Introduction: Despite considerable interest in noninvasive diagnosis of brain glioma with MRI in vivo, high sensitivity and specificity for glioma diagnosis to define the tumor anatomy for surgical section, chemotherapy and radiation therapy need to further research[1]. Superparamagnetic iron oxide nanoparticle (SPIONPs) delivery system has become a model system in which to study the target molecule-specific biodistribution, rapid exertion and undesired side-effects using in vivo small animal MRI. As a cellular transmembrane receptor, EGFR regulates important cellular processes and is linked to a poor prognosis in various human cancers[2]. Although EGFR offers a useful new tool as a brain glioma biomarker, its monoclonal antibody has not been widely used or translated for use in medical imaging. In this study, we developed a potentially valuable new targeted nanocarrier based on SPIO delivery system, EGFRmAb-bioconjugated nanoparticles—EGFRmAb-SPIONPs. Magnetic targeting is a promising strategy for developing the diagnosis of brain glioma. The purpose of this study was to elucidate strategies for further improvement of this promising approach.

Method and Materials: EGFRmAb-SPIONs were prepared and characterized. The preferential accumulation of the EGFRmAb-SPIONPs within gliomas and subsequent magnetic resonance imaging (MRI) contrast enhancement were demonstrated in vitro in C6 cells and in vivo in tumors of rat model. MRI scanning was performed using a 3.0T MRI scanner (Signa HDxt GEMR) and a research coil insert designed specifically for imaging rats was used to MRI.

Results: The average particle size of about 10.21 nm, hydrodynamic diameter of about 161.5 nm, saturation magnetization of 55 emu/g Fe and T2 relaxivity of 92.73 S⁻¹mM⁻¹ of the EGFRmAb-SPIONs suggested its applicability for MRI. MR T2WI of iron uptake in C6 cells treated with the nanoparticles (EGFRmAb-SPIONPs and SPIONPs) of various iron concentrations were shown in Fig. 1. This result demonstrated that, EGFRmAb-SPIONPs could efficiently and specifically label the C6 cells compared to SPIONPs. Using a rat model of C6 glioma, EGFRmAb-SPIONs provided a better picture or more sensitivity to depict brain glioma on MR images than that of SPIONPs. Significantly enhanced T2-weighted images of brain glioma were documented in vivo with EGFRmAb-SPIONs until 48h after injection (Fig. 2). Histochomical analysis of the tumor tissue shown in Fig. 3. The results from cytotoxicity, histopathology and blood toxicity assays suggested that the EGFRmAb-SPIONPs had good biocompatibility and exhibited no toxicity.

Discussion and Conclusions: we showed the following main findings: first, EGFRmAb-SPIONPs is suitable for use as negative MRI contrast agent, specially T2WI; secondly EGFRmAb-SPIONPs could be specifically and efficiently uptaken by C6 glioma cells, and selectively improve the detection of tumor by MRI; thirdly EGFRmAb-SPIONPs could produce the remarkable contrast change of brain glioma in vivo following intra-carotid administration of EGFRmAb-SPIONPs; and fourthly EGFRmAb-SPIONPs had good biocompatibility and exhibited no toxicity, which was very important for the clinical application. Thus, as prolonged retention in tumors, relatively safer toxicity profile and strong T2-relaxation on MR images—an attractive property for their real-time, in vivo monitoring, EGFR MAb-SPIONPs may allow for earlier cancer detection, assessment of the recurrent tumor after tumor resection and postoperative radiotherapy.