Dokumenttyp: journal article

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Titel des Beitrags:
Model Matters: Differences in Orthotopic Rat Hepatocellular Carcinoma Physiology Determine Therapy Response to Sorafenib.

Abstract:
Preclinical model systems should faithfully reflect the complexity of the human pathology. In hepatocellular carcinoma (HCC), the tumor vasculature is of particular interest in diagnosis and therapy. By comparing two commonly applied preclinical model systems, diethylnitrosamine induced (DEN) and orthotopically implanted (McA) rat HCC, we aimed to measure tumor biology noninvasively and identify differences between the models. DEN and McA tumor development was monitored by MRI and PET. A slice-based correlation of imaging and histopathology was performed. Array CGH analyses were applied to determine genetic heterogeneity. Therapy response to sorafenib was tested in DEN and McA tumors. Histologically and biochemically confirmed liver damage resulted in increased (18)F-fluorodeoxyglucose (FDG) PET uptake and perfusion in DEN animals only. DEN tumors exhibited G1-3 grading compared with uniform G3 grading of McA tumors. Array comparative genomic hybridization revealed a highly variable chromosomal aberration pattern in DEN tumors. Heterogeneity of DEN
tumors was reflected in more variable imaging parameter values. DEN tumors exhibited lower mean
growth rates and FDG uptake and higher diffusion and perfusion values compared with McA tumors.
To test the significance of these differences, the multikinase inhibitor sorafenib was administered,
resulting in reduced volume growth kinetics and perfusion in the DEN group only. This work depicts
the feasibility and importance of in-depth preclinical tumor model characterization and suggests the
DEN model as a promising model system of multifocal nodular HCC in future therapy studies.