and efficient method for classifying and modelling.

Small animal imaging is extensively used as a preclinical experimental tool in many animal models of human diseases. More recently, it has been applied for the development of stem cell-based therapies. There have also been advances wherein researchers are increasingly using imaging for phenotyping and characterisation of transgenic disease models [2].

This project work is mainly centre on pre-clinical MRI scanner, because, animal model used widely are based on pre-clinical scanner owing to the substantial benefits in the quality of image acquisition, sensitivity, and spatial resolution that can be acquired using smaller scanner with high magnetic field like the 4.7T. As rat and mouse brain are about 3,000 times much smaller compare to the brain of human, the pre-clinical scanner is necessary to achieve high resolution [3].

THEORETICAL BACKGROUND

Generally, physiological monitoring for preclinical MRI is achieved using a high field magnets B_O with a very small bore specifically designed for rodents (rats and mice). The B_o is a static magnetic field, and the significant of using the high magnetic field B_O is the high resolution that is achieved due to increase in signal, as a result of increase sample magnetisation cause by greater number of aligned spin from the Boltzmann distribution and the increased Faraday induction from the higher frequency given as;

$$fL=(\gamma/2\pi)B_O \qquad (1)$$

where γ is the gyromagnetic, fL is the Larmor frequency and B_O is the magnetic field.

Usually, preclinical uses higher magnetic field B_O range of 4.7T to 7T. For the purpose of this research work, magnetic field of 4.7T (200 MHz) is used [4]. MRI scanner for a whole body always has the main magnet, the gradient coils, and the RF coils for receiving and sending signals. Mostly, the contemporary clinical scanner uses superconducting magnet range of 1.5T to 3T. The magnet is designed to maintain good homogeneity in static magnetic field B. In determining image quality, magnetic fields(B_O) strength is very important. SNR is increase by higher magnetic field strength, allowing faster scanning and high resolution. Although, higher magnetic field strength need more expensive magnets and high cost of maintenance, and concern for safety [5].

METHODOLOGY

Since monitoring small rodents are always anaesthetized for a considerable period up to 2 hours or more, there is need to measure some important physiological parameters such as, the body temperature, respiration rate, and the heart rate need monitoring during scanning. For instance, a sedated rats or mice usually have their heart rate and respiratory rate decreased when exposed to room temperature environment by more than a factor of two.

Thermistor is used because is the most widely sued temperature sensor, and it gives voltage output of ± 5v, and is linearly related to temperature. The thermistor is a resistor with a very strong negative temperature coefficient of resistance, also known as NTC sensor.

The temperature sensor used was a chip thermistor with dimensions x mm, y mm, z mm (NTCS0603E3103JHT, Vishay, US) [6], with b value of 3960K, tolerance of $B_{25/85}$ = ±1, and R_{25} value of 10kΩ. The thermistor obeys exponential law. Given as

$$R=Ae^{(b/T)} \qquad (2)$$

where b is the constant temperature in Kelvin (K), and depends on the composition; 3000 – 4000K, value within the datasheet, and A is in (Ω) depends on the sensor shape. Supplied with calibration value of R_O at T_O which allows the elimination of A from equation (2) to give

$$R=R_Oe^{b(1/T-1/To)} \qquad (3)$$

where R is unknown resistance, R_o is the calibrated resistance, 1/T is the unknown temperature and $1/T_O$ is the calibrated temperature.

The pressure transducer's datasheet is, Freescale; MPX5100AP/GP [7] pressure transducer with Graseby sensor pad, use for respiration. It is an on-chip condition integrated silicon pressure sensor, suitable for microcontroller or microprocessor. The MPX5100 is a piezoresistive transducer series.

Abdominal respiratory sensor uses a small pressure pad designed for infant apnoea alarms (MRI0, Graseby, UK) [8] A small volume of air pass through the sensor tube to the monitor, cause by the expansion of the abdominal wall during breathing. Other components datasheet use are; LM285Z – 2.5RAG 2.5V reference, and TC 7660S [9] Charge pump (negative voltage generator).

RESULTS

First among the measurement was the thermistor designed to be inserted inside the body of the animal to determine the body temperature. The NTC thermistor was soldered to a twisted pair of 0.2 mm enamelled copper wires to allow resistance measurements. The thermistor was temporarily glued to a copper block of approximate dimensions of 5 mm x 20 mm x 40 mm to which a silicon temperature sensor with a 10 mV/^{0}C output (LM35, Texas Instrument, USA) [8] was also attached. The copper block was heated up to approximately 40^{0}C by applying a lot of soldering iron for a few seconds, and then was place on a polystyrene block and cover so that it cooled to room temperature over a period of several minutes. Copper has high thermal conductivity and a high heat capacity, so this help the thermistor and reference sensor at the same temperature during cooling. The measurement of resistance versus temperature shows that, as temperature increases it lead to decrease in resistance as seen in Figure1, below.

Figure1: Resistance against temperature of an NTC thermistor.

The negative temperature coefficient (NTC) thermistor (NTCS0603E3103JHT,Vishay, Germay) used is a dual op-amp (LF353), the choice of the NTC thermistor is because from the experimental measurement as temperature rises, the resistance decreases.

The gradient echo measurement of the parameters were carried out to test interactions between the imager's RF and gradient pulses and physiological sensors. The tests used a gradient echo pulse

sequence with a bandwidth of 50kHz, 256 x 256 pixels, slice thickness 1mm with a field of view (FOV) of 50mm. The gradient ramp time is 1000μs, the repetition time (TR) of 200ms, echo time (TE) of 11ms and flip angle of 45^0, as shown below.

Figure 2: Image outside magnet

Where channel 0: pulse, channel 1: temperature, channel 2: battery voltage and channel 3: ECG.

Figure3: Image near the magnet

Here channel 0: ECG, channel 1: pulse, channel 2: temperature and channel 3: battery voltage.

DISCUSSION

Figure1. show how temperature and resistance relate with thermistor. A thermistor chip is connected with copper enamelled wire of thickness 0.2mm, twisted together to avoid magnetic field interference. One end of the wire is connected to a multi meter as a resistance monitor, and a reference voltage is connected to another multi meter, power by the 6V battery use as temperature monitor. A copper metal is used because of it high thermal conductivity and high electrical conductivity, for heat and electric conductor, and the thermal copper is with thermal equilibrium with the copper. When heat was applied to the thermistor attach to the copper metal with the Vref, as temperature rises, resistance decreases as seen in Figure 1.

And before starting the MRI measurement, the force of attraction including field strength between the 4.7T MRI scanner and the circuit board was tested as the board was constructed from standard components which contain small amount of ferromagnetic material. It was important to assess whether the attractive force could present a hazard or at least make the board difficult to handle. The magnetic force was balanced with the gravitational force of a test mass attached to the board via a nylon thread passing over a low friction pulley.

CONCLUSION

The testing and measurement carried out in this project show that, all the monitoring parameters do not perform as expected in the MRI system. The components interaction with the MRI need more research for MRI compatibility to be achieve. And non-ferromagnetic components should be use.

The use of signal gating generator should be explored in a future work, this could make the monitoring parameters to be independent of the RF pulse influence as seen in Figure:2 and 3.

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