Purpose: The integration of molecular therapies into chemoradiation treatments has motivated improved tools for treatment assessment. We used hypoxia, proliferation, and perfusion imaging techniques for multimodality response assessment in patients receiving combined therapy.

Methods: Ten HNSCC patients received anti-angiogenic therapy (Avastin). After three weeks, patients began chemoradiation and continued Avastin. Patients were imaged at baseline, after Avastin monotherapy, and during combined therapy. Imaging modalities were CuATSM-PET (tumor hypoxia), FLT-PET (proliferation), dynamic FLT-PET (FLT kinetics) and dynamic contrast-enhanced CT (perfusion). Mean SUV was calculated from PET data and dynamic FLT data were analyzed for kinetics with a two-compartment, four-parameter model. DCE-CT data were analyzed with GE Advantage software. Paired t-tests were used to evaluate tumor response and mean imaging values were correlated with Pearson's R.

Results: After Avastin monotherapy, significant decreases were measured in CuATSM_SUV ($p=0.05$), FLT_SUV ($p<0.01$), FLT_Ki ($p<0.01$), and CT_Enhancement ($p<0.01$). During combined therapy, further decreases were measured in CuATSM_SUV and FLT_SUV ($p=0.05$, $p<0.001$). Across the study, significant correlations were found between CuATSM_SUV and CT_BloodVolume ($R=0.72$), CT_BloodFlow ($R=0.59$), and FLT_K1 ($R=0.53$). Additionally, FLT_Ki was significantly correlated to FLT_SUV ($R=0.80$) and CT_Enhancement ($R=0.50$).

Conclusions: Multimodality imaging has been used to identify clinically relevant tumor characteristics over the course of therapy. Significant decrease in tumor proliferation suggests effective combination of Avastin and chemoradiotherapy, and FLT imaging endpoints could potentially be used to optimize combined therapy. Decrease in hypoxia was also measured, and given the established prognostic value of hypoxia, mid-therapy hypoxic status is another potential therapeutic endpoint. Decrease in CT_Enhancement after Avastin may indicate reduction in vascular permeability, and correlation between CuATSM_SUV and perfusion-related parameters such as FLT_K1, CT_BloodVolume, and CT_BloodFlow suggests further importance of vascular status in effectiveness of combined therapies. As outcome data becomes available, these imaging biomarkers could eventually be used to personalize delivery of combined therapy.

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