patients, and explores which structure may be most sensitive to radiation dose.

Material and Methods

The residual setup errors of 780 NSCLC patients treated with a 5mm action threshold correction protocol were estimated and parameterized as the mean and standard deviation of the residual shifts in each direction per patient. Shift parameters related to survival were selected using an elastic net penalised multivariate Cox model. Their significance was determined through multivariate Cox regression correcting for age, performance status, GTV volume and fractionation. The effect of shift directionality was studied by comparison of subgroups with the tumour located in the left and right lung, and by consideration of the residual shift of the high dose region towards or away from the heart. The main finding was validated in an independent cohort of oesophageal cancer patients (n = 177).

Results

The residual shifts were not correlated with any clinical variables, yet strong associations with survival were found in 5 out of the 9 summary shift parameters. The left and right lung cohorts, split for survival analysis by their mean lateral shifts, showed opposite directional shift effects (Figure 1), demonstrating the negative effect of residual shifts towards the mediastinum on survival. Vector projection showed that patients with a residual shift towards the heart have significantly worse overall survival (p = 0.001, HR 1.310) (Figure 2). The same effect was observed in the oesophageal patient validation cohort (p = 0.030, HR 1.531).

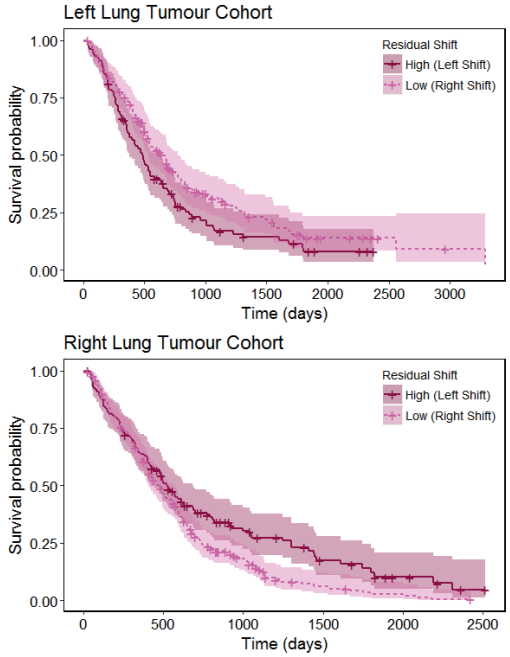

Figure 1: Multivariate corrected survival curves for patients with left (n = 261) and right (n = 367) lung tumours, split on the mean lateral shift. Patients with high shifts in the left cohort (> 0.1mm) have worse overall survival (p = 0.027), while patients with high shifts in the right cohort (> 0.4mm) have improved overall survival (p = 0.016), demonstrating the detrimintal effect of shifts towards the mediastinum.

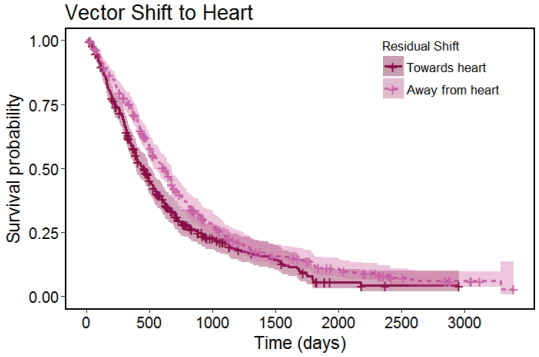

Figure 2: Multivariate corrected survival curves for NSCLC patients stratified on whether their residual shift moves the high dose region towards or away from the heart (p = 0.001)

Conclusion

To our knowledge, this is the first study of its type. We showed that residual systematic shifts after IGRT are strongly associated with overall survival in NSCLC patients, with residual shifts towards the heart significantly associated with worse survival. The effect was confirmed in an independent cohort of oesophageal patients. This analysis provides direct evidence in a large patient cohort of the importance of ensuring correct patient positioning through the use of IGRT. Furthermore, it highlights the heart as a dose sensitive organ in thoracic radiotherapy with early effects on survival.

