Grade 3 toxicities included visual disturbance, cataract, facial disfigurement, chronic sinusitis/otitis, and hearing loss. Severe facial disfigurement was noted in 8 (29%) patients, and 2 patients underwent subsequent cosmetic surgery. Patients with severe facial disfigurement were treated at younger ages (median 5.2 years versus 7.8 years for patients with no or non-severe facial disfigurement) and were more likely to have infratemporal fossa tumors. Three patients (12%) had grade 1 neurocognitive dysfunction. Two patients exhibited decreased processing speed with no special education requirements and one patient, whose past medical history was also complicated by epidual hematoma requiring craniotomy, exhibited slowed processing speed and weakness in memory retrieval. There were no secondary solid malignancies but two patients (7.4%) developed secondary acute myeloid leukemia (grade 4), presumably secondary to chemotherapy.

Conclusion: Late radiation toxicities are commonly seen in pediatric RMS survivors treated with IMRT to the head and neck. The majority of late effects are mild-moderate in severity; however, they can significantly impact quality of life. Facial disfigurement was the most devastating late effect of IMRT, especially in younger children with infratemporal fossa tumors. Future research efforts are needed to minimize this problem. These data on late effects with IMRT for head and neck RMS will be useful for comparison to proton therapy data which will soon mature.


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Predicting Secondary Breast and Lung Malignancy Risk After Combined Chemoradiation Treatment
C. Grassberger,1 V. Manem,2,3 B.R. Eaton,1 T.I. Yock,1 and H. Paganetti1,4
1Massachusetts General Hospital, Boston, MA. 2Princess Margaret Hospital, Toronto, ON, Canada. 3Massachusetts General Hospital, Harvard Medical School, Boston, MA.

Purpose/Objective(s): Predict the secondary cancer risk of breast and lung cancer stemming from different treatment regimens used in the treatment of childhood cancers. The aim is to provide a framework based on clinical data that helps personalize therapy for high-risk patients and to design trials aimed on minimizing these late toxicities.

Materials/Methods: A well-known framework, the initiation-inactivation-proliferation formalism, was used to model the secondary cancer induction from chemotherapy only and radiation therapy only. The parameters are based on published clinical data of >17 000 patients. The resulting model was further applied to combined chemoradiation regimens currently in use and under investigation in clinical trials.

Results: The application of the model to combined chemoradiation regimens revealed that there is no interaction between chemotherapy and radiation regarding secondary cancer induction in breast and lung. This agrees with published secondary malignancy data for combination regimens used in all. Toxicity was assessed with CTCAE 4.0. Local control (LC) was defined as patients without clinical or radiographic evidence of progression from end of treatment.

Conclusion: The model enhances the understanding of the impact of timing and dosing in treatment regimens on secondary cancer induction in breast and lung. It could serve as a tool to design clinical trials aimed at minimizing these toxicities, or provide guidelines in the treatment of rare tumors and high-risk patients.


3271
WITHDRAWN

3272
Acute Toxicity and Local Control in Pediatric Cancers Treated With Stereotactic Body Radiation Therapy (SBRT)
N.K. Taunk, and S.L. Wolden: Memorial Sloan Kettering Cancer Center, New York, NY

Purpose/Objective(s): Pediatric cancers often respond to conventionally fractionated RT, but some are inherently radioresistant and others resistant after extensive therapy. Stereotactic body radiation therapy has emerged as an effective tool in ablating relatively radioresistant tumors in adults, particularly recurrent or metastatic tumors. Interest in SBRT for pediatric tumors is growing rapidly. It is now included in Children’s Oncology Group (COG) protocols; yet, safety and efficacy are not yet established. Here, we reported toxicity and control data in recurrent and metastatic pediatric tumors.

Materials/Methods: Patients from 2011-15 with pediatric tumors treated with SBRT were included. Indication for SBRT was progression of previously irradiated tumor in 12 cases and treatment for oligometastases of Ewing sarcoma or pheochromocytoma in eight cases. Stereotactic body radiation therapy was defined as hypofractionated, intensity modulated, high-dose per fraction RT in ≤5 fractions, daily cone beam CT (CBCT), custom immobilization, and small margins (<3 mm); 6MV photons were used in all. Toxicity was assessed with CTCAE 4.0. Local control (LC) was defined as patients without clinical or radiographic evidence of progression from end of treatment.

