

defined as ischemia, obstructive coronary disease, at least moderately severe valve disease, cardiac arrhythmias requiring mechanical intervention, and cardiomyopathy with LVEF <50%. Continuous variables were summarized by mean  $\pm$  standard deviation (SD). Categorical variables were reported as frequencies and percentages. Univariate logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

**Results:** A total of 182 HL survivors (59% female, mean age  $44.1 \pm 8.7$  yrs, follow-up time  $15.1 \pm 7.2$  years) were studied. Overall, 81% (148) have at least 1 modifiable CRF: 26% (48) had HTN, 55% (101) patients had hyperlipidemia, 20% (37) were obese and 43% (79) were physically inactive. Only 6% were current smokers. Seven percent (13) of patients (77% male, mean age  $48.1 \pm 6.1$  years, follow-up time  $19.1 \pm 8.0$  years) were found to have significant CVD. HTN (OR 3.6; 95% CI 1.6-11.5,  $p = 0.03$ ) and hyperlipidemia (OR, 4.8; 95% CI 1.04-22.4,  $p = 0.04$ ) were associated with significant screen-detected CVD.

**Conclusions:** This prospective screening study identified modifiable CRF in 81% of long-term HL survivors, with HTN and hyperlipidemia being significantly associated with risk for screen-detected CVD. Routine screening of modifiable CRF is prudent in long-term HL survivors treated with RT. Management of CRF, along with modern RT techniques and lower treatment doses, may result in reduced CVD risk for long-term HL survivors.

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## 2765 Predicted Risk of Radiation-Induced Cancers after Involved Field- and Involved-Node Radiotherapy with or without Intensity Modulation for Early Stage Hodgkin Lymphoma in Female Patients

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**Purpose/Objective(s):** To assess the excess relative risk (ERR) of radiation-induced cancers (RIC) in Hodgkin lymphoma (HL) female patients treated with 3D conformal (3DCRT), intensity modulated (IMRT) or volumetric modulated arc (RA) radiation therapy.

**Materials/Methods:** Plans for 10 early stage HL female patients were computed for 3DCRT, IMRT and RA with involved-field (IFRT) and involved-node (INRT) radiation fields. The organ at risks (OAR) Dose-Volume Histograms (DVHs) were computed and inter-compared for IFRT vs. INRT and 3DCRT vs. IMRT/RA, respectively. The excessive relative risk (ERR) for cancer induction in breasts, lungs and thyroid was estimated, using both linear and non-linear models.

**Results:** The mean estimated ERR for breast, lung and thyroid were significantly ( $p < 0.01$ ) lower with INRT than with IFRT planning, regardless of the radiation technique delivery used, assuming a linear dose-risk relationship. Using the non-linear model, mean ERR were significantly ( $p < 0.01$ ) increased with IMRT or RA when compared to 3DCRT planning for the breast, lung and thyroid using an IFRT paradigm. After INRT planning, IMRT or RA increased the risk of RIC for lung and thyroid only.

**Conclusions:** Regardless of the technique delivery, these data suggest that INRT when compared to IFRT planning may reduce the ERR of breast, lung and thyroid RIC for HL female patients, when risk is predicted using a linear model. A non-linear dose-risk relationship suggests that IMRT or RA increase the risk of RIC for these OARs.

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## 2766 Mid-treatment Metabolic Tumor Volume Predicts Progression and Death among Patients with Hodgkin's Disease

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**Purpose/Objective(s):** Considerable evidence has demonstrated the predictive value of positron emission tomography (PET) imaging using fluorodeoxyglucose in patients with lymphomas. We hypothesized that pre- and mid-treatment quantitative PET metrics may have increased predictive strength as compared to traditional clinical factors such as the International Prognostic Score (IPS).

**Materials/Methods:** Thirty pediatric and adult patients with Hodgkin's disease (HD) treated at presentation or relapse had initial staging and mid-treatment PET-CT scans. The majority of patients (53%) had stage III-IV disease and 67% had an IPS of 2 or greater. Mid-treatment scans were performed at a median of 55 days from the staging PET-CT, corresponding to 2 cycles of Stanford V chemotherapy. Hypermetabolic tumor regions were segmented semiautomatically on the pre-treatment scans using custom software and the metabolic tumor volume (MTV), mean standardized uptake value (SUVmean), maximum SUV (SUVmax) and integrated SUV (iSUV) were recorded. Mid-treatment scans were then registered to the corresponding pre-treatment scans and the identical regions interrogated. We analyzed whether IPS, PET parameters or the calculated ratio of mid- to pre-treatment PET parameters (e.g., mid-treatment MTV/pre-treatment MTV) were associated with differences in progression free survival (PFS) or overall survival (OS).

**Results:** At the time of this analysis, median follow-up of the study group was 50 months. Six of the 30 patients progressed clinically (defined as death, biopsy-proven recurrence or radiographic findings warranting a change in management). SUV parameters from pre-treatment scans were not significant. Two PET parameters from mid-treatment scans were significantly associated with OS as determined by Cox proportional hazards: MTV ( $p = 0.03$ ) and SUVmax (0.008). Two calculated PET

parameters were significantly associated with PFS: MTV ( $p = 0.008$ ) and iSUV ( $p = 0.01$ ). Three calculated SUV parameters were associated with OS: MTV ( $p = 0.005$ ), SUVmax ( $p = 0.046$ ) and iSUV ( $p = 0.007$ ). IPS was associated with PFS ( $p = 0.03$ ) and OS ( $p = 0.008$ ).

**Conclusions:** Calculated PET metrics may provide predictive information beyond that of traditional clinical factors. These findings suggest quantitative metrics as a means to identify patients at high risk of treatment failure, at a early time point when treatment intensification could be considered and may be useful in adaptive clinical trials of HD.

