Monitoring Response to Convection Enhanced Taxol Delivery in Brain Tumor Patients Using Diffusion Weighted MRI

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Introduction

Recurrent malignant brain tumors are almost universally fatal within weeks to months of diagnosis of recurrence. Chemotherapy does not confer any significant survival advantage, in part due to the poor penetration of most chemotherapeutic drugs across the blood brain barrier and into the tumor.

Convection is a novel approach to deliver drugs into brain tumors (1). It is based on enhancing the penetration of various molecules into the malignant tissue. Paclitaxel (Taxol) is a powerful antineoplastic agent that is effective against brain tumors in vitro, but does not cross the blood brain barrier. A new Phase II clinical trial was designed in an attempt to deliver taxol using convection into recurrent malignant brain tumors.

Diffusion-weighted (DW) MRI enables non-invasive characterization of biological tissues based on the diffusion of water molecules. It has been shown that there is an order of magnitude difference between the diffusion of intra- and extracellular water molecules. Therefore, it is anticipated that the diffusion of the water molecules will correlate with early changes in morphology and physiology of tissues reflecting responses to treatment (2-5), such as changes in the permeability of cell membranes, cell swelling and cell lysis.

Since convection-enhanced taxol delivery is a new type of treatment there is no established way to follow its progress. In this work we demonstrate the feasibility of using DWMRI as a non-invasive tool to continuously monitor the progression of the convection process or its effects.

Methods

Patients with recurrent malignant glioma received intratumoral placement of a catheter through which Taxol (1 mg/ml) was continuously administered for 5 days at a rate of 5 micro-l/min.

Line Scan DWMRI, contrast enhanced T1 weighted and T2 weighted MRI were used to daily monitor 3 patients with brain tumors before, during (5 days) and following treatment. One patient was treated twice in different regions. All images were acquired with 4mm slices, 2-signal averages and a 22x16cm field of view. T2 weighted MRI were acquired with a 256x128 matrix, TR=3000 ms and TE=19/95 ms. T1 weighted MRI were acquired with a 256x128 matrix, TR=500 ms and TE=105.2 ms. Diffusion curves were calculated from additional DWMRI obtained with 14 b values ranging from 15 to 4000 s/mm². Data were acquired using a 0.5T interventional MRI machine at Sheba Medical Center.

Results

Significant changes in water diffusion were observed within the first 24 hr after the treatment began (see fig.). The shape, magnitude and nature of this effect changed continuously throughout the treatment period. The initial effect was the appearance of a bright area, corresponding to a decrease in the apparent diffusion coefficient (ADC) and an increase in the fraction of slow/fast water volumes (R). This region changes later on to a dark area that appears within the bright ring, corresponding to an increased ADC and decreased R (this can be seen in the images taken 4 and 6 days after treatment began). These changes were compared with contrast enhanced T1 weighted and T2 weighted MRI, histology when available, and DWI data of other brain pathologies.

References