Results: Included were 20 lesions in 15 patients with neuroblastoma (9), Ewing sarcoma (7), rhabdomyosarcoma (2), osteosarcoma (1), or pheochromocytoma (1). Median age at treatment was 17 years (range 4-31). There were 19 metastatic and 1 primary lesions. All lesions were osseous. Twelve of 20 were previously irradiated to doses of 21Gy-79.2Gy in 10-44 fractions. Median clinical follow-up after SBRT was 22 (range 1-33) months. Local control for the entire cohort was 75%; 4 of the 5 failures had prior conventional RT. Median interval between conventional RT and SBRT was 34 (range 3-152) months. Total SBRT dose ranged from 20Gy-40Gy, in 3 to 5 fractions (median 27Gy in 3 fractions). Common toxicities were grade 1 dermatitis (45%) and fatigue (40%). Both patients treated in the thoracic spine experienced Grade 1 esophagitis. Crude grade 3 toxicity was 15%. A 4 year old patient with neuroblastoma experienced extremely painful, grade 3 myositis one month after 27Gy to the right scapula and left distal femur. Both sites received 30Gy in 10 fractions within the previous 6 months. The patient with sacrum osteosarcoma experienced grade 3 neuropathy after 30Gy in 3 fractions; SBRT was 6 months after initial 79.2CGE fractionated proton RT.

Conclusion: Stereotactic body radiation therapy is effective in managing bone lesions in pediatric cancers, particularly in the re-irradiation setting. Local control is excellent. Further follow-up and study is required to
determine if the risk of significant (grade 3) toxicity increases with higher biologically equivalent dose (e.g., 9-10Gy x 3), short interval re-irradiation, and young age. Careful patient selection and long-term toxicity monitoring is absolutely necessary to further explore SBRT in pediatric tumors.

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3273
Predisposing Factors for Short Stature in Long-term Survivors of High-Risk Neuroblastoma

Purpose/Objective(s): Survivors of high-risk neuroblastoma who received abdominal radiation (RT) are at risk for short stature. These prepubertal children received multi-modality therapy, which included chemotherapy, surgery, immunotherapy, isotretinoin, and autologous stem cell transplant (SCT), but predisposing factors for short stature other than RT have not been carefully analyzed.

Materials/Methods: This was a retrospective review of long-term neuroblastoma survivors treated with abdominal RT at our institution from 1984 through 2011. All patients were prepubertal at the time of treatment and postpubertal at follow-up. Patients treated with craniospinal or total body RT were not eligible. Data on final standing height, expressed as percentiles for national references, and sitting to standing height ratio were abstracted.

Results: A total of 42 patients (20 males > 15 years; 22 females > 13 years) diagnosed at a median age of 2 years (range: 2 months-10 years) were analyzed. All patients had stage 4 disease and underwent chemotherapy, surgery, and RT with 10-36 Gy to the abdomen. Seventy-six percent of patients (n = 32) received 21 Gy in 14 twice-daily fractions. Twenty patients received RT to additional sites of disease, including 7 who received 21 Gy to the mediastinum and 5 patients who received 21-22 Gy to the orbit. Sixty percent of patients had short stature, which was defined as height below the 5th percentile: 60% of the immunotherapy group, 63% of the isotretinoin group, and 66% of the SCT group. All patients had a normal sitting to standing height ratio of 0.5. Patients who did not fit the strict definition of short stature had final heights in the 9th to 95th percentiles. In univariate analysis, there was no significant association between short stature and SCT (P = 0.27), isotretinoin (P = 0.76), or immunotherapy (P = 0.99) individually by Fisher exact test. Patients with short stature were more likely to have started treatment at a younger age (P = 0.048, Wilcoxon rank sum test). Two-thirds of all patients had x-rays to assess bone age; 93% of these patients had a normal bone age.

Conclusion: Though all included patients received abdominal RT, only half of these long-term, high-risk pediatric neuroblastoma survivors had short stature. The normal sitting to standing height ratios indicate that growth delays were global rather than limited to the torso where patients were irradiated. Patients who started treatment at a younger age were more likely to have short stature. Since no single treatment variable was associated with short stature, the role of abdominal RT cannot be ruled out. We believe that the cause of short stature among these survivors is likely multifactorial and a larger cohort would be needed to explore its etiology.


