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Matthew D. Cheney

Harvard Medical School, Boston

Yen-Lin Chen

Massachusetts General Hospital

Ruth Lim

Massachusetts General Hospital

Barbara K. Winrich

Massachusetts General Hospital

Anca L. Grosu

Massachusetts General Hospital

See next page for additional authors

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Abstract

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Authors

Matthew D. Cheney, Yen-Lin Chen, Ruth Lim, Barbara K. Winrich, Anca L. Grosu, Alexei V. Trofimov, Nicolas Depauw, Helen A. Shih, Joseph H. Schwab, Francis J. Hornicek, and Thomas F. Delaney

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

M.D. Cheney,¹ Y. Chen,² R. Lim,² B.K. Winrich,² A.L. Grosu,² A.V. Trofimov,² N. Depauw,^{2,3} H.A. Shih,² J.H. Schwab,² F.J. Hornicek,² and T.F. DeLaney²;

¹Harvard Radiation Oncology Program, Boston, MA, ²Massachusetts General Hospital, Boston, MA,

³University of Wollongong, Wollongong, Australia

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.