

Assessment and monitoring tumor vascularity with contrast-enhanced ultrasound maximum intensity persistence imaging

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OBJECTIVES

Contrast-enhanced ultrasound imaging is increasingly being used in the clinic for assessment of tissue vascularity. The purpose of our study was to evaluate the effect of different contrast administration parameters on the in vivo ultrasound imaging signal in tumor-bearing mice using a maximum intensity persistence (MIP) algorithm and to evaluate the reliability of in vivo MIP imaging in assessing tumor vascularity. The potential of in vivo MIP imaging for monitoring tumor vascularity during antiangiogenic cancer treatment was further evaluated.

MATERIALS AND METHODS

In intraindividual experiments, varying contrast microbubble concentrations (5×10^5 , 5×10^6 , 5×10^7 , 5×10^8 microbubbles in 100 μ L saline) and contrast injection rates (0.6, 1.2, and 2.4 mL/min) in subcutaneous tumor-bearing mice were applied and their effects on in vivo contrast-enhanced ultrasound MIP imaging plateau values were obtained using a dedicated small animal ultrasound imaging system (40 MHz). Reliability of MIP ultrasound imaging was tested following 2 injections of the same microbubble concentration (5×10^7 microbubbles at 1.2 mL/min) in the same tumors. In mice with subcutaneous human colon cancer xenografts, longitudinal contrast-enhanced ultrasound MIP imaging plateau values (baseline and at 48 hours) were compared between mice with and without antiangiogenic treatment (antivascular endothelial growth factor antibody). Ex vivo CD31 immunostaining of tumor tissue was used to correlate in vivo MIP imaging plateau values with microvessel density analysis.

RESULTS

In vivo MIP imaging plateau values correlated significantly ($P = 0.001$) with contrast microbubble doses. At 3 different injection rates of 0.6, 1.2, and 2.4 mL/min, MIP imaging plateau values did not change significantly ($P = 0.61$). Following 2 injections with the same microbubble dose and injection rate, MIP imaging plateau values were obtained with high reliability with an intraclass correlation coefficient of 0.82 (95% confidence interval: 0.64, 0.94). In

addition, in vivo MIP imaging plateau values significantly correlated ($P = 0.01$; $R^2 = 0.77$) with ex vivo microvessel density analysis. Tumor volumes in treated and nontreated mice did not change significantly ($P = 0.22$) within 48 hours. In contrast, the change of in vivo MIP imaging plateau values from baseline to 48 hours was significantly different ($P = 0.01$) in treated versus nontreated mice.

CONCLUSIONS

Contrast-enhanced ultrasound MIP imaging allows reliable assessment of tumor vascularity and monitoring of antiangiogenic cancer therapy in vivo, provided that a constant microbubble dose is administered.

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