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Abstract

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18F-FMISO PET/CT Visualization of Tumor Hypoxia in Patients With Chordoma of the Mobile and Sacrococcygeal Spine

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Purpose/Objective(s): Local recurrence rates in reported series of chordoma patients following treatment with surgery ± radiation therapy (RT) or definitive RT are high. Tumor hypoxia is associated with radioresistance and local recurrence in animal models and human patients. [¹⁸F] fluoromisonidazole positron emission tomography/computed tomography (FMISO-PET/CT) has been used to visualize hypoxic sub-volumes (HSV) in skull base chordoma and the feasibility of its use in RT dose-escalation has been demonstrated in head and neck cancer. The feasibility of FMISOPET/CT use for detection of targetable HSVs in patients with chordoma of the mobile and sacrococcygeal spine is unknown and investigated in the current study.

Materials/Methods: A prospective, pilot study of 20 patients with primary or locally recurrent chordoma of the mobile or sacrococcygeal spine treated with proton or combined proton/photon RT ± surgery was completed. FMISO-PET/CT was performed prior to RT and again after 19.8-34.2 GyRBE (relative biologic effectiveness). Gross tumor volumes were delineated and HSVs defined including all voxels with a standardized uptake value (SUV) ≥ 1.4 times the mean muscle SUV. The pre-specified threshold for FMISO-PET/CT feasibility was positive tracer uptake in 4/20 patients. Distributions of clinical characteristics and treatments received were compared between patients with and without HSVs. Treatment outcomes are reported.

Results: FMISO-PET/CT detected HSVs in 12 (60%; 12/20) patients, 8 of which were of sufficient size (≥ 5 cc) to potentially allow for delivery of an intensity modulated proton therapy boost. Patients with HSVs had significantly larger gross tumor volumes (median = 410.0 cc vs 63.4 cc; p = 0.02) and were significantly more likely to have stage T2 tumors (5/12 vs 0/8; p = 0.04) compared to those without HSVs. After a median followup of 1.8 years (range: 0.2-4.4), a local recurrence has yet to be observed. Three patients developed metastatic disease, 2 of whom had HSVs.

Conclusions: FMISO-PET/CT is feasible for detection of targetable HSVs within patients undergoing RT ± surgery for treatment of chordoma of the mobile and sacrococcygeal spine. Further study of its application in hypoxia-directed, dose-escalated RT, particularly in patients at high risk for local recurrence, is warranted.