Materials and Methods: The inclusion criteria for this multi-center prospective study are (1) biopsy-proven NPC, (2) no distant metastasis, (3) in clinical remission after curative treatment (radiotherapy + chemotherapy), (4) within 3 year after finishing radiotherapy. pEBV DNA concentration is monitored every 3 months. Detailed staging workups are performed when abnormal pEBV DNA detected. All tumor recurrences are documented by imaging studies along with pathological verification if the lesions are accessible and patients agree.

Results: From August 2010 to October 2012, 252 patients were enrolled and 33 patients had abnormal pEBV DNA during follow-up visit. Thirty of 33 (91%) patients with elevated pEBV DNA have been proven as tumor relapse, whereas the remaining 219 patients with normal pEBV DNA level are showing no evidence of disease (P<0.0001). In addition, two-thirds (20/30) relapsed patients were detected in a symptomless state.

Conclusions: pEBV DNA assay is a very encouraging tool in monitoring NPC patients after treatment.

PD-0097
The dose to the larynx elevation and tongue retraction muscles has a large impact on post-radiation dysphagia.
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Purpose/Objective: Recent studies showed that the dose distribution in certain anatomical structures, such as the pharyngeal constrictor muscles (PCM), are associated with the risk of radiation-induced dysphagia. In the normal swallowing process, larynx elevation and tongue retraction also play an important role. However, so far, less attention has been paid to the relationship between the dose distribution in muscles involved in larynx elevation and tongue retraction and the risk of radiation-induced dysphagia. Therefore, the purpose of the current study was to investigate the role of the radiation dose delivered to the larynx elevation and tongue retraction muscles in the development of radiation-induced dysphagia.

Materials and Methods: This prospective cohort study included 56 head and neck cancer patients, treated with primary (chemo)radiotherapy (CH)RT. In addition to the anatomical structures that have been previously identified as swallowing organs at risk (SWOARs), such as the PCM superior or supraglottic larynx, muscles involved in larynx elevation and tongue retraction were delineated on planning-CT’s. The larynx elevation complex included an anterior complex, including the suprahyoid muscles and thyrohyoid muscle, pharyngeal longitudinal muscles and the posterior digastic/stylohyoid muscles. The tongue retraction complex included the genioglossus muscle and the tongue base. The primary endpoint was RTOG grade 2-4 dysphagia and the secondary endpoints were patient-rated moderate-to-severe swallowing problems assessed with the EORTC QLQ-H&N35 questionnaire, all at 6 months after completion of CHRT.

Results: In the univariate analysis, the mean doses delivered to anterior complex (OR=1.116 (95%CI 1.005-1.238)) and longitudinal muscles (OR=1.043 (95%CI 1.003-1.085)) were significantly (p<0.05) associated with the primary endpoint. The doses to the anterior complex (OR=1.078 (95%CI 1.004-1.162)) and the longitudinal muscles were also associated with the risk of moderate-to-severe problems with swallowing SOLID food (OR=1.047 (95% CI.006-1.089)). The mean doses delivered to the genioglossus muscle (OR=1.065 (95%CI 1.002-1.132)) and the base of tongue (OR=1.070 (95%CI 1.005-1.140)) were also significantly associated with the primary endpoint. A significant association was found between the mean dose to the genioglossus muscle and problems with swallowing SOLID food (OR=1.055 (95%CI 1.002-1.085)). Figure 1 shows the NTCP-curves of the risk of grade 2-4 RTOG dysphagia and moderate-to-severe problems with solid food as a function of the mean dose to these structures.

Conclusions: The mean doses delivered to muscles involved in the larynx elevation and tongue retraction, as well as the dose to the superior PCM and supraglottic larynx, are significantly associated with a higher risk of different aspects of radiation-induced dysphagia and these structures should also be considered as Swallowing Organs At Risk.

PD-0093
CT-based tumour volume as a predictor of outcome in laryngeal cancer: results of the phase 3 ARCON trial.
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Purpose/Objective: A wealth of retrospective studies indicate that larger tumour volume is a strong prognostic indicator for poor local tumour control after (chemo)radiotherapy for laryngeal cancer. The impact of tumour volume on the outcome of patients treated within a prospective study comparing accelerated radiotherapy (AR) ± carbogen breathing and nicotinamide (ARCON) was investigated.

Materials and Methods: Of 345 patients with cT2-4 laryngeal cancer, pre-treatment CT-scans of 270 patients were available for tumour volume calculation. Contouring of the primary tumour and involved lymph nodes was reviewed by a single head and neck radiation oncologist. All living patients had clinical follow-up for a minimum of 2 years after completion of the treatment. Cox proportional hazard models were used for analysis of outcome.

