Purpose or Objective
Postmastectomy radiation therapy (PMRT) reduces locoregional recurrence of breast cancer and improves survival in patients with lymph node involvement. A SEER analysis demonstrated an intermediate prognosis for pN1mi patients between lymph node negative (pN0) and lymph node positive (pN1) patients. This study addresses whether the subset of patients with lymph node micrometastasis (pN1mi) benefit from PMRT.
Material and Methods
We queried the surveillance, epidemiology, and end results (SEER) cancer registry version for women older than 18 years, with a diagnosis of primary breast cancer based on International Classification of Diseases for Oncology codes, diagnosed between 1998 and 2013, with invasive ductal or invasive lobular carcinoma histology, pathologic T1 or T2 primaries, micrometastatic nodal disease, who underwent mastectomy. Patients with distant metastatic disease, multiple primary cancers, unknown grade or undifferentiated carcinomas, and those who received neo-adjuvant radiotherapy were excluded. Univariate survival analysis was performed using the Kaplan-Meier method. Multivariate analysis was performed using a Cox proportionate hazards model. Variables included in multivariate analysis included age (continuous), menopausal status (as determined by age <50 or ≥50), race, histology (invasive ductal, lobular, or mixed), tumor grade (low and intermediate vs. high), T stage (T1 vs. T2), estrogen receptor status, progesterone receptor status, type of surgery (simple or radical mastectomy), and use of post-mastectomy radiation. The primary endpoint was overall survival. We then defined a risk of women with at least two of three high risk features (age <50, grade 3, T2) and evaluated the effect of radiotherapy on this subset.
Results
The analysis included 8,820 patients who met the inclusion and exclusion criteria as described above. The use of PMRT in pN1mi patients was associated with a higher risk of all cause mortality on multivariate analysis (HR 1.17, 95% CI 1.01 – 1.35, p=0.04). Other factors of worse all cause mortality include African American race, older age, premenopausal status, high grade, lobular histology, ER/PR negativity, and simple mastectomy. The subset of women with at least two of three high risk features included 3,242 patients. For this subset, PMRT was not significantly associated with overall survival (HR 1.11, 95% CI 0.92 – 1.33, p=0.29).
Conclusion
The use of PMRT in women with nodal micrometastasis without additional established indications for PMRT is associated with worse overall survival. For women with lymph node micrometastases and additional risk factors, PMRT is not associated with overall survival. Caution should be used in considering PMRT based on the finding of lymph node micrometastasis even in the setting of additional risk factors.

Poster: Clinical track: Lung

PO-0746 NTCP modelling of pulmonary toxicity after stereotactic radiotherapy for central lung tumors
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Purpose or Objective
Although stereotactic ablative radiotherapy and hypofractionated radiotherapy are established treatments for central lung tumors, reliable predictors for pulmonary toxicity are lacking. We evaluated the incidence of clinical pulmonary and radiographic bronchial toxicity, and performed normal tissue complication probability (NTCP) and multivariable analysis to identify predictors for toxicity.
Material and Methods
A pooled analysis was performed of patients with a central lung tumor treated using ≤12 fractions at two centers, between 2006-2015. Airways were manually contoured on planning CT scans and doses were recalculated to an equivalent dose of 2Gy per fraction with an α/ß ratio of 3. Grade ≥3 (≥G3) clinical pulmonary toxicity was evaluated by ≥2 physicians. Radiographic toxicity was defined as a stenosis or an occlusion with or without atelectasis using follow-up CT scans. Logistic regression analyses were used for statistical analyses.
Results
A total of 585 bronchial structures were studied in 195 patients who were mainly treated using 5 or 8 fractions (60%). Median patient survival was 27.9 month s (95% CI 22.3-33.6). Clinical ≥G3 pulmonary toxicity was observed in 24 patients (12%), and radiographic bronchial toxicity in 55 patients (28%), both mainly manifesting ≤12 months post-treatment. All analyzed dosimetric parameters correlated with clinical and lobar bronchial radiographic toxicity, with the $V_{130Gy,EQD}$ having the highest odds ratio. NTCP modelling showed a volume dependency for the development of both clinical and radiographic toxicity. On multivariate analyses, significant predictors for ≥G3 toxicity were a planning target volume overlapping the trachea/main stem bronchus (p=0.005), COPD (p=0.034), and the total $V_{130Gy,EQD}$ (p=0.012). Radiographic bronchial toxicity did not significantly correlate with clinical toxicity (p=0.663).
Conclusion
We identified patient and dosimetric factors associated with clinical and radiographic toxicity after high-dose radiotherapy for central lung tumors. Additional data from prospective studies are needed to validate these findings.

PO-0747 Validation of the survival model including cardiac substructure dosimetry in NSCLC
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Purpose or Objective
In lung cancer radiotherapy (RT) high doses are delivered to the heart. We found significant associations between death rate (DR) and high left atrial wall (LAWall) volumes receiving 63-69Gy ($LAWall_{V63-69}$) and any new or worsening ischaemic or rhythm ECG changes within 6 months of RT in a prospective isotoxic dose-escalation trial of 78 locally advanced non-small cell lung cancer (LA-NSCLC) patients. Here we aim to validate these findings in an independent retrospective cohort.

