local control (LC), regional control (RC) and metastasis-free survival (MFS). A strong correlation between total lymph node tumour volume and N-stage was found (R²=0.93, P=0.01). MFS was worse with involvement of the lower neck levels (R²=0.345, P=0.01). Patients with larger total lymph node tumour volumes had poorer RC and MFS rates, independent of treatment regimen. For total lymph node volumes up to 3.5 cm³, MFS can be improved by ARCON (P=0.01).

Conclusions: The strong prognostic value of T-stage and primary tumour volume, observed in retrospective analyses was not confirmed in patients treated in a prospective randomised trial with accelerated radiotherapy with or without carbogen breathing and nicotinamide. Results of this study indicate that (biological) factors other than primary tumour volume and T-stage are needed to select patients with laryngeal cancer for treatment intensification.

PD-0094

EGFR inhibition radiosensitizes NSCLC cells via permanent G1 arrest but only when p53/p21 signaling is intact

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Purpose/Objective: Radiotherapy combined with targeting of the epidermal growth factor receptor (EGFR) is considered to be a promising new tool to increase tumor control. However, the data available so far, indicate that probably only a subgroup of patients may actually benefit from this new treatment. In order to identify these patients the mechanisms of EGFR targeting has to be known. We asked whether cell cycle effects as caused by EGFR targeting may play a critical role when combined with irradiation and whether biomarkers can be established for this interaction.

Materials and Methods: Study was performed with cell lines differing in p53 status (A549, H1299, H460, H3122, HCT116, FaDu) as well as in A549 grown as xenografts. Cell cycle analysis was measured via FACScan and kinetics of G1 population was followed using colcemid assay. Protein expression was determined via Western, p21 was knocked down via siRNA; cell survival by colony assay, for xenograft model tumor control probability was determined after conventional fractionation. Results: Targeting of EGFR alone by tyrosine kinase inhibitors (Erlotinib and Gefitinib) was able to induce a strongly pronounced accumulation of cells in G1. But this effect was mostly transient. In combination with X-irradiation both TK inhibitors were found to enhance the radiation-induced permanent G1 arrest to a great extend. This effect, however, only occurred in cells with intact p53/p21 signaling. No such an effect was seen in tumor cells mutated in p53 or p21 status (A549, H1299, H460, H3122, HCT116, FaDu) as well as in A549 grown as xenografts. Cell cycle analysis was measured via FACScan and kinetics of G1 population was followed using colcemid assay. Protein expression was determined via Western, p21 was knocked down via siRNA; cell survival by colony assay, for xenograft model tumor control probability was determined after conventional fractionation.

Conclusions: Overall these data suggest that both in vitro as well as in vivo EGFR inhibition may lead to a moderately increased cellular radiosensitivity and vice versa. In a xenograft model, blockage of EGFR was also found to result in a trend towards higher local control. However, the data available so far, indicate that probably only a subgroup of patients may actually benefit from this new treatment. In order to identify these patients the mechanisms of EGFR targeting has to be known. We asked whether cell cycle effects as caused by EGFR targeting may play a critical role when combined with irradiation and whether biomarkers can be established for this interaction.

PD-0095

Dosimetric parameters predictive for radiation pneumonitis after SABR for high-risk lung tumors

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Purpose/Objective: Treatment of larger and more centrally located lung tumors with SABR results in high local control, but higher rates of radiation pneumonitis (RP) have been reported. We studied predictors of RP in high-risk patients treated with SABR, to optimize treatment planning objectives.

Materials and Methods: A review was performed of 79 SABR patients and 27 patients treated with CRT for NSCLC and 16 patients treated with CRT for SCLC and 25 patients treated with SABR for SCLC. A total of 38 NSCLC and 22 SCLC patients were included.

Results: Of these, 14 NSCLC (37%) and 9 SCLC (41%) developed at least grade 3 RP. Multivariable analysis showed contralateral MLD (p=0.007) and ITV (p=0.063) to best predict grade ≥3 RP, and the model achieved excellent discrimination with a C-statistic of 0.87. The highest risk for RP was found if the contralateral MLD was ≥3.6Gy (for 3 out of 8 patients) or if ITV size was ≥145cc (2 out of 7 patients). Lowest risk (1 case out of 54) was found for patients outside these two groups.

Conclusions: The contralateral MLD and ITV strongly correlated with risk of Grade ≥3 pneumonitis after SABR. New strategies are needed to minimize this risk.

