Assessment of preconditioning on LNCaP tumors by a TNF-α nanoparticle construct using MRI

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The outcome of systemic and local therapies (e.g., chemotherapy, radiotherapy, surgery, focal ablation) for prostate cancer can be significantly improved by using tumor-specific adjuvants prior to treatment (“preconditioning”). We propose to use dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) to monitor the in vivo response of a mouse model of prostate cancer treated with a vascular disruptive agent, TNF-α, delivered on a gold nanoparticle (NP-TNF). Six male nude mice bearing 4-5 weeks old LNCaP tumors were scanned at 9.4T. DCE-MRI was performed two days before and 4-5 hours after treatment with NP-TNF. An intraperitoneal bolus of Gadolinium-DTPA (Gd) was administered and contrast enhancement was measured for 90 minutes. Concentration time curves of Gd were calculated and the area under the Gd curve (AUGC) was determined pre and post treatment. NP-TNF treatment caused an increase in contrast uptake in tumors. Interestingly, the early concentration (10 minutes post Gd bolus i.p.) was similar in both untreated and treated conditions; however, 90 minutes after injection, [Gd] was 3.4 times higher after treatment compared to before. AUGC doubled from 11 ± 6 [Gd] × min before treatment to 22 ± 9 [Gd] × min after treatment. An increase in signal enhancement was also observed in the muscle but to a lesser degree. We also evaluated the kinetics of intravenous gadolinium administration in mice bearing a jugular vein catheter to mimic the delivery method used in clinical trials. The overall treatment effects were independent of the delivery pathway of the contrast agent. In conclusion, we show that DCE-MRI is suitable to detect changes associated with a vascular disruptive agent in a mouse model of prostate cancer. The ability to characterize the effects of nanoparticle therapy in vivo with non-destructive methods is important as such compounds, in combination with treatment strategies, progress towards clinical trials.