Material and Methods

We analysed 64 LA-NSCLC patients prescribed radical RT 66Gy in 33# in our centre. Heart and LAWall were delineated on planning scans. $LAWall_{V63\text{-}69}$ in 30# in the previous cohort is equivalent to $LAWall_{V65\text{-}71}$ in 33# in this cohort according to the LQ model (α/ß=3). So, $LAWall_{V65\text{-}71}$ was extracted for all patients. Recorded cardiac events (RCE) defined as symptomatic or asymptomatic, new or worsening cardiac events within 1 year of RT were collected from records. Patients were dichotomised according to the presence or absence of RCE. As ECGs were unavailable, RCE substituted this in the univariable (UVA) and multivariable (MVA) models. Death certificates were examined to determine recorded cardiac-related deaths (RCD). DR was modelled using cox regression from start of RT. To validate the model these variables were analysed: $LAWall_{V65\text{-}71}$, planning target volume (PTV), RCE.

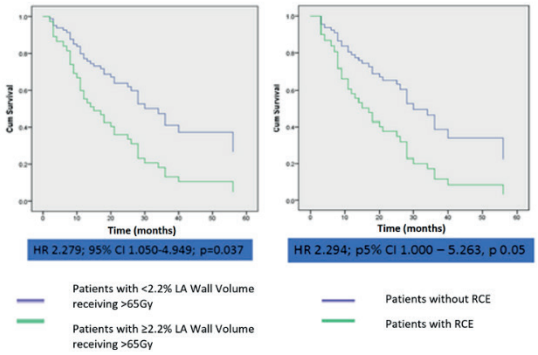
Results

Doses of 66, 64, 62, 60 and 58Gy in 2Gy per fraction were delivered to 56, 3, 2, 2, and 1 patients respectively. 17 patients had concurrent, 16 had sequential and 29 had no chemotherapy. Median PTV was $319cm^3$ (Range 82-1120). 17 patients had baseline cardiac comorbidity and 9 patients had RCE (6 fast AF/tachycardia, 3 pericardial effusion, 1 angina, 2 heart failure). 5 patients had RCD. 51 were ex/current smokers. 34 were PS1 and 17 were PS0.

On UVA, RCE and high $LAWall_{V65\text{-}71}$ were significantly associated with DR, and $LAWall_{V65\text{-}71}$ remained significant on MVA (Table). The hazard ratios (HRs) of $LAWall_{V65\text{-}71}$ were similar in the original and current cohorts (1.04 and 1.09 respectively). The HRs of cardiac events (ECG changes in original cohort and RCE in this cohort) were also similar (2.43 and 2.20 respectively). The scale of association between DR and $LAWall_{V65}$ and RCE are shown in the figure. Mean $LAWall_{V65\text{-}71}$ was higher in patients with RCD than in patients with non-RCD or alive patients (4.25%, 2.78% and 1.11% respectively). Baseline cardiac morbidity and smoking status were not significantly associated with DR.

	UVA		**MVA**	
	HR *p-value*	(95%CI)	HR *p-value*	(95%CI)
PTV	1 *.17*	(1-1)	1 *.84*	(1-1)
$LAWall_{V65\text{-}71}$	1.08 *.01*	(1.02-1.13)	1.09 *.01*	(1.03-1.15)
RCE	2.29 *.05*	(1-5.26)	2.20 *.08*	(.92-5.27)

Figure: Kaplan Meier overall survival (OS) curves dichotomising according to ≥/<2.2% LA wall volume receiving >65Gy (left) and the presence or absence of Recorded Cardiac Event within 12 months of radiotherapy (RCE) (right)



Conclusion

We validated in this independent cohort, despite the small size, our previous finding that high $LAWall_{V65\text{-}71}$ is associated with higher DR. RCD rate was low likely due to under recording. Patients with RCD had higher $LAWall_{V65\text{-}71}$. Prospective studies to elucidate the mechanism of damage and better recording of cardiac and cancer deaths is required.

PO-0748 Inter-observer delineation variation and dose to hippocampus in hippocampus avoidance PCI

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Purpose or Objective

To reduce radiation damage to the hippocampus, hippocampus avoidance prophylactic cranial irradiation (HA-PCI) techniques are used, in which the hippocampus is delineated and a 5mm planning organ at risk volume (PRV) margin defines the avoidance zone. In this study, we analyzed inter-observer delineation variability and estimated the effect of this variability on dose to the hippocampus.

Material and Methods

From the Dutch-Belgian randomized phase III HA-PCI trial (NCT01780675) 3D T1-weighted MPRAGE MRI were collected of five patients and seven observers outlined both left and right hippocampus according to the RTOG instructions (https://www.rtog.org/CoreLab/ContouringAtlases/HippocampalSparing.aspx). To quantify inter-observer outlining variability the intra-class correlation (ICC) with absolute agreement was calculated for volumes and the generalized conformity index (CI_{gen}) was computed to quantify overlap. In addition, standard deviations (SD) expressed as local observer variation were computed from the distance of all delineations to the median surface and projected on the median surface to observe regional outlining differences. Finally, for the five median surfaces HA-PCI dose treatment plans were generated and we investigated whether trial dose constraints in the hippocampus were met for individual delineations. The trial constraints for the hippocampus are: $D_{1\%} \leq 10Gy$; $D_{mean} \leq 8.5Gy$ and $D_{mean\ biological} \leq 6.2Gy$.

Results

The ICC across all observers' delineations was 0.56 for the left hippocampus volume and 0.69 for the right hippocampus volume. CIgen values ranged from 0.55 to 0.7. Regional hippocampal SD maps showed that most variations were in the anterior-medial hippocampal regions with SDs ranging from approximately 1-2.5mm. For the $D_{1\%}$ we observed a few constraint violations, especially for patient number four where for the