Purpose/Objective: Loco-regional recurrences remain frequent in locally advanced non-small cell lung cancer (NSCLC) patients and are predominantly located in the area of the primary tumor. Improved tumor control might be accomplished by dose-escalation and dose-redistribution. The PET-boost trial (NCT01024829) is an ongoing randomized phase II trial investigating individualized accelerated dose-escalation to the entire primary tumor (arm A) or redistributed to regions of high FGD-uptake within the primary tumor (arm B). We present a planned interim analysis of the toxicity of 63 randomized patients.

Materials and Methods: Patients with NSCLC stage IB-III, a primary tumor (PT) ≥4 cm and a SUVmax ≥5 are treated with chemo-radiation or radiotherapy alone. Treatment plans are designed using a pre-treatment FDG-PET-CT-scan with similar dose limits to OAR as in conventionally treated patients. If normal tissue constraints allow dose-escalation using an integrated boost ≥72 Gy in 24 fractions to the PT and with equal mean lung dose for both study arms, a patient is randomized to arm A or arm B. Involved lymph nodes are treated to a fractionation dose of 66 Gy in 24 fractions. Toxicity is scored according to the CTCAEv3.0 criteria. Endpoints are local progression-free survival at 1 year, toxicity, overall survival and quality of life.

Results: From April 2010 to March 2014, 32 patients were randomized to arm A and 31 patients to arm B. Forty-eight patients received concurrent chemo-radiotherapy. Median follow-up was 25.5 months. The mean PT volume in arm A was 123.4cc and in arm B 181.5cc. Mean prescribed dose to the planning target volume of the primary tumor was 3.3 Gy (range 3.0-4.0 Gy) in arm A and 3.9 Gy (range 3.2-5.4 Gy) in arm B. Grade ≥3 dysphagia and dyspnea during treatment occurred in 7 and 2 patients (11 and 3%). Grade ≥3 esophagitis and pneumonitis after treatment was seen in 11 and 6 patients (17.5% and 9.5%). Hematologic toxicity grade ≥3 was observed in 5%. Four out of 63 patients (6.3%) died due to pulmonary hemorrhage.

Conclusions: This interim toxicity analysis of the randomized phase II PET-boost trial shows that dose-escalation is feasible in 63 randomized patients. The toxicity observed during and after treatment shows no excess or unexpected toxicity.

OC-0205
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Purpose/Objective: The prognostic value of standardized uptake value (SUV) distribution of the fluorine-18 labeled glucose analog (FDG), has been widely studied for the primary tumor in non-small cell lung cancer (NSCLC) patients. However, nodal stage determines treatment choice and is related to disease progression and its capability to metastasize. We hypothesize that more PET-related prognostic information can be extracted from affected hilar/mediastinal lymph nodes than in the primary tumor. Therefore, we analyzed the SUV distribution and volume of the primary tumor and affected lymph nodes prior to radiotherapy.

Materials and Methods: A cohort of 352 stages I-III NSCLC patients referred for primary (chemo)radiotherapy was included. The gross tumor volume of the primary tumor (GTV_{prim}) and the metastatic lymph nodes (GTV_{ln}) had been manually delineated for treatment planning purposes. The nodal positive subset of patients (272) was selected for a comparison analysis based on volume and SUV descriptors (maximum, mean and peak), as derived from both the primary tumor and the affected lymph nodes, of the pre-radiotherapy PET scan. The prognostic value of each of the metrics to overall survival (OS), recorded from start of radiotherapy until last day of follow-up or death by any cause, was evaluated through a Cox Proportional Hazards regression.

Results: We first compared the distribution of volume and common SUV descriptors of the primary tumor for N=0 (80) and N+ (272) NSCLC patients. The GTV_{prim} of patients without affected lymph nodes was metabolically more active (SUV_{max} = 13 ± 6.3; p<0.01, and SUV_{peak} = 10.3 ± 5.1; p<0.02) and larger (volume = 127.3 ± 235.4; p<0.01) than the GTV_{prim} of patients with affected lymph nodes. Mean ranks difference (Wilcoxon test) of volume and SUV descriptors of both GTV_{prim} and GTV_{ln} was conducted for the nodal positive subset of patients, for which statistically significant (p<0.001) differences between metrics derived from the two structures could be shown (see table). The prognostic value of each of the metrics to OS was evaluated through a Cox Proportional Hazards regression. None of the metrics derived from the primary tumor were associated with OS in our cohort. However, the same metrics, extracted from the involved lymph nodes, were prognostic for survival with mean SUV showing the strongest correlation with OS (HR=1.14, p<0.01). Also, tumor load, defined as GTV_{prim} + GTV_{ln} showed a statistically significant correlation with OS. Currently, a multivariate analysis and collection of an external dataset for validation is ongoing.