PD-0096

Contralateral hilar or supraclavicular lymph node doses do not impact OS in PET-staged patients with stage I-II SCLC.

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Purpose/Objective: Traditionally patients with contralateral hilar or supraclavicular lymph node doses are often denied curative treatment for stage III small cell lung cancer (SCLC). We hypothesized that the prognostic impact of these lymph nodes is less pronounced in PET-staged SCLC patients due to more accurate staging.

Materials and Methods: Analysis of 111 patients in our prospective database with stage I-II SCLC referred for concurrent chemoradiotherapy. All patients received a PET-scan as part of their staging work-up. Standard treatment was 45 Gy in 1.5 Gy fractions twice daily concurrently with carboplatin-etoposide, followed by prophylactic cranial irradiation (PCI) in case of non-progression. Only PET-positive or pathologically proven lymph nodes were included in the Gross Tumor Volume (GTV). Survival was calculated from diagnosis (Kaplan-Meier method).

Results: Out of 111 patients, 10 (9%) had contralateral hilar and 29 (26%) had supraclavicular lymph nodes. Median overall survival for the entire cohort was 20 months (95% CI 17.8-22.1 months), 2-year survival 39%. In univariate analysis neither having supraclavicular or contralateral hilar lymph nodes did not have a significantly worse prognosis.

Conclusions: In stage I-II SCLC staged with PET and treated with modern concurrent chemoradiotherapy, the presence of supraclavicular or contralateral hilar lymph nodes does not have a significant impact on overall survival. These patients should therefore be offered treatment with curative intent.

PD-0097

Impact of new Dutch guideline on patient selection for WBRT in a large lung cancer cohort

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Purpose/Objective: During the course of their disease, 30-60% of lung cancer patients (pts) develop brain metastasis (BM). Despite local and/or systemic treatment survival is dismal. Depending on the Recursive Partitioning Analysis (RPA) class median survival is 7 months for class 1 and 3 months for class 3. In 2011 the Dutch national guideline on BM was revised, advising to actively treat pts with more than 3 BM both in RPA class 1 and the majority of pts in class 2 with Whole Brain Radiotherapy (WBRT). With lacking evidence of benefit, pts in RPA class 3 should be strictly treated palliatively. In this retrospective study in a large lung cancer patient cohort we evaluate the guideline's use in daily practice.

Materials and Methods: Data of all lung cancer pts who underwent WBRT for BM referred from one of three collaborating hospitals in the South of the Netherlands between March 2004 and July 2012 were retrospectively analyzed. Details on performance score (according to WHO/Karnofsky(KPS)), age, locally controlled disease, extracranial metastasis, time from diagnosis of lung cancer to development of BM, histology and survival after diagnosis of BM were collected. The RPA class was determined using the first four items.

Results: 292 WBRT pts had NSCLC. Average age (range) was 62.6 years (40.5-83.5), 59.2% was male, 252 (68.3%) had a KPS of ≥ 70. In 215 (73.6%) pts the primary tumor was not controlled, 116 (39.7%) had extra-cranial metastasis, 93 (31.1%) had BM at primary diagnosis. 96 WBRT pts had SCLC, average age was 62.1 years (44.7-83.5), 64.0% was male, 86 (89.6%) had a KPS of ≥ 70. In 71 (74.0%) pts the primary tumor was not controlled, 37 (38.5%) had extracranial metastasis and 24 (25.0%) had BM at primary diagnosis.

For NSCLC, 45 (15.4%) of 292 pts were classified as RPA 1, 210 (71.9%) as RPA 2, and 37 (12.7%) as RPA 3. For SCLC this was 7 (7.3%), 75 (78.1%), and 14 (14.6%), respectively. Before the revised guideline was implemented in 2011, on average 10.8% of WBRT pts were annually classified as RPA 3. In the year after implementing the guideline, this was 7.7% (p<0.353). Median survival for NSCLC RPA class 1, 2, and 3 was 6.5 [95% CI = 3.8-9.2]; 3.0 [95% CI = 2.3-3.7] and 1.3 [95% CI = 0.7-2.2] months, respectively. For SCLC this was 9.0 [95% CI = 8.0-10.0]; 4.4 [95% CI = 2.9-6.0] and 2.0 [95% CI = 0.2-3.8] months, respectively (see figure 1).

