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Monitoring the Effect of Doxorubicin Liposomal in VX2 Tumor Using Magnetic Resonance Imaging

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Abstract : Cancer is still one of the serious diseases threatening the lives of human beings. How to have an early diagnosis and effective treatment for tumors is a very important issue. The animal carcinoma model can provide a simulation tool for the study of pathogenesis, biological characteristics and therapeutic effects. Recently, drug delivery systems have been rapidly developed to effectively improve the therapeutic effects. Liposome plays an increasingly important role in clinical diagnosis and therapy for delivering a pharmaceutic or contrast agent to the targeted sites. Liposome can be absorbed and excreted by the human body, and is well known that no harm to the human body. This study aimed to compare the therapeutic effects between encapsulated (doxorubicin liposomal, LipoDox) and un-encapsulated (doxorubicin, Dox) anti-tumor drugs using Magnetic Resonance Imaging (MRI). Twenty-four New Zealand rabbits implanted with VX2 carcinoma at left thigh were classified into three groups: control group (untreated), Dox-treated group and LipoDox-treated group, 8 rabbits for each group. MRI scans were performed three days after tumor implantation. A 1.5T GE Signa HDxt whole body MRI scanner with a high resolution knee coil was used in this study. After a 3-plane localizer scan was performed, Three-Dimensional (3D) Fast Spin Echo (FSE) T2-Weighted Images (T2WI) was used for tumor volumetric quantification. And Two-Dimensional (2D) spoiled gradient recalled echo (SPGR) dynamic Contrast-enhanced (DCE) MRI was used for tumor perfusion evaluation. DCE-MRI was designed to acquire four baseline images, followed by contrast agent Gd-DOTA injection through the ear vein of rabbits. Afterwards, a series of 32 images were acquired to observe the signals change over time in the tumor and muscle. The MRI scanning was scheduled on a weekly basis for a period of four weeks to observe the tumor progression longitudinally. The Dox and LipoDox treatments were prescribed 3 times in the first week immediately after VX2 tumor implantation. ImageJ was used to quantitate tumor volume and time course signal enhancement on DCE images. The changes of tumor size showed that the growth of VX2 tumors was effectively inhibited for both LipoDox-treated and Dox-treated groups. Furthermore, the tumor volume of LipoDox-treated group was significantly lower than that of Dox-treated group, which implies that LipoDox has better therapeutic effect than Dox. The signal intensity of LipoDox-treated group is significantly lower than that of the other two groups, which implies that targeted therapeutic drug remained in the tumor tissue. This study provides a radiation-free and non-invasive MRI method for therapeutic monitoring of targeted liposome on an animal tumor model.

Keywords : doxorubicin, dynamic contrast-enhanced MRI, lipodox, magnetic resonance imaging, VX2 tumor model
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