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Monitoring sunitinib-induced vascular effects to optimize radiotherapy combined with soy isoflavones in murine xenograft tumor.

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Abstract: Using dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) to monitor vascular changes induced by sunitinib within a murine xenograft kidney tumor, we previously determined a dose that caused only partial destruction of blood vessels leading to "normalization" of tumor vasculature and improved blood flow. In the current study, kidney tumors were treated with this dose of sunitinib to modify the tumor microenvironment and enhance the effect of kidney tumor irradiation. The addition of soy isoflavones to this combined antiangiogenic and radiotherapy approach was investigated based on our studies demonstrating that soy isoflavones can potentiate the radiation effect on the tumors and act as antioxidants to protect normal tissues from treatment-induced toxicity. DCE-MRI was used to monitor vascular changes induced by sunitinib and schedule radiation when the uptake and washout of the contrast agent indicated regularization of blood flow. The combination of sunitinib with tumor irradiation and soy isoflavones significantly inhibited the growth and invasion of established kidney tumors and caused marked aberrations in the morphology of residual tumor cells. DCE-MRI studies demonstrated that the three modalities, sunitinib, radiation, and soy isoflavones, also exerted antiangiogenic effects resulting in increased uptake and clearance of the contrast agent. Interestingly, DCE-MRI and histologic observations of the normal contralateral kidneys suggest that soy could protect the vasculature of normal tissue from the adverse effects of sunitinib. An antiangiogenic approach that only partially destroys inefficient vessels could potentially increase the efficacy and delivery of cytotoxic therapies and radiotherapy for unresectable primary renal cell carcinoma tumors and metastatic disease.