Figure -- Fused pre-radiotherapy PET-CT scans of two NSCLC patients with de-histiated primary tumor and corresponding lymph nodes.

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Conclusions: The most common SUV descriptors as well as the volume of the involved lymph nodes of NSCLC patients are significant prognostic factors for overall survival for NSCLC. Likelihood of a worse prognosis increases with an increase of the mean SUV of the nodes. This is consistent with our hypothesis that there is more PET-related prognostic information in the nodes compared to the primary tumor.

OC-0206
Dose-response modelling in SBRT for stage I NSCLC and pulmonary metastases based on a multi-institutional database

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Purpose/Objective: Stereotactic body radiotherapy (SBRT) is the treatment of choice in medically inoperable patients with stage I NSCLC. Today, SBRT is used with increasing frequency for pulmonary metastases; however, dose prescriptions are adapted from primary NSCLC experiences without their validation for metastases. It was therefore the aim of this study to analyze a potential dose-effect relationship for local tumor control in SBRT for pulmonary metastases and compare results to SBRT for stage I NSCLC.

Materials and Methods: This retrospective multi-institutional study is based on 582 and 964 patients treated with SBRT for stage I NSCLC and pulmonary metastases at 13 centres; only patients with follow-up >6 months were analyzed resulting in 399 and 525 patients, respectively. Patients with primary NSCLC and pulmonary metastases were treated with a median of 3 (range 1-17) and 3 (1-12) fractions to a total dose of 60Gy (range 19-86) and 55Gy (16-80) (maximum PTV dose at isocenter; PTV-max), respectively. BED was calculated using the LQ-model with α/β=10Gy resulting in PTV-max doses of 168Gy (48-263) and 138Gy (24-288) BED for primary NSCLC and metastases, respectively. Dose-effect models were compared using the second-order bias corrected Akaike Information Criterion (AICc). We used Bayesian logistic regression to estimate regression parameters and their standard errors.

Results: Median tumor diameter was 2.6cm (0.8-4.8) and 1.9cm (0.4-9.0) for patients with primary NSCLC and pulmonary metastases, respectively (p<0.001, Wilcoxon rank sum test); tumor diameter was lacking in 47% (primary NSCLC) and 12% (pulmonary metastases) of the patients. Most frequent histologies for pulmonary metastases were NSCLC (28%), colorectal (25%) and renal cell cancer (11%). Median follow-up was 19 months (6-139; primary NSCLC) and 16 months (6-125; pulmonary metastases) (p<0.05). For pulmonary metastases, a strong dose response relationship was observed (evidence ratio 98.6), but only for PTV-max BED and not for the PTV encompassing BED; the latter is in contrast to findings from SBRT for primary NSCLC, where a strong evidence for a minimum PTV dose-effect was observed (Guckenberger et al. Radiother Oncol 2013). Overall, there was no difference in the dose response relationship between primary NSCLC and pulmonary metastases: the PTV-max BED required for 90% TCP was 176±17Gy and 167±18 Gy for primary NSCLC and pulmonary metastases, respectively.

Conclusions: A significant dose-response relationship was observed in SBRT for pulmonary metastases with local tumor control as endpoint. The observed dose response relationship was not different to primary stage I NSCLC. We will, however, further investigate the influence of histology and tumor size on the dose-effect relationship in pulmonary metastases.

Symposium: Elderly should be treated as their younger counterparts

SP-0207
The role of postoperative radiotherapy in the older patient: impact on local control and quality of life

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The incidence of breast cancer is rising in the elderly, reflecting the age related incidence of the disease and, in the UK, the impact of the breast screening programme. The evidence base for the role of postoperative radiotherapy (RT) after breast conserving surgery in older patients has been limited, in part reflecting the historical exclusion of the elderly from randomised trials. Extrapolating outcomes from younger to older patients may not be valid. In older patients there are also competing risks of non breast cancer mortality. The Oxford overview (1) of over 10,000 women treated with breast conserving surgery with or without adjuvant radiotherapy shows that RT halves the risk of first recurrence (most of which are local). However the absolute reduction in risk of recurrence from RT is very modest in older good prognosis patients. The main source of level 1 evidence in older patients is the CALGB 9343 trial (1) which randomised over 700 women >/= 70 years with T1, NO,MO hormone receptor positive breast cancer treated by breast conserving...