

patients. The plans allow geometrical ad-hoc adaptation to large interfractional deformations of patient geometry.

Materials and Methods: Patients with intermediate or high-risk prostate cancer are normally treated using VMAT technique with Simultaneously Integrated Boost at our department. The CTV is defined as the prostate and the base of seminal vesicles. The Boost (PTV) is obtained by expanding the CTV by 5 (10) mm. Prescription doses to PTV and Boost are respectively 60.1 and 74 Gy given in 33 fractions.

Our method of IMAT for prostate cancer uses three arcs. We analyze the geometry of the structures of interest (PTV and rectum), and generate segments to deliver three fluence steps: conformal (Step 0, first arc), sparing the rectum (Step 1, second arc), and narrow segments compensating for the underdosage in the PTV due to rectum sparing (Step 2, third arc). The width of Step 2 segments is calculated for every MLC leaf pair based on the PTV and rectum geometry in the corresponding CT layer to have best dose homogeneity. The segments are then fed into the DMPO engine of Pinnacle for weight optimization and fine-tuning of the form. We call this method '2-Step IMAT'. 2-Step IMAT and reference VMAT plans show highly equivalent target coverage, rectum sparing, and dosimetric quality, with 2-Step IMAT taking on average 230 sec to deliver vs 100 sec for VMAT.

We adapt 2-Step IMAT plans to changed geometry preserving the number of Monitor Units (MU) calculated for each segment at initial geometry. The leaves of Step 0 segments follow the edges of the PTV in Beam Eye View to keep PTV conformally irradiated. The leaves of Step 1 segments follow the edges of the rectum to keep it spared. For Step 2 segments, the opening of each leaf pair is adapted to the geometry change in the corresponding CT layer to have best dose homogeneity under the condition of MU preservation.

Results: Four adaptation cases have been considered. The ones having best and worst improvement of target coverage between relocated and adapted plan are shown in Fig.1 a,b and Tab. 1. The target coverage is measured by S_D index which sums up violations of dose requirements for Boost and PTV-Boost:

$$S_D = \sum_j \begin{cases} |(Obtained\ dose)_j - (Required\ dose)_j|, & \text{if requirement is violated} \\ 0 & \text{otherwise} \end{cases}$$

To characterize rectum sparing we measure absolute rectum volumes cut out by 95%, 80%, and 50%-isodose.

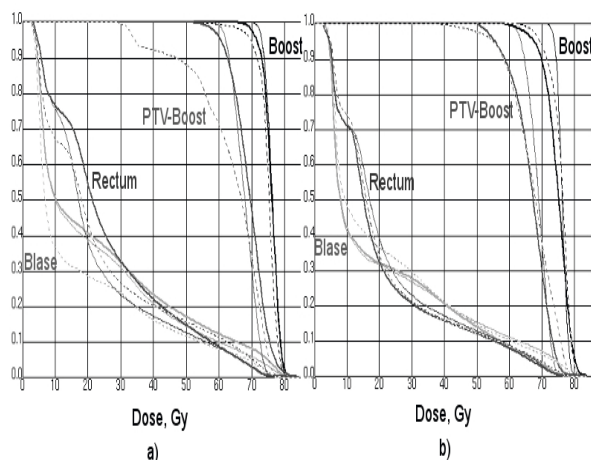


Fig.1. DVHs for the adaptation cases with the best (a) and the worst (b) target coverage: dotted - relocation, thin - new optimization, thick - adaptation.

	Required	Obtained					
		Best improvement of target coverage ($\Delta S_D = -56.9$ Gy)			Worst improvement of target coverage ($\Delta S_D = -0.8$ Gy)		
		relocated	new	adapted	relocated	new	adapted
Boost, Gy							
$D_{95\%}$	76.2Gy±1%	74.9	76.2	75.9	75.8	76.2	74.7
$D_{80\%}$	>70	62.5	71.6	68.7	65.2	72.5	61.3
$D_{65\%}$	74Gy±2%	69.7	73.0	71.4	69.2	73.8	67.5
$D_{50\%}$	<80	79.8	79.8	80.7	80.6	79.4	81.5
PTV-Boost, Gy							
$D_{95\%}$	>56	31.2	60.0	55.9	43.9	61.4	51.4
$D_{80\%}$	60.1Gy±2%	34.4	62.0	60.5	54.9	63.5	55.4
Rectum, ccm							
$V_{95\%}$		4.0	1.3	1.7	4.2	2.1	1.7
$V_{80\%}$		14.4	10.3	10.6	13.1	13.1	11.6
$V_{50\%}$		29.4	24.9	32.4	27	29.5	26.9
S_D , Gy		60.1	0.7	3.2	24.8	2.2	24

Tab.1. Evaluation for Fig.1.

Conclusions: The 2-Step IMAT method delivers prostate plans equivalent to the reference VMAT plans. On the expense of 2-3 longer delivery time 2-Step IMAT plans offer the possibility to adapt to large interfractional changes of patient geometry.

