Material and Methods: Eligibility criteria were age ⩽80 years, PSA ⩽ 50 ng/ml, N0M0 and either tumour stage cT2a (1997 UICC TNM) or cT1b-c combined with PSA⩾10 ng/ml and/or Gleason score ⩾7.
We report toxicity for all eligible patients who received the planned RT with documented acute toxicity (CTCAEv.2) and RT-quality assurance parameters. The RT dose (70 Gy, 74 Gy or 78 Gy) and technique (3D-CRT vs IRMT) were per institution choice, the randomization was stratified for institution. Statistical significance was set at 0.05. (ClinicalTrials.gov: NCT00021450)
Results: Of 819 randomized patients, 28 were excluded from the analysis (3 with <60 Gy RT, 25 with missing information). Of the 791 analysed patients, 652 (82.4%) were treated with 3D-CRT, 139 with IMRT. In the 3D-CRT group, 195 patients (29.9%) were treated with a total prescribed dose of 70 Gy; 376 (57.7%) with 74 Gy and 81 (12.4%) with 78 Gy. In the IMRT group, 28 (20.1%) were treated to a total dose of 74 Gy and 111 (79.9%) with 78 Gy.
Overall, only 7 of 791 patients (0.9%) had grade 3 GI toxicity during RT: diarrhea (N = 6), rectal bleeding (N = 1) and proctitis (N = 1). Fifty patients (6.3%) had grade 3 GU toxicity: urinary frequency (N = 38, 4.6%), dysuria (N = 14, 1.7%), urinary retention (N = 11, 1.3%), urinary incontinence (N = 2) and hematuria (N = 1). No grade 4 toxicity was reported. Hormonal treatment did not influence the risk of side effects (p>0.05). The risk of grade ⩾2 GI toxicity significantly correlated to D50%-rectum (p = 0.004) with a cut-of value of 44 Gy. The risk of grade ⩾2 GU toxicity was moderately affected by Dmax-bladder (p = 0.051). Overall, only 14 patients (1.8%) had residual grade 3 toxicities one month after RT.
Conclusion: 3D-CRT and IMRT up to 78 Gy is well tolerated. Dmax-bladder and D50%-rectum were related to the risk of grade⩾2 GU and GI toxicity, respectively. IMRT lowered D50% rectum and Dmax-bladder. An irradiated volume >400 cc for 3D-RT and a dose of 78 Gy, even for IMRT, negatively affected those parameters and increased the risk for toxicity.

2002 ORAL

Development and external validation of a nomogram for prediction of radiation-induced dysphagia in 493 lung cancer patients treated with chemo-radiotherapy or radiotherapy alone

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Background: Acute dysphagia is a distressing dose-limiting toxicity occurring frequently during concurrent chemo-radiation or high-dose radiotherapy for lung cancer. It can lead to treatment interruptions and subsequently jeopardize tumor control. Although a number of predictive factors associated with dysphagia have been identified it is still not clear how these factors should be used in daily clinical practice and how they could offer assistance for treatment decision making. We have therefore developed and validated a nomogram to predict acute severe dysphagia in lung cancer patients who are receiving (chemo)radiotherapy.
Material and Methods: Clinical data from 493 lung cancer patients, treated with curative intent with chemo-radiation (CT-RT) or radiotherapy (RT) alone were collected. An ordinal regression analysis was performed to predict severe acute dysphagia (according to the CTCAEv3.0). The start model consisted of age, gender, World Health Organisation performance status (WHO-PS), mean esophagus dose, maximum esophagus dose, overall treatment time (OTT), radiation once (QD) or twice daily (BID) and chemotherapy. Odds ratios (OR) were reported. The final model was validated using bootstrap techniques as well as an external dataset from Ghent University (n = 117). The performance of the model was expressed as the C-statistic. The interpretation is similar to the interpretation of the Area Under the Curve (AUC) of the Receiver Operator Curve (ROC). The maximum value of the C-statistic is 1.0; indicating a perfect prediction model. A value of 0.5 indicates that patients are correctly classified in 50% of the cases, e.g. as good as chance. In addition, the results of the multivariate analysis were used to develop a nomogram.
Results: Fifty-three patients (11%) developed acute severe dysphagia ⩾grade III. The final model consisted of mean esophagus dose (OR 1.06, p < 0.0001), maximal esophagus dose (OR 1.04, p < 0.0001), OTT (OR 0.94, p < 0.0001), chemotherapy treatment (OR sequential 1.02, OR concurrent 2.86; p < 0.0001) and gender (female OR 1.99; p = 0.0003). The C-statistic was 0.77 (0.76 internal validation). External validation using the dataset from Ghent yielded a C-statistic of 0.86.
Conclusions: The performance of the model, C-statistic of 0.76, was good. In addition, external validation yielded a C-statistic of 0.86 and was thus successful. The nomogram could be used in clinical practice to identify patients at high risk for developing severe acute dysphagia.