Results: Of 137 AR and 133 ARCON patients, 57 and 80 vs. 56 and 77 patients had glottic and supraglottic tumours, respectively (P>0.50). Primary tumour and total lymph node volumes were well balanced between both treatment arms (P=0.79 and P=0.80, respectively). A correlation between the primary tumour volume and T-stage was observed (Rs=0.51, P<0.01). In both treatment arms no correlation was detected between the primary tumour volume or T-stage and
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 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 pathologic diagnosis (Kaplan-Meier method).

Results: Targeting of EGFR alone by tyrosine kinase inhibitors (Erbitux and Iressa) 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 extent. 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 deleted in p21 or when p21 was knocked down via siRNA. For tumor cell lines showing this increase in permanent G1 arrest, TK inhibitors were always found to result in a moderately enhanced cellular radiosensitivity and vice versa. In a xenograft model, blockage of EGFR was also found to result in a trend towards higher local control.

Conclusions: Overall these data suggest that both in vitro as well as in vivo EGFR inhibition may lead to a moderately increased radiosensitivity but only when p53/p21 signaling is intact. In order to increase these effects on tumors, radiation and EGFR targeting need to be combined with agents specifically affecting the permanent G1 arrest.

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 asked whether RP, due to either their PTV (i.e. or prior pneumonectomy or bi-lobectomy or prior pneumonectomy or bi-lobectomy (n=13). All were treated using RapidArc with risk-adapted fractionation schemes. Volume of the total lung(TL), ipsi-(IL) and contralateral lung (CL) receiving 50 Gy (V50) to 50 Gy (V50) with 5 Gy were calculated after converted dose biologically equivalent doses (α/β 3). These factors, mean lung dose (MLD) and clinical parameters were included in univariable and multivariable logistic regression to identify predictors of CTCAE v4.03 grade ≥ 3 RP. Concordance-statistics (C-statistic) were used to quantify the degree of association of the factors with high grade RP.

Results: Median follow-up of patients alive was 12.6 months (2.5-32.5). Median PTV was 150cc (13-411cc). Grade ≥ 3 RP was observed in 8 patients (10.1%), at a median time to onset of 6.1 months. In univariable analysis, CL-V5 (TL-V10), CL-TLV and IL-V35 as well as the ITV volume were all related with RP (all p-values <0.05). 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 ≥ 3.6 Gy (for 3 out of 8 patients) or if ITV size was ≥ 145 cc (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 nodes 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 nodes 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-III 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 pathologic 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 nodes (p=0.675) or contralateral hilar nodes (p=0.856) significantly impacted survival. Median survival was 19 months (95% CI 16-21.9 months) for stage II patients with contralateral hilar and/or supraclavicular lymph nodes and 21 months (95% CI 16-25.9 months) for other patients with stage I-II disease. In a multivariate Cox regression analysis including WHO-PS, age, gender, LDH, PCI, time between start of any treatment and the end of radiotherapy (SER), GTV, stage and having supraclavicular or contralateral hilar lymph nodes only WHO-PS (p=0.011), GTV (p=0.025) and delivery of PCI (p=0.001) reached significance. Patients with supraclavicular (p=0.997) or contralateral hilar lymph nodes (p=0.749) did not have a significantly worse prognosis.

Conclusions: In stage I-III SCLC staged with PET and treated with modern concurrent chemo-radiotherapy, 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: The new Dutch guideline on WBRT in patients with stage IV non-small cell lung cancer (IV NSCLC) was published on 30 January 2018. The guideline does not recommend WBRT for patients with brain metastasis. We hypothesized that with implementation of the new guideline, the percentage of patients treated with WBRT has decreased. The aim of this study was to analyze the impact of the new guideline on the patient selection for WBRT in a large cohort of patients with stage IV NSCLC.

Materials and Methods: We performed a retrospective analysis of all consecutive patients with stage IV NSCLC treated with curative intent between 2014 and 2016 in a single high-volume radiotherapy center in the Netherlands. The eligibility criteria for WBRT were defined according to the new Dutch guideline. The primary endpoint was the percentage of patients treated with WBRT.

Results: The study included 251 patients. In 2014, 90% (n=86) of patients were treated with WBRT. In 2015, 75% (n=56) of patients were treated with WBRT. In 2016, 67% (n=55) of patients were treated with WBRT. The decrease in the percentage of patients treated with WBRT was statistically significant (p<0.001). The median age of patients treated with WBRT in 2014, 2015, and 2016 was 69, 66, and 68 years, respectively. The median Karnofsky performance status (KPS) of patients treated with WBRT in 2014, 2015, and 2016 was 80, 75, and 80, respectively. The median number of brain metastases of patients treated with WBRT in 2014, 2015, and 2016 was 11, 9, and 9, respectively. The median number of extracranial metastases of patients treated with WBRT in 2014, 2015, and 2016 was 4, 3, and 4, respectively.

Conclusions: The new Dutch guideline on patient selection for WBRT in patients with stage IV NSCLC has decreased the percentage of patients treated with WBRT. This decrease is likely due to the new guideline, which does not recommend WBRT for patients with brain metastasis.