Difference in Early Intratumoral Changes Induced by Single Dose and Fractionated Radiotherapy in Rat Rhabdomyosarcoma Measured with Diffusion- and Perfusion-Weighted Magnetic Resonance Imaging

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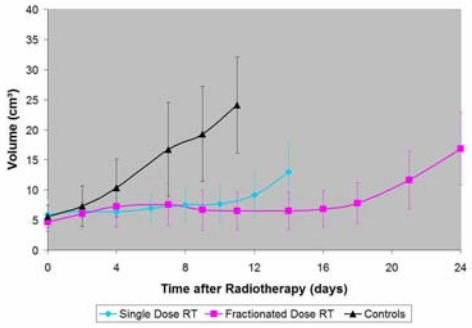
Introduction:

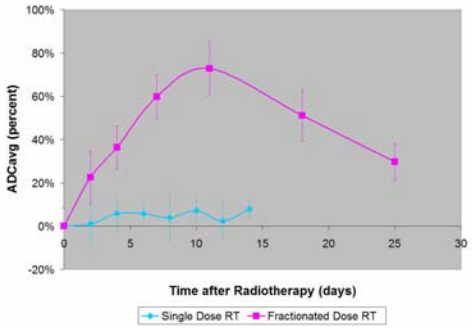
Visualization of early therapy-induced tumoral changes can be used to predict tumor response, allowing treatment modulation in case of nonresponding lesions. The purpose of this study was to examine the difference in early intratumoral changes after single dose or fractionated irradiation, using a combination of diffusion-weighted (DW) and dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) in a rat rhabdomyosarcoma model.

Material and Methods:

Male WAG/Rij rats with bilateral subcutaneous rhabdomyosarcoma in the flanks underwent a baseline MRI scan on a clinical 1.5T system (SONATAVision; Siemens, Erlangen, Germany) using a 4-channel phased-array wrist coil. The MRI protocol consisted of anatomic T1- and T2-weighted turbo spin-echo sequences, a dynamic series of 100 T1-weighted 'Volumetric Interpolated Breath-hold Examination' (VIBE) scans with Gd contrast injection after 12 scans, and a diffusion-weighted spin-echo echo-planar sequence using a large range of b-values (between 0 and 1000 s/mm^2).



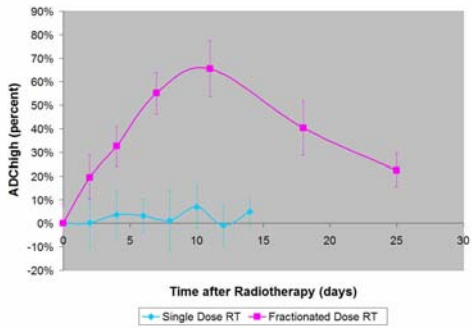
Four rats received a single dose of 8 Gy, and 4 other rats were given a clinically relevant dose of 3 Gy administered daily for five days. All rats were examined repeatedly in the first three weeks after the start of radiotherapy. Apparent diffusion coefficient (ADC) values were calculated for all b-values (ADCavg), and separately for low (b<150 s/mm^2; ADClow) and for high b-values (b>400 s/mm^2; ADChigh). From the DCE-MRI images, the maximal contrast inflow ('initial slope', IS), the maximal contrast-enhancement (Cpeak) and the time between start of injection and maximal contrast-enhancement ('time to peak', TTP) were calculated.

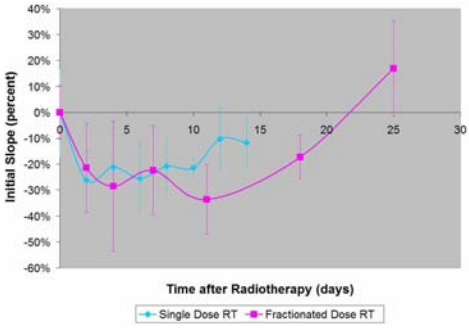


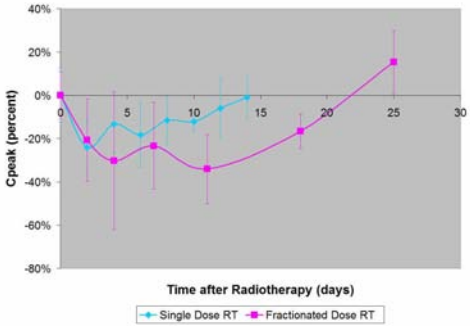
Results:

The tumors treated with a single dose irradiation showed a strong decrease in IS and in Cpeak already at two days post-treatment, with slow recuperation afterwards; no TTP changes were found. No substantial ADCavg, ADClow, ADChigh changes were found during the entire follow-up period in this group. In this group a tumor growth delay of 12 days was seen.

The group of rats treated with a fractionated radiotherapy scheme showed a slightly later, but stronger decrease in IS and Cpeak early post-treatment, again without substantial changes in TTP. However, a very strong increase in all ADC values (ADClow, ADChigh and ADCavg) occurred in the first 10 days after the start of radiotherapy. In this group a growth delay of 18 days was observed. The similar response found in ADChigh and ADClow indicates that the effect of the fractionated radiation treatment in this tumor model is both at the level of the vasculature as well as the individual tumor cells directly.







Conclusion:

The combined use of DW-MRI and DCE-MRI was used to show early intratumoral changes induced by radiotherapy, comparing single dose and fractionated irradiation of rat rhabdomyosarcoma. The single dose radiotherapy seems to induce a strong immediate perfusion decrease, but the induced necrosis, as well as the tumor growth delay, is limited. The fractionated radiotherapy scheme resulted in a similar perfusion decrease, but induces more intratumoral necrosis (indicated by the ADC increase) and a longer tumor growth delay. The results furthermore suggest the potential of combining DCE- and DW-MRI for the prediction of tumor regrowth.