2003 ORAL

Angiotensin converting enzyme inhibitors (ACE-I) protect against the clinical and radiological manifestations of radiation pneumonitis (RP) in patients undergoing radical radiotherapy for lung cancer

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Background: Previous laboratory investigations have highlighted a possible role of the renin angiotensin system in the pathogenesis of RP. ACE-I have also been shown to reduce radiation pneumotoxicity in animal studies. However a previous clinical study, which predates modern 3-dimensional treatment techniques, did not find an association between these agents and the development of RP.
Material and Methods: The records of 145 patients (pts) who had undergone radiotherapy for stage I-III NSCLC were reviewed. Median age 70, male:female 102:43, induction chemotherapy administered in 52. All pts were treated with a single radiotherapy dose, 54 Gy in 36 fractions over 12 days (CHART). 3-dimensional conformal treatment was used in all cases. Medications taken at the time of treatment were noted. 19 pts were taking ACE-I for hypertension or congestive cardiac failure. The development of RP was recorded prospectively using the RTOG criteria. All pts had a diagnostic CT scan performed 3 months following completion of RT. Radiation induced radiographic abnormalities within the lung were graded using the system of Libshitz and Shuman (G0 = no change, G1 = 'ground glass' changes, G2 = patchy consolidation, G3 = confluent consolidation)
Results: In total 24 (17%) pts developed clinical RP ⩾G3 (requiring steroids). Radiographic intrapulmonary abnormalities were seen in 92 (63%). These were grade as: G1 – 15 (10%), G2 – 19 (13%) and G3 – 58 (40%). The association of lung injury and medication with ACE-I is shown in the table.

	ACE-I	No ACE-I	p-value
Clinical RP ⩾G2	0/19 (0%)	24/126 (19%)	0.037
Radiological injury ⩾G2	2/19 (11%)	75/126 (60%)	<0.001
V_{20} (mean)	19.1%	20.9%	0.33
Mean lung dose (mean)	10.6 Gy	11.4 Gy	0.37

Conclusions: In this series of pts treated in the modern era, ACE-I appear to offer significant protection against radiation induced lung injury. Their use as pulmonary radioprotectants warrants further investigation. The results of the randomised RTOG trial (0123) are awaited with interest.

2004 ORAL

Intraperitoneal delivery of Chitosan/siRNA nanoparticles targeting TNF-a prevents radiation-induced fibrosis

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Introduction: Ionizing radiation therapy plays a pivotal role in cancer treatment but one of the most common long-term adverse effects of ionizing radiotherapy is radiation-induced fibrosis (RIF). Recent studies suggested Tumor Necrosis Factor (TNF-a), produced by macrophages might promote radiation-induced fibrosis.
This work describes intraperitoneal delivery of chitosan/siRNA nanoparticles targeting TNF-a as prevention for radiation-induced fibrosis. CDF1 mice treated with TNF-a siRNA at least until day 22 after radiation did not develop fibrosis whereas the control groups treated either with buffer or mismatch siRNA develop severe fibrosis.
Experimental Methods: Chitosan was dissolved in sodium acetate buffer (0.2 M NaAc, pH 4.5) to obtain a 1 mg/ml solution and then adjusted to pH 5.5. 20 μl of siRNA (100 μm) in nuclease free water was added to 1 ml of filtered chitosan (1000 μg/ml) whilst stirring and left for 1 h.
Male CDF1 mice were divided into 9 groups of 3. Except of the control group with no treatment, all mice received a single irradiation dose of 45 Gy. Mice were i.p. dosed with 200 μl of chitosan/siRNA nanoparticles (5 μg TNF-a siRNA and 5 μg mismatch siRNA) 2 days before irradiation or 1 day after irradiation. The chitosan/siRNA nanoparticles treatment was continued twice a week and terminated on days 10, 22, 34 and 258.
The irradiated hind leg of the mice was scored for clinical symptoms of radiation-induced fibrosis by using the leg contracture model.
Results: The irradiated hind leg of the mice was scored for clinical symptoms of radiation-induced fibrosis by using the leg contracture model for level of severe fibrosis (scale: 0 = normal, 1−2 = mild to moderate