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A comparison of MR imaging of a mouse model of glioma at 0.2 T and 9.4 T

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ABSTRACT

Both 0.2 T and 9.4 T MRI systems were used to image a mouse model of glioma. RF coils were designed for both fields. A spin-echo, multi-echo pulse sequence was used to determine T_2 relaxation times of both brain and tumor tissues. Contrast-to-noise ratio was calculated based on the selected echo time. The results showed that 0.2 T is suitable for mouse model imaging, however total scan time must be long to achieve high enough SNR. T_2 relaxation times of the tumor and brain tissues can be measured at 0.2 T and are 2.1 and 1.8 times respectively longer at 0.2 T than at 9.4 T. Contrast to noise ratio for tumor and brain was better at high field than at the low field. We concluded that 0.2 T may be used to study mouse model of glioma using spin echo pulse sequence, yet the total scan time is long (about 40 min), resolution is lower (~250 μm × 250 μm) and slice thickness (3 mm) must be large enough to obtain sufficient SNR.

1. Introduction

Magnetic resonance imaging (MRI) is currently an important diagnostic technique. In the last few years, MRI has become the method of choice over other diagnostic methods, such as computer tomography or positron emission tomography as it provides high-quality images of soft tissue without ionizing radiation (Lauffer, 1987). It is known, that the stronger magnetic field provides higher signal-to-noise ratio (SNR) and thus better image quality (Chen et al., 1986). Therefore high field human (3 T and higher) and animal (7 T, 9.4 T and 14 T) MRI systems have been used for studies. However the optimum field strength remains unknown and depends upon many factors. Higher fields (above 3 T for human systems) bring issues associated with RF power deposition, image inhomogeneities (Hoult, 2000) and often eddy currents induced by fast switching gradients of the magnetic field gradients. Furthermore the optimum field strength depends on tissues and pathologies of interest due to dependence of tissue relaxation times on the magnetic field strength (Orrison et al., 1991; Bonart and Kormaro, 1997). T_1 relaxation time decreases, T_2 increases and susceptibility-caused artifacts are lessened with decreasing B_0 (Parizel et al., 1995). Therefore different parameters and different pulse sequences must be used at the lower field to obtain maximum SNR and CNR.

While the most popular human system remains 1.5 T MRI, the number of low field (0.2 T and 0.35 T MRI) installations have also been increasing due to the low purchase and maintenance costs (Hayashi et al., 2004; Kuhl et al., 1995a,b). In order to compensate for low SNR, signal averaging is needed, resulting in longer acquisition times for scanners with lower field strengths. This often results in motion artifacts that are avoided at higher fields. However, due to the vertical direction of the main magnetic field, low field systems allow application of the most efficient solenoidal radiofrequency (RF) coils (Blasiak et al., 2009). These coils cannot be used in the high field systems (1.5 T and higher) which have a horizontal magnetic field. The solenoidal coils, when properly designed, provide higher SNR than other volume coils (e.g. birdcage) working at the same Larmor frequency (Chen et al., 1986). This reduces the difference in SNR caused purely by the lower field. However SNR remains significantly lower at lower fields (e.g. 0.2 T or 0.35 T) than at the higher fields (e.g. 1.5 T). Despite that, some authors reported that there is no significant difference in high field MRI diagnosis capabilities of certain diseases compared to low-field MRI (Hoult et al., 1986; Crooks et al., 1984; Passariello et al., 1996; Barnettt, 1993), such as kidney (Merl et al., 1999) or white mater diseases (Bonart and Kormaro, 1997; Orrison et al., 1991; Hayashi et al., 2004; Allmann et al., 1998; Merl et al., 1999). In addition, open configuration of low field MRI allows access to the patient during the examination, does not aggravate claustrophobia, and permits bone and joint

Abbreviations: FOV, field of view; RF, radio-frequency; SNR, signal-to-noise ratio; CNR, contrast-to-noise ratio; PBS, phosphate-buffered saline.

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motion studies, (Spouse and Gedroyc, 2000). Open design also helps to reduce discomfort for the oversized patient (Evers, 1999) and allows interventional MRI (Lenz and Drobnitzky, 1998). Therefore low field systems are being developed and utilized in parallel to high field systems. As glioma is the most common among primary brain tumors and the most difficult to treat (Fisher et al., 2007) we investigated possible detection of glioma in an animal model using low field (0.2 T) MRI. Studies of glioma including animal models are needed to improve patient outcome as the mean survival rate is only 9 months following diagnosis (Surawicz et al., 1998). While there have been many studies of animal models of glioma at 9.4 T (e.g. Blasiak et al., 2010) the studies at low field (0.1 T) have been introduced only recently (Choquet et al., 2009; Breton et al., 2010). As some centers are equipped only with low field systems, such as 0.1 T or 0.2 T, studies comparing low and high field are needed. Therefore we designed and manufactured optimized RF coils operating at for both magnetic fields for mouse brain MRI. We have also calculated T_2 values of tumor and normal brain tissue at both 9.4 T and 0.2 T to show, that different pulse parameters should be used depending on the field strength.

2. Materials and methods

2.1. Tumor cell preparation

The U87MGdEGFRvIII cell line, which overexpresses the EGFR type III variant and is highly malignant, was derived from a human tumor known to express high levels of VEGF and EGFR [36]. U87MG cells were cultured in DMEM solution supplemented with 10% fetal calf serum and maintained in a humidified 5% CO_2 atmosphere at 37 °C. Cells were harvested by trypsinization in ethylenediaminetetraacetic acid/trypsin, washed in phosphate-buffered saline (PBS), and centrifuged three times at 200 G. Viability was assessed using a 0.4% trypthan blue exclusion test. After cell density was determined, cells were brought into suspension at a final concentration of 5×10^4/2.5 μL and mixed with 2.5 μL of PBS for a total volume of 5 μL. Cells were kept on ice until inoculation.

