

## S10-5 Tumor permeability of nanocarriers observed by dynamic contrast-enhanced MRI

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The structure of tumor vasculature is crucial for the nanocarrier-mediated chemotherapy. Recently, transforming growth factor- $\beta$  (TGF- $\beta$ ) inhibitor was reported to increase the tumor accumulation of nanocarriers by changing the structure of tumor vasculature. To identify the parameters of tumor vasculature function following TGF- $\beta$  inhibitor (A-83-01) treatment, dynamic contrast-enhanced MRI (DCE-MRI) was performed using Gd-DTPA and its liposomal formulation (Gd-L) as contrast agents. Observation of tumor MR image before, during, and after injection of contrast agent could calculate the parameters of vascular function, such as volume transfer constant between blood plasma and extracellular space ( $K^{\text{trans}}$ ) and fractional plasma volume ( $v_p$ ). A-83-01 treatment significantly increased these parameters within 24 h, that was positively related to pericyte coverage and tumor cell proliferation. Furthermore, apparent diffusion coefficient (ADC) determined by diffusion-weighted imaging was decreased by A-83-01 treatment, suggesting the decrease of tumor interstitial fluid pressure. Vascular function of the tumor improved by A-83-01 treatment well assessed on post-Gd-L-enhanced MR images, which predicted delivery of liposomal drug to the tumor. These findings suggest that DCE-MRI and, in particular,  $K^{\text{trans}}$  and  $v_p$  quantitation, provide important additional information about tumor vasculature by A-83-01 treatment.