**Purpose:** To explore the basis for quantitative in-vivo tumor imaging during radiation therapy with the aim to adaptively modify the treatment according to the response.

**Method and Materials:** Two positron emission tomography (PET) imaging agents were used to assess the response. Fluorodeoxygluocose (<sup>18</sup>F-FDG), a metabolic marker, is not ideal agent for monitoring tumor tissue response, because increased metabolism in response to radiotherapy due to inflammatory cells. 3'-deoxy-fluorothymidine (<sup>18</sup>F-FLT) has recently been proposed as a marker for imaging tumor proliferation. Several canine subjects with recurrent soft tissue sarcomas were repeatedly imaged with PET/CT before, during and after the radiation treatment. The tumors were treated with <sup>60</sup>Co with one or two fractions of 8Gy. Approximately 200 MBq of FDG/FLT activity was administered per scan. Standard uptake values (SUV) were calculated to evaluate uptake in the tumor region, as well as in the surrounding organs. The CT data between the imaging sessions was co-registered and PET data compared.

**Results:** Tumor response to therapy varied significantly between the subjects. High heterogeneity (up to 50%) of the tumor was observed in some of the cases. Early post treatment scans (3 days) showed already significant decrease in FLT uptake, followed by an increase 6 days after the treatment due to accelerated repopulation. Severe redistribution of the tumor proliferation potential was observed during the treatment. In the follow-up study 6-weeks post-treatment both, FDG and FLT PET showed low uptake in the tumor region (SUV=1.9 vs. SUV=1.0) with the slightly elevated FDG uptake on the periphery of the tumor.

**Conclusions:** FLT proved to be a better treatment response monitoring agent than FDG. High heterogeneity of the proliferation activity, as well as redistribution of the proliferation potential indicates strong potential for treatment adaptation as well as potential problems with treatment planning.