Purpose: Tumors are known to be heterogeneous but it is unclear whether and how heterogeneity changes throughout therapy. The purpose of this work was to quantitatively assess proliferative heterogeneity over time course of treatment.

Method and Materials: Tumor heterogeneity and its temporal development were investigated for patients undergoing either radiotherapy or chemotherapy. Six radiotherapy patients were imaged prior to radiation therapy and 2-3 weeks after the first scan while receiving treatment. Four chemotherapy patients were imaged with FLT-PET prior to treatment, during Sunitinib malate therapy (week 4) and during withdrawal (week 6). Spatial statistics were used to assess proliferative heterogeneity over tumor volume. Global Moran I statistics with inverse distance weighting were used to estimate the overall degree of spatial autocorrelation in cell proliferation. Proliferation clusters were visualized using local G statistics, which identified local regions of strong autocorrelation.

Results: No significant changes in tumor heterogeneity during radiation therapy were seen, with the mean change in Moran I throughout treatment of only -2.5±6.9 %. On the contrary, chemotherapy patients showed changes in tumor heterogeneity over the time course of treatment. Moran I changed by -14.5±3.7 % from pre-treatment to week 4 and 13.0±8.1 % from week 4 to week 6. The correlation coefficient between chemotherapy response and change in Moran I from pre-treatment to week 4 was 0.75. On the other hand, no strong correlation between the initial heterogeneity and response to treatment was observed.

Conclusion: Results showed that spatial statistics successfully provide a measure of tumor heterogeneity and its changes over the course of treatment. The heterogeneity changes depend upon treatment type and response to treatment.