

Monitoring Tumor Cellular and Tissue Response to Photodynamic Therapy by Choline PET imaging and Diffusion-weighted MRI

Baowei Fei, Hesheng Wang, Chunying Wu, Song-mao Chiu, Nancy Edgehouse

Department of Radiology, Emory University, Atlanta, GA

Email: bfei@emory.edu

This study is to develop multimodality imaging (PET/MRI) as an early biomarker for monitoring tumor response to photodynamic therapy (PDT) at the cellular and tissue levels.

Methods: A human prostate cancer cell line (CWR22) was used to generate tumors in athymic nude mice. A second-generation photosensitizing drug Pc 4 (0.6 mg/kg body weight) was delivered to each animal by tail vein injection 48 h before laser illumination (672 nm, 100 mW/cm², 150 J/cm²). For Group I (N=5), dynamic microPET images with ¹¹C-choline were acquired from each mouse pre-PDT and 24 h and 48 h after PDT. For Group II (N=18), diffusion-weighted MR images were acquired pre- and post-PDT, 24 h, and/or 7 d after PDT. Apparent diffusion coefficient (ADC) maps were obtained and analyzed for each tumor. Prostate specific antigen (PSA) levels were measured 1 d before PDT and 24 h and 7 d after PDT.

Results: The PSA values decreased by 30.3% and 64.1% 24 h and 7 d after PDT, respectively, indicating the treatment effect. For Group I, the choline uptakes dramatically decreased 24 h (75.5%) and 48 h (43.5%) after PDT, compared to those pre-PDT. Histologic analysis showed that PDT-treated tumors demonstrated apoptosis, necrosis and inflammation. For Group II, ADC values significantly increased (47.5%) 24 h after PDT. In four mice, the ADC histogram demonstrated a biphasic response 7 d after PDT, *i.e.* some tissue within the tumor had increased ADC values and other maintained approximately the same values as those before treatment. On MR images, tumor tissue was automatically classified into two tissue types (necrotic and viable), which were well correlated (R=89%) with tissue quantification from histology. The changes in choline uptake and ADC values are consistent with the PSA levels.

Conclusions: Changes in tumor choline uptake detected by PET imaging can determine whether or not the tumor responds the therapy within 48 h after PDT. Diffusion-weighted MR imaging can detect and quantify viable and necrotic tumor tissue within one week after the treatment. The noninvasive imaging techniques can provide an assay that could be useful for clinical monitoring of photodynamic therapy at an early stage (1-7 days).

Research Support: This work was supported by NIH grant R21CA120536 (PI: Fei).