1144 POSTER