PROFFERED PAPERS: CLINICAL 2: LUNG AND HEAD & NECK

OC-0138

Phase III study of concurrent cisplatin with pemetrexed or vinorelbine and RT for unresectable stage III NSCLC

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Purpose/Objective: Concurrent chemoradiotherapy has been a standard treatment for good performance status patients with unresectable stage III non-small cell lung cancer (NSCLC). However, the toxicities were not neglected. To evaluate pemetrexed in combination with cisplatin in these patients, a randomized phase III study of concurrent cisplatin with pemetrexed or vinorelbine and late course accelerated hyperfractionated radiotherapy (LCAHRT) was performed.

Materials and Methods: Total of 86 patients were randomly assigned to two concurrent regimens before March 2012. Arm1 included cisplatin at 25 mg/m² on days 1-3, 22-24 and vinorelbine at 25 mg/m² on days 1,8 and 22,29 with concurrent late course accelerated hyperfractionated radiotherapy. Arm 2 used cisplatin at 25 mg/m² on days 1-3, 22-24 and pemetrexed at 500 mg/m² on days 1 and 22 with the same radiotherapy protocol. The primary endpoint was overall survival (OS), and secondary endpoints included toxicities. Kaplan-Meier analyses were used to assess survival, and toxic effects were examined using the Pearson Chi-Square test. All statistical tests were two-sided.

Results: 84 patients were analyzed for 2 patients in arm 1 were not finished treatment according to the protocol. The mean radiation dose in arms 1-2 was 66.2±7.5 Gy and 67.9±7.4 Gy. 76 patients used 2 cycle concomitant chemotherapy, 4 cases 3 cycles, and 4 ones 1 cycle (3 in arm 1 and 1 in arm 2). Median OS were 23 and 25 months for arms 1 and 2, respectively (p=0.224). Concerning toxicities of grade 2 or more in the arms 1 and 2, the white blood cell was 32/41 and 20/43 (p=0.003), esophagitis 14/41 and 10/43 (p=0.269), pneumonitis 8/41 and 6/43 (p=0.494), vomiting 13/41 and 9/43 (p=0.261), hemotoblatin 8/41 and 5/43 (p=0.318), platelet 9/41 and 5/43 (p=0.204), respectively.

Conclusions: Concurrent cisplatin with pemetrexed and LCAHRT was as effective as with vinorelbine for unresectable stage III non-small cell lung cancer, however, the treatment compatibility was better.

OC-0139

SBRT for stage I NSCLC: patterns-of-care and outcome analysis in Germany and Austria between 1998 and 2011

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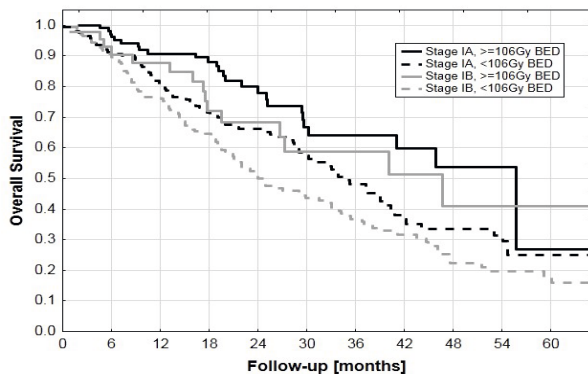
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Purpose/Objective: To evaluate patterns-of-care and patterns-of-outcome after stereotactic body radiotherapy (SBRT) for stage I non-small cell lung cancer (NSCLC).

Materials and Methods: The working group 'Extracranial Stereotactic Radiotherapy' of the German Society of Radiation Oncology (DEGRO) performed a multi-center analysis of practice and outcome after SBRT for stage I NSCLC: 16 German and Austrian centers with experience in pulmonary SBRT were asked for participation.

Results: Data of 582 patients treated in 13 institutions between 1998-2011 were collected; all but one institution were academic hospitals. In 2010, the last full year covered in this analysis, 95 patients in total were treated with SBRT. The median number of patients per institution was 39 (range 8-110) and the median number of patients per institution and year was 5 (range 1-29). Median patient age was 72 years (range 31-92) and median pre-treatment FEV1 was 58% (range 16-129%). Median maximum tumor diameter was 2.5cm. NSCLC was biopsy confirmed in 84.5% of the patients. A time trend to more advanced radiotherapy technologies (nodal staging using FDG-PET, advanced type B dose calculation algorithm, in-room image guidance) was observed. The PTV encompassing dose was increased continuously and reached a plateau of 94Gy±26Gy BED ($\alpha/\beta=10\text{Gy}$) on average in 2006-2011. Patient characteristics (age, performance status, pulmonary function) remained stable over time. Inter-institutional variability was substantial in all treatment characteristics. In contrast, there was no inter-institutional variability in pre-treatment patient age and pulmonary function. After average follow-up of 21 months, three-years freedom from distant recurrence (FFDR), regional recurrence (FFRR) and local progression (FFLP) were 63.4%, 75.4% and 79.6% for all 582 patients, respectively. Three-years overall survival (OS) was 47.1%. The biological effective dose (BED) was the most significant factor influencing all patterns of failure and OS in uni- and multivariate analysis. After $\geq 106\text{Gy}$ BED as planning target volume encompassing dose ($n=164$), three-years FFDR, FFRC, and FFLP were 74.8%, 90.4% and 92.5%, respectively; three-years OS was 62.2%. The figure below shows OS depending on stage and irradiation dose.