Proffered Papers: Highlights of proffered papers

OC-0323 Patterns of recurrence in the randomised PORTEC-3 trial of chemoradiotherapy for endometrial cancer

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Purpose or Objective
Women with high-risk endometrial cancer (HREC) are at increased risk of distant metastasis and endometrial cancer-related death. The international, randomised PORTEC-3 trial was initiated to investigate the benefit of adjuvant chemotherapy during and after radiotherapy (CTRT) versus pelvic radiotherapy alone (RT) for women with HREC. The aim of the current analysis was to determine the patterns of vaginal, pelvic and distant recurrence and survival after recurrence.
Material and Methods
Women with HREC (FIGO stage I grade 3 with deep myometrial invasion and/or LVSI; stage II or III; or serous/clear cell histology) were randomly allocated (1:1) to RT (48.6Gy in 1.8Gy fractions) or CTRT (two cycles of cisplatin 50 mg/m² in week 1 and 4 of RT, followed by four cycles of carboplatin AUC5 and paclitaxel 175 mg/m² at 3-week intervals).
The co-primary endpoints were overall survival (OS) and failure-free survival (FFS). Secondary endpoints were vaginal, pelvic and distant recurrences; these were analysed according to first site of recurrence. The Kaplan-Meier method, log-rank test and Cox regression analysis were used for final analysis according to intention-to-treat, and competing risk methods for FFS and recurrence. PORTEC-3 is registered with ISRCTN (ISRCTN14387080) and ClinicalTrials.gov (NCT00411138).
Results
686 women were enrolled between 2006 and 2013 of whom 26 were excluded for consent withdrawal or ineligibility, leaving 660 patients in the final analysis, 330 CTRT and 330 RT. Median follow up time was 60.2 months (IQR 47.1-72.9). OS at 5 years was 81.8% for CTRT versus 76.7% for RT; hazard ratio (HR) 0.81 [95% CI 0.58-1.13, p=0.2123]. Five-year FFS was 75.5% versus 68.6%, HR 0.76 [0.57-1.02, p=0.067] and 69.3% vs 58.0% (p=0.032) for stage III. The final database had 186 FFS events. Isolated vaginal or pelvic recurrences were rare (0.3% vaginal and 1.2% pelvic recurrences). Most were distant metastases: 22.4% (n=76, CTRT) vs 28.3% (n=93, RT) [HR 0.78 CI 0.58-1.06; p=0.108), of which 6.1% vs 9.7% were combined with a vaginal or pelvic recurrence, and 17% vs 18.5% were isolated dist ant recurrences. Patients were treated for a first recurrence with chemotherapy in 33.7% (CTRT) vs 47.6% (RT), and hormonal therapy in 15.7% vs 15.5%. Median survival after any recurrence was 1.1 (CTRT) vs 1.4 years (RT p=0.36), with 3-year survival after recurrence of 29 vs 31%. Median survival after isolated vaginal or pelvic recurrence was 1.2 (CTRT) vs 2.3 years (RT), p=0.46.
Conclusion
Adjuvant chemotherapy given during and after pelvic radiotherapy for HREC showed 7% improvement of failure-free survival compared with radiotherapy alone, with a significant 11% improvement in stage III disease. The majority of recurrences were distant metastasis. Treatment included chemotherapy for most patients in both treatment arms, with similar 3-year survival after recurrence of about 30%, indicating prolonged survival of a substantial number of patients even after relapse.

OC-0324 Immune contexture in SCCHN and outcome after chemoradiotherapy in an uni- and multicentric cohort.
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Purpose or Objective
We examined the prognostic value of tumor infiltrating lymphocytes, tumor associated macrophage markers and the PD1/PD-L1 axis in patients with squamous cell carcinoma of the head and neck (SCCHN) in two cohorts treated with definitive or postoperative chemoradiotherapy (CRT).
Material and Methods
We evaluated the CD3, CD4, CD8, FOXP3, CD163, CD68, CD11b, CD56 and PD1/PD-L1 expression according to immunohistochemical staining of biopsies for definitively treated patients or of the tumor resection specimen for adjuvant CRT, respectively. Overall, 110 patients treated with definitive CRT in the DKTK-subsite Frankfurt and 155 patients treated with postoperative CRT with carcinomas of the oral cavity, oropharynx and hypopharynx from all eight DKTK-partner sites have been included in this retrospective analysis. All patients were treated between 2004 and 2012 with postoperative radiotherapy (RT) to a cumulative dose of 60-66 Gy or with definitive RT to a dose of 70-72 Gy and concomitant, cisplatinum-based chemotherapy. We performed a statistical correlation with clinicopathological parameters and oncological endpoints depending on HPV-DNS/p16 - status.
Results
After a median follow-up of 40 months for the definitive cohort and 48 months for the adjuvant cohort, a high infiltration with CD3- and CD8-positive cells correlated with a significantly improved overall survival in both cohorts. CD163 positive ("M2") macrophages were associated with significantly worse survival in the definitively irradiated cohort and PD-L1 with significantly improved survival in the postoperatively treated cohort. All of the findings above were also true for the endpoints local progression free survival and