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Beam Edges and Safety: Correlation With Imaging Radiation Necrosis in Pediatric Brain Tumor Patients Treated With Proton Radiation Therapy
J. Buchsbaum, C. Haskins, W. Finke, S. Kralik, C. Ho, and C.S. Shih; Indiana University, Indianapolis, IN

Purpose/Objective(s): To test the hypothesis that beam edges are causative in imaging radiation necrosis (IRN) in pediatric brain tumor patients treated with proton radiation therapy where range modulation or feathering is being employed.

Materials/Methods: We performed a retrospective study of 55 pediatric patients with primary brain tumors who treated with proton radiation therapy. In addition to pediatric neuroradiologists assessing radiation necrosis by examining serial MRIs in conjunction with clinical records to determine the incidence, timing, risk factors, imaging patterns and clinical significance associated with development of radiation necrosis in these patients, we looked at beam edges and ends in our treatment planning system to see if beam components contributed to radiation necrosis in a uniform active scanning system. Imaging radiation necrosis was defined as areas of new enhancement with subsequent decrease on follow-up imaging without changes in chemotherapy within an anatomic region with previous exposure to proton beam therapy.

Results: Thirty-one percent developed IRN with a median time to development of IRN of 5.0 months (range 3-11). Full resolution on imaging median time was 5.3 months (range 3-12). Among the IRN patients, 25% demonstrated symptoms requiring medical intervention (7.5% of the total population). Multivariate analysis of age, conformal dose (focused portion of total dose), beam ends, beam edges, and intensive chemotherapy use (shown in our non-dosimetric review to be significant) revealed that only edge number (0 or 1 versus 2 to 6, P = 0.009) and conformal dose (continuous variable from 18 to 59.4 Gy, p = 0.035) were significant. In our cohort, 33 patients had no beams ending in the area of IRN and 22 had 1 to 6 beams ending in the area (defined as within 3mm). Beam ends were not significantly correlated with necrosis (P = 0.989) in the background of active clinical use of our published range modulation method.

Conclusion: Pediatric brain tumor patients treated with proton radiation therapy demonstrate a high incidence of IRN. Changes are correlated with beam edge number and conformal dose. The number of beam ends does not correlate with IRN when using a technique to feather the beam end in this context. It is possible that modulation of the beam edges in a similar fashion to how this data set modulates beam ends would help decrease overall IRN.


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Feasibility and Acute Toxicity of Supine Craniospinal Irradiation With Image Guided Volumetric Modulated Arc Therapy in Pediatric Patients
K. Wong,1 O.M. Ragab,2 A. Aguilar,3 N.G. Dholakia,4 and A.J. Olch3;1 Children’s Hospital Los Angeles / University of Southern California, Los Angeles, CA, 2LAC+USC Medical Center, Los Angeles, CA, 3Children’s Hospital Los Angeles, Los Angeles, CA, 4Children’s Hospital Los Angeles, Los Angeles, CA

Purpose/Objective(s): To evaluate the feasibility of craniospinal irradiation (CSI) with volumetric modulated arc therapy (VMAT) for treatment of pediatric patients with solid tumors presenting with disseminated or recurrent disease, treated with high-dose chemotherapy and autologous stem cell rescue (HD-AuSCR), or requiring anesthesia. Acute effects are assessed for tolerability.

Materials/Methods: From 2013 to 2015, we treated 19 patients with CSI in the supine position with custom head and spine immobilization; CSI doses were 18-23.4 Gy (n = 11) or 30.6-36 Gy (n = 8). The most common plan utilized 2 isocenters with 2 arcs covering the brain/upper spine and a partial arc for the mid-to-lower spine; a third isocenter was sometimes needed in taller patients to cover the lumbosacral spine.; QA was performed with a cylindrical detector array and ion chamber measurements at the arc junctions. All plans passed with 3% and 3mm thresholds. Daily CBCT and optical surface imaging was used. Radiation therapy data and acute toxicities were recorded.

Results: The median age at CSI was 11 years (range 3-17) with 13 boys and 6 girls. Patients had medulloblastoma or supratentorial primitive neuroectodermal tumor (n = 14, 11 high-risk), germ cell tumors (2), relapsed neuroblastoma (2), and an ATRT. Disease dissemination (M1-3)