Conclusions: Although it is not advised that RPA class 3 pts should receive WBRT, approximately 13% of the analyzed WBRT pts were classified as RPA 3. Despite the release/implementation of the new national guideline in 2011, we did not find a significant difference regarding the treatment of RPA class 3 pts thereafter. The survival of RPA class 3 pts is poor and in agreement with RTOG validation studies. In our view, guidelines should be implemented more precisely. Better awareness amongst physicians would prevent some patients from being treated unnecessarily.

PD-0098
Biological summation of conventional and stereotactic radiation treatment planning in non-small cell lung cancer

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Purpose/Objective: Standard treatment of locally advanced non-small cell lung cancer (NSCLC) corresponds to concomitant chemoradiotherapy (2 Gy per fraction until 60-66 Gy). A phase I trial was initiated in order to analyze toxicity of standard chemoradiotherapy (CTR: 46 Gy, 2 Gy per fraction) with a stereotactic ablative radiotherapy (SABR) boost. The aim of the present study was to develop an algorithm able to determine biological equivalent dose received by every organ at risk and target volume during radiotherapy using two different fractionation schedules.

Materials and Methods: A phase I trial began in our center in 2010 and analyzes toxicity after chemoradiotherapy (46 Gy with docetaxel and cisplatinum, 2 Gy per fraction) and a boost delivered by SABR (3 X 7 Gy). For the last 3 x 12 Gy for the last conventional treatment dose matrix and stereotactic dose matrix were fused on the same CT-scan (used for SABR treatment). Histogram dose volume was evaluated by summation of physical dose after biological conversion for each voxel by using the linear quadratic-linear model (LQ-L) and the α/β ratio of the delineated organ (ARTVIEW, AQUILAB SAS, France).

Results: With a median follow-up of 21 months (5-26), 14 patients (pts) were treated and 12 (85.7%) experienced grade 1-2 toxicities (no grade 3-4 toxicities). One patient died of massive heart failure 6 months after treatment, but also after local and metastatic relapse, and bevacizumab treatment. The most frequent toxicity was G1-2 pulmonary alveolitis (8 pts, 57.1%). When considering dose constraints under chemo, conventional treatment, post hoc analysis of matrix-dose revealed that bioequivalent cumulative dose were above the usual recommended dose in 3 pts for brachial plexus, 6 pts for pulmonary arteries, 4 for superior cave veins, 2 for heart, 3 for bronchial tree, 8 for bone, and 3 for lung. When comparing biological summation for both conventional and SABR treatment, with only conversion for the SABR part there was a median difference of -0.35 Gy (-5.1 ;+0.8). Patient with hemoptysis had the highest dose delivered to the big vessels (141.7 Gy).

Conclusions: One toxic death was suspected in this trial and correlated with the highest dose received to the big vessels but other factors could also explain this event. Otherwise a lot of pts received a dose over the limit of dose constraint but with up to now, no grade 3-5 toxicities suggesting that the LQ-L might not well predict toxicities when mixing conventional and SABR treatments, and might overestimate bioequivalent dose. This has to be confirmed with longer follow-up and a larger number of patients.

AWARD LECTURE: VAN DER SCHUEREN AWARD LECTURE

SP-0099
The role of medical physicists in implementing advanced technology in radiotherapy

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The last decade has shown a tremendous increase in technological developments in radiotherapy in which many types of advanced technology emerged. These steps forward concerned: 1) Access of RT departments to new diagnostic imaging equipment; 2) Installation of new treatment modalities allowing dose delivery that are more precise, faster or with greater biological effectiveness; 3) Availability of numerous QA devices to verify the dose delivery and patient position before or during their treatment; 4) Electronic data transfer. Not all potential improvements have led to large scale clinical implementation. Cost and reimbursement are obvious reasons, but the implementation of new treatment modalities depends also on the availability of sufficient expertise and manpower in a department. A large number of physical, technical and clinical problems have to be solved before advanced technology can be used in an optimal way. For instance, combination of diagnostic imaging information may yield improved knowledge of the position of target volume and organs at risk, while more advanced optimization and dose calculation algorithms may allow better target coverage and sparing of organs at risk. However, knowing the possibilities and limitations of these procedures is a prerequisite for their safe use by the treatment planning team; a process in which medical physicists play an essential role. Implementation of new treatment modalities such as proton and carbon-ion therapy is still far from routine practice and requires