Comparison of Diffusion-weighted with Necrosis Avid Contrast Agent –enhanced MRI for the Assessment of Spontaneously Developed Necrosis in a Rat Rhabdomyosarcoma Model

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Introduction:

When treating tumors with chemo- or radiotherapy, one of the main indications of treatment response is the formation of tumor cell death and necrosis. A larger induction of necrosis usually corresponds to a better response to therapy. For this reason, accurate *in vivo* delineation and quantification of necrosis is important for therapeutic assessment. The current study examines the correlation between two noninvasive necrosis detection techniques, namely diffusion-weighted (DW-) and necrosis avid contrast agent –enhanced (NACA-) magnetic resonance imaging (MRI) for quantification of spontaneous necrosis in a rat rhabdomyosarcoma model.

Material and Methods:

Four male WAG/Rij rats with bilateral subcutaneous rhabdomyosarcoma in the flanks (n=8 tumors) underwent a first 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 (TSE) sequences and a diffusion-weighted spin-echo echo-planar sequence using a large range of b-values (between 0 and 1000 s/mm^2). In order to reduce susceptibility artifacts during the MRI examination and improve reproducibility of the positioning, the anesthetized rats were placed in a mold (Fig 1, *). After the MRI scan, a dose of 0.05 mmol/kg of NACA (bis-Gd-DTPA-pamoic acid derivative, ECIII-60) was administered using an intravenous injection. Twenty-four hours later, the rats underwent a second MRI scan with identical sequences. On the latter T1-weighted TSE sequences, regions of interest (ROIs) were placed on each tumor covering (a) the entire tumor and (b) the NACA enhanced volume. The necrotic fraction of the tumor was then calculated as the ratio (in percentages) of the pixel counts of the necrotic area and the entire tumor volume. From the DW-MRI images, an apparent diffusion coefficient (ADC) map was calculated, on which the same delineations were performed yielding a second quantification of the necrotic fraction.

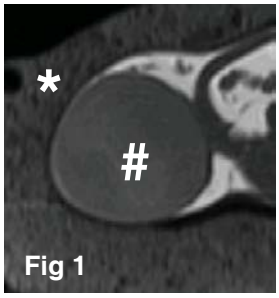


Fig 1

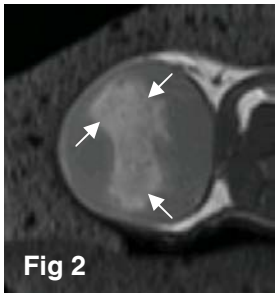


Fig 2

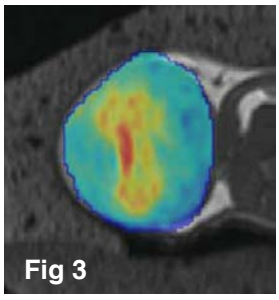


Fig 3

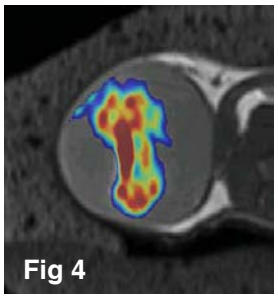
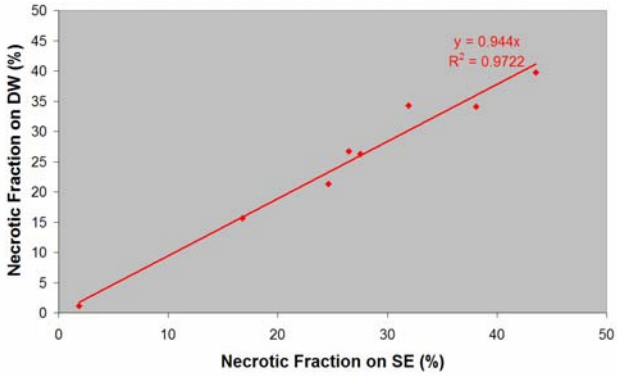


Fig 4

Results:

Figure 1 shows a T1-weighted TSE image of a randomly chosen tumor displaying a rather homogeneous mass (#). One day after the injection of NACA, the same sequence shows this tumor with a large region of enhancement (Fig 2, arrows), indicative of necrosis. The superposed ADC map shows a similar area with a high ADC value surrounded by low-ADC tumoral tissue (Fig 3). Using a threshold of 150 mm^2/s, the ADC map closely approximates the NACA-enhanced area (Fig 4). Plotting the necrotic fraction on the T1-weighted TSE versus the DW-MRI images (Graph), a significant correlation can be found ($p<0.001$), with a slight, non-significant, lower value on DW-MRI as compared to the TSE images.



Conclusion:

Both necrosis avid contrast agent –enhanced and diffusion-weighted MRI show spontaneous necrosis in a rat rhabdomyosarcoma model, with high agreement on necrotic fraction between the two different methods. This correlation holds true over a large range of necrotic fractions (in the current study between 2% and 45%). The current results indicate that both techniques could be used interchangeably according to subject agreement and time constraints.