

Monitoring the Effect of a Vascular Targeting Agent on Rhabdomyosarcomas in Rats by Diffusion-Weighted MRI.

H. C. Thoeny^{1,2}, F. De Keyzer¹, F. Chen^{1,3}, Y. Ni¹, R. R. Peeters¹, E. K. Verbeken⁴, H. Bosmans¹, G. Marchal¹, W. Landuyt⁵, R. Hermans¹

¹Radiology, University Hospitals Leuven, Leuven, Belgium, ²Diagnostic Radiology, University & Inselspital Berne, Berne, Switzerland, ³Radiology, Zhong Da Hospital, Nanjing, China, People's Republic of, ⁴Pathology, University Hospitals Leuven, Leuven, Belgium, ⁵Experimental Radiobiology/LEO, University Hospitals Leuven, Leuven, Belgium

Introduction:

Vascular targeting agents act selectively on preexisting blood vessels of solid tumors causing a rapid shutdown in the blood supply^{1,2}. Intratumoral changes after this kind of treatment are important to recognize, as in contrast to other anticancer therapies such as cytotoxic agents and irradiation, a decrease in tumor volume is not an expected treatment response³. In this work, the potential value of diffusion-weighted MRI (DW-MRI) was compared to conventional spin-echo imaging for monitoring tumor response in rats after administration of a vascular targeting agent.

Material and Methods:

Thirty-four rhabdomyosarcomas implanted subcutaneously in both flanks of seventeen rats were evaluated with a 1.5T MR unit using a 4-channel wrist coil. All sequences were obtained with a GRAPPA-factor of 2. Axial T2-weighted turbo spin-echo (TR/TE = 5860/99 ms), T1-weighted spin-echo (TR/TE = 553/15 ms) sequences (before and after Gd-application) and echo-planar DW-MRI (TR/TE = 3300/124 ms, voxel size 1.4x1.0x2.0 mm, 4 averages) were performed before, 1 and 6 hours as well as 2 and 9 days after intraperitoneal injection of a vascular targeting agent (Combretastatin A-4 phosphate, CA-4-P, OXiGENE, Watertown, MA; 25mg/kg). The apparent diffusion coefficient (ADC) was automatically calculated from the DW-MRI. These findings were correlated with histopathology at each time point.

Results:

The T1-weighted images (Fig) before CA-4-P administration showed enhancement of the solid tumor tissue but not of the central necrosis; early (1 and 6 hours) after CA-4-P injection the enhancement of the solid tissue disappeared almost completely with the exception of a small peripheral rim. Later, at 2 and 9 days, enhancement progressively reappeared in the tumor periphery. The ADC (Fig) however, showed a decrease early after CA-4-P injection, histologically corresponding to vessel congestion and vascular shutdown in the periphery but no necrosis. Later an increase of ADC was paralleled by histologically proven progressive necrosis. A significant decrease in ADC nine days after treatment corresponded to regrowth of the tumor.

Discussion:

DW-MRI allows to assess intratumoral changes noninvasively after administration of a vascular targeting agent. In contrast to conventional MRI, DW-MRI provides more accurate information for differentiating between viable and necrotic tumor tissue after administration of a vascular targeting agent. Therefore, it is a promising tool for monitoring the effects of tumor blood vessel-directed agents. Improved tumor tissue characterization would be a better guide to the management of patients with malignant tumors. It could potentially predict treatment outcome and help to make decisions about different treatment options.

References:

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