

ACOUSTICS2008/277
Ultrasound contrast imaging of angiogenesis in a murine tumor model

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Microvascularization modifications should precede tumor size-changes during anti-angiogenic therapy. We applied contrast functional ultrasound imaging (fUSI) to detect changes in Wilms tumors with anti-angiogenic treatment (Bevacizumab). Human Wilms tumor cells were grafted in left kidney of 32 mice. Once tumors had >5mm diameter, mice received : placebo, N=14; Bevacizumab for 21days, N=11; and Bevacizumab for 10days followed by placebo for 11days, N = 7. On days -1, +1, +9, +14 and +21 with respect to treatment start, fUSI was performed (CPS mode, SonoVue). Linear time intensity curves were obtained from regions in kidney cortex and matched-depth of tumor for first bolus passage and 50s following acoustic destruction of contrast. Excised tumor weight decreased with increased treatment duration: 3.7+/-1.8 g (placebo), 2.3+/-1.9 g (Bevacizumab-10days, placebo-11days), 1.4+/-0.7 g (Bevacizumab-21 days) [p<0.05]. Area under the bolus-passage curve (AUC) and the plateau intensity of the destruction-reperfusion were greater from D+9 to D+21 [p<0.04] in the placebo than Bevacizumab-21day. For the group treated during the first 10 days, fUSI values were comparable to those of the treated group until D+14, then increased to become slightly superior to those of the placebo group by D+21. Noninvasive fUSI demonstrated revascularization after suspension of anti-VEGF therapy.