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## 2767 Preliminary Experience with Proton Radiotherapy in Mediastinal Lymphoma

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**Purpose/Objective(s):** Long-term cardiopulmonary toxicity and second malignancy risks of mediastinal radiation therapy are well recognized sequelae of lymphoma radiotherapy. Efforts to reduce dose to lungs, cardiac structures, spinal cord, and uninvolved tissue are needed. We report our early single institutional experience using proton radiotherapy in patients with bulky mediastinal Hodgkin's or non-Hodgkin's lymphoma.

**Materials/Methods:** Twenty patients with Hodgkin's lymphoma ( $n = 16$ ) or mediastinal DLBCL ( $n = 4$ ) underwent definitive or salvage involved field radiotherapy from 2006-2009. Indications for proton included prior mediastinal radiation ( $n = 2$ ) or bulky mediastinal disease involving pericardial, hilar, and/or subcarinal nodes ( $n = 18$ ). 3D conformal photon plans were generated and compared to proton plan for target coverage, organs at risk, and integral dose. We analyzed disease control as well as acute and subacute toxicities.

**Results:** Median age of patients was 30.5 years (16 to 62 years); 10 male and 10 female. In all patients, protons provided superior dosimetry compared to 3D conformal photon plans. Patients were treated with median dose of 36 GyE (proton RBE of 1 Gy photon) (25.5-39.6 Gy) at 1.5 to 1.8 Gy/fraction using either a single anterior beam and/or a superior anterior beam depending on the curvature of the anterior thorax contours. Proton plans provided an average reduction of mean lung dose reduction by 52% and V20 reduction by 49%. Right coronary artery dose did not reduce significantly with protons due to proximity to precardial target volumes; however, left coronary artery dose significantly decreased by 30 to 90% (mean dose 12 Gy) and left ventricle dose reduction was 72%. Mean dose to spinal cord was 8 Gy (5-30 Gy). The significant reduction in spinal cord dose with protons allowed retreatment in patients who had prior conventional radiotherapy. Acute side effects were limited to grade 1 or 2 anterior chest wall radiation dermatitis and grade 1 or 2 esophagitis in all patients, one pericarditis improved with NSAIDS, and one grade 3 radiation pneumonitis which resolved with short course steroids. At median follow-up of 25.5 months, one patient relapsed distantly in iliac bone and a new nodal area requiring further therapy. All 19 other patients remain without any evidence of recurrence. No severe cardiac or pulmonary toxicities have been observed so far, although long-term follow-up is necessary.

**Conclusions:** Proton radiotherapy appears to be a feasible and safe option in selected patients with bulky mediastinal/precordial lymphoma which can significantly reduce cardiac, lung, spinal cord, and integral dose with minimal acute/subacute toxicity and excellent control at this preliminary time point. Additional follow-up is needed to assess long-term control and late toxicity.

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## 2768 Salvage Radiotherapy in Patients with Recurrent or Refractory CNS Lymphoma

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**Purpose/Objective(s):** High-dose methotrexate (HD MTX) and whole-brain radiation therapy (WBRT) prolong survival in primary CNS lymphoma (CNSL). However, there is limited data for the optimal management of patients with recurrent or refractory primary or secondary CNSL after initial MTX. This study analyzes the outcome of salvage RT for these patients.

**Materials/Methods:** We reviewed records of 36 patients (22 male, 14 female) with primary ( $n = 15$ ) or secondary ( $n = 21$ ) CNSL who failed initial MTX therapy and received salvage RT between 1997 and 2009. Median age at CNSL diagnosis was 56 years (range, 20-83) and median time from diagnosis to start of RT was 3.3 months (range, 0.1-55.3). Included were 33 patients (92%) with diffuse large B-cell, 2 (6%) with marginal zone and 1 (3%) with mantle cell lymphoma. At diagnosis, 28 patients (78%) had brain involvement (including 1 with brain and spinal cord and 1 with brain and ocular), 4 (11%) had only spinal cord, and 4 (11%) had only leptomeningeal disease. Thirty-three patients (92%) received HD MTX with a median dose of 3.5 g/m<sup>2</sup> (range, 2.5-6.5) and the median number of cycles was 4 (range, 1-15). Three patients (8%) received only intrathecal MTX. Thirty-three patients (92%) received WBRT (median dose 40 Gy), 2 (6%) received RT to only the bilateral orbits (median dose 36 Gy) and 1 (3%) received RT to only the spine (40 Gy). Primary endpoints were radiographic response and overall survival (OS). Variables associated with OS were determined by the log-rank test.

**Results:** After RT, 18 patients (50%) achieved a complete radiographic response (CR) and 6 (17%) achieved a partial response (PR), for an overall response rate of 67% [95% CI: 49%, 82%]. One patient (3%) had stable disease, 10 (28%) progressed, and 1 died prior to response assessment. Of the 24 patients with a CR or PR, 10 had CNS relapse at a median of 7.9 months (range, 2.8-31.9). The median OS from start of RT was 11.7 months (range, 0.6-94.7) and 47% were alive 1 year after start of RT. Median follow-up time among patients still alive is 43.1 months. Patients treated with  $\leq 5$  cycles of MTX had shorter median OS than patients with  $\geq 5$  cycles of MTX (9.2 months vs. not reached,  $p = 0.04$ ). Patients with CNSL in only the brain had longer median OS than patients with disease in the brain and other CNS locations (16.5 vs. 4.5 months,  $p = 0.01$ ). Age, gender, type of CNSL, response to MTX, and multiple CNS lesions were not associated with OS.