2.2. Tumor model

Animal procedures were performed according to a protocol approved by a Local Animal Care Committee.

A CD-1 nude mouse (male, 6 weeks old, Charles River Laboratories, Cambridge, MA, USA) was anesthetized by intraperitoneal injection of a mixture of ketamine (8–120 mg/kg) and xylzine (6 mg/kg) and placed in a stereotactic head frame. Tumor cells were inoculated using procedures described previously (Blasiak et al., 2010). Briefly, the scalp was shaved and swabbed with iodine and alcohol. The skin was incised and a 0.18-mm diameter hole was drilled in the skull. Approximately 5×10^4 U87MGdEGFRvIII glioma cells, suspended in a total volume of 5 μL, were injected intracerebrally into the frontal lobe of each mouse with a chromatography syringe at a depth of 2.5–3 mm, 1 mm anterior and 1.8 mm lateral to the bregma using a Kopf stereotactic apparatus (Kopf Instruments, Tujunga, CA, USA). Subsequently, the bony calvarium was sealed by a droplet of bone wax to prevent reflux and the skin was sutured. After the surgery animals were allowed to recover from the anesthesia and were placed in the cages.

2.3. RF coils design and manufacturing

As a properly designed RF coil is crucial to obtain maximum SNR at any frequency we selected the well known birdcage RF coil (Hayes et al., 1985) that provides the maximum SNR and optimum B_1 homogeneity and is commonly used in systems with horizontal magnetic field. For imaging at 0.2 T we optimized a standard solenoidal coil.

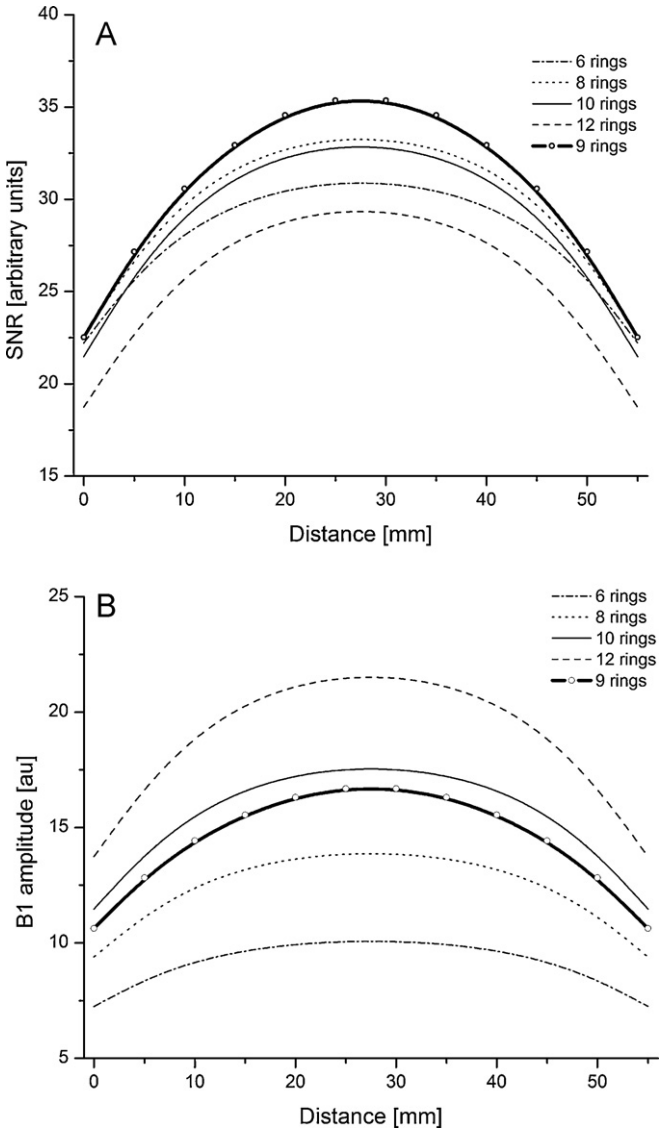

Fig. 1. The results of the simulation for the mouse head RF coil at 0.2 T: SNR (A) B_1 distribution (B) along z axis as a function of number of turns. The coil was 55 mm long and its center was at 27.5 mm along the axis. Region of interest was ±5 mm from the center (27.5 ± 5 mm).

2.3.1. Solenoidal coil for 0.2 T

MR images at 0.2 T were obtained with a 4-post magnet (MRI-TECH, Canada, Poland) equipped with TMX console (NRC, Canada) used for human imaging. This system produces vertical magnetic field and therefore a solenoidal RF coil was used. It was previously shown that this type of coil provides the best SNR (Hoult and Richards, 1976). However an optimized design of solenoidal RF coil for mouse brain was not available. Therefore we performed computer calculations based on already presented theory (Blasiak et al., 2009). Briefly, the theory applies Bio-Savart law to calculate the distribution of B_1 field produced by an n turn coil. SNR is calculated based on reciprocity theory (Hoult and Richards, 1976) and takes into account both sample and coil losses including proximity and skin effects. The following parameters were assumed for the calculation of the RF coil for mouse MRI: 2 mm conductor diameter, 35.6 mm coil diameter (center to center of the wire), 55 mm coil length, resonance frequency 8.2 MHz (Larmor frequency of protons