Characterization of neuro-endocrine tumors using MRI: Longitudinal study in an athymic nude mouse model

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Introduction

As the main cause of treatment failure in humans, liver metastasis is an important target for therapeutic intervention. Furthermore, liver metastases are the most important predictor of poor survival in patients with neuroendocrine tumors. Experimental model of endocrine tumors with liver dissemination is available for evaluation of new medical therapeutics such as antiangiogenic therapy. The aim of this longitudinal study was to evaluate the performance of the detection and characterization of the liver metastases using high field MR Imaging.

Methods

We designed a longitudinal in vivo study with intrasplenic injection of enteroendocrine cell line STC-1 in 8 immunosuppressed newborn mice during one month. Magnetic resonance imaging (MRI) was performed at D7, D12, D17 and D24 after intrasplenic injection. Mice were sacrificed for histological analysis at D24.

A cylindrical volumetric coil with a 32 mm internal diameter for both RF emission and reception was used. Mice were imaged under isoflurane anesthesia and internal temperature was preserved with a water-flow heating apparatus. A respiratory sensor, placed on the abdomen was used in order to detect the movement due to respiration and cardiac cycle.

Axial images covering the whole liver were acquired *in vivo* at 7T on a Biospec system (Bruker, Ettlingen, Germany) using a respiratory-triggered fat suppressed Spin-Echo (SE) with 3 echo times (TE = 20, 40 and 60 ms). Other parameters were TR = 6000 ms, 0.5 mm slice thickness, 36 slices; 30 mm FOV; 256 square matrix and about 20 min acquisition time.

Image analysis was performed with software developed under IDL (RSI, Boulder, CO) programming language. Specifically, regions of interest were drawn manually in each slice to delimit the volume of the liver. Thresholding was performed using a dual reference limit based on average signal calculated in air (S_{air}) and reference water tube (S_{water}). The threshold was set up to 30% of (S_{water} - S_{air}). This adaptative threshold was chosen to segment image into a "lesion" phase and a "parenchymal" phase. The fraction of lesion over the total liver volume was quantified.

Results

Representative images obtained at three echo times from a mouse at D24 are shown in Figure 1. For the images with a short TE (20 ms) almost all the lesions appear in hyper intensity signal. For longer TE (60 ms), fewer lesions are visible which represent cystic lesions on histopathologic analysis. Quantification results of the lesion fraction are summarized in Figure 2. Figure 2 shows that for each stage the fraction of visible lesions of the liver decrease with TE. As expected, lesion fraction increases with time (Figure 3).

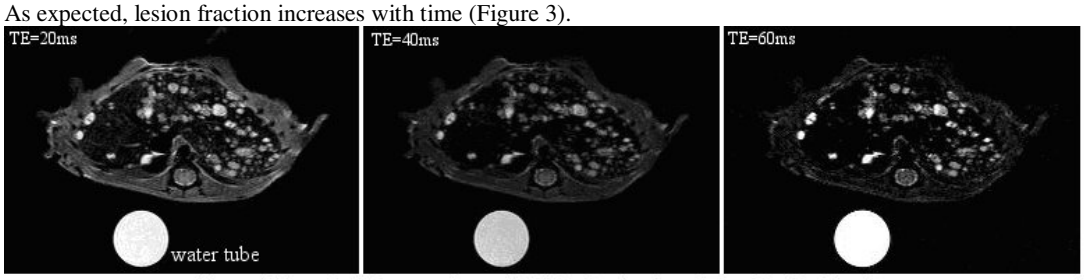

Figure 1: Example of a mouse liver at D24 for 3 echo times (TE = 20, 40, 60 ms).

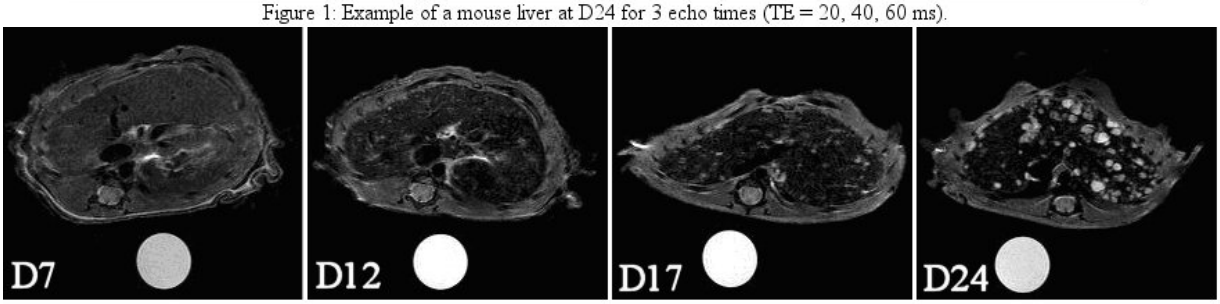

Figure 2: Lesions evolution

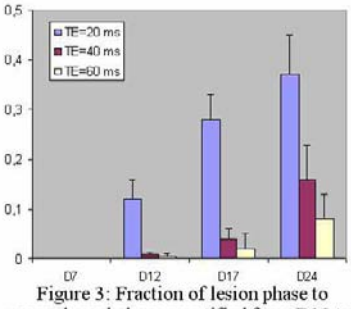

Figure 3: Fraction of lesion phase to parenchymal phase quantified from D12 to D24 for each echo time.

Discussion

The lesions were detected and quantified from D12 to D24. The maximum of lesions is visible at D24. In the MR images, two types of liver lesions depending on TE used. Short TE allows detecting all lesions and long TE allows detecting only cystic lesion according to histopathologic findings. The threshold used provides good discrimination between parenchymal phase and lesion phase. With these results, MR imaging could be used with relevance in the evaluation of new therapeutics protocol for treatment of liver metastasis in neuroendocrine tumors using small animal model.

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