No evidence for a learning curve of improved results with larger SBRT experience or practice was observed. Radiation induced pneumonitis grade ≥ 2 was observed in 7.4% of the patients and grade 5 pneumonitis was documented in only two patients. Thirty day mortality after SBRT was 0.5% ($n=3$).

Conclusions: After irradiation doses $\geq 106\text{Gy}$ BED, favorable and consistent outcome after SBRT for stage I NSCLC was observed in this multi-institutional analysis despite substantial time-trends and inter-institutional variability in the methodology of SBRT.

OC-0140

A prospective study to compare doctor versus model predictions for outcome in lung cancer patients: pick the winner!

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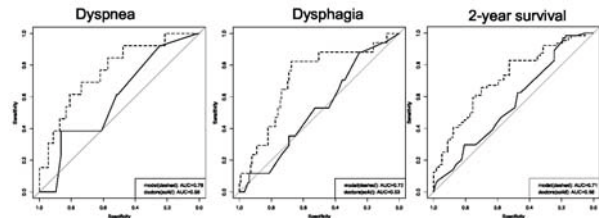
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Purpose/Objective: Despite the increasing number of decision making tools, many are not used in daily clinical practice. Implementation might be stimulated if it is obvious that models can offer valuable extra information. We previously reported that prediction models outperformed physicians' predictions based on chart review. However, physically seeing a patient provides the doctor with extra information. The purpose of this prospective study was to compare predictions

based on statistical models to predictions made by the physicians after they had seen the patient.

Materials and Methods: Based on the performance of already published and validated prediction models for lung cancer, we hypothesized that these models would outperform the doctors' prediction by at least 0.1 in Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC). The required sample size for the primary outcome, 2-yr survival, was 128 patients. Model predictions were obtained and experienced radiation oncologists were asked to predict 2 year survival, dyspnea (\geq grade III) and dysphagia (\geq grade III) at two time points: 1) after they had seen the patient for the first visit, and 2) after the treatment plan was made. For survival prediction NSCLC patients, stage I-IIIb, were included; for dyspnea and dysphagia both NSCLC and SCLC were included. All patients were treated with radiotherapy with or without chemotherapy, did not have surgery, no other tumor <5 years ago, and no distant metastasis. We compared the performance of the models to the doctors' in terms of AUC. To gain more insight in the benefit of using predictions in clinical practice we analysed the positive (PPV) and negative predictive value (NPV) for all possible cut-off values of the probabilities. In addition, Kaplan Meier curves based on TNM stage were made.



Results: At time point 1 the doctors predicted outcome for 121, 139 and 146 patients (2-yr survival, dyspnea and dysphagia respectively). The AUCs of the doctors were 0.56, 0.59 and 0.52, while the models yielded AUCs of 0.71, 0.76 and 0.72, with p-values for difference in AUC of 0.02, 0.06 and 0.03 respectively. The Kaplan Meier curves based on TNM stage could not identify survival risk groups ($p=0.33$). Predictions at time point 2 were only available for 35, 39 and 41 patients (survival, dyspnea and dysphagia). Results were in line with those at time point 1. The PPVs of the models were generally higher, while the NPVs of doctors and models were comparable, indicating that the models could better identify high risk patients.

Conclusions: Prediction models for lung cancer patients substantially outperformed the physicians' prediction for all outcomes. The difference between doctors and models did not decrease after the doctors had seen the treatment planning. The models were especially superior in identifying high risk patients and should therefore be implemented in clinical practice to guide decisions.

OC-0141

Reduction of the dose to the elective CTV in HNSCC using IMRT. Dosimetrical analysis and effect on acute toxicity.

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Purpose/Objective: Radiation induced toxicity is an important issue in head and neck cancer patients. With the introduction of IMRT into daily practice we are able to minimize doses to organs-at-risk while maintaining adequate tumor coverage. However, the commonly used elective nodal site doses might result in neck fibrosis and dysphagia. The goal of this randomized, multicenter trial was to investigate whether a reduction of the dose to the elective nodal sites and off-target regions of the swallowing apparatus delivered by IMRT would result in a reduction of both acute and late side effects without compromising tumor control.

Materials and Methods: Two-hundred patients with histologically proven head and neck squamous cell carcinoma were randomly assigned to the standard and experimental arm. In the standard arm the elective nodal volumes ($\text{PTV}_{\text{elective}}$) were irradiated up to an equivalent dose of 50Gy in 2 Gy fractions. In the experimental arm an equivalent dose of 40Gy in 2 Gy fractions was delivered to the nodal volumes and the dose to the swallowing apparatus was kept as low as reasonably possible without compromising coverage of the therapeutic PTV (PTV_{ther}). Toxicity was recorded using CTCAE v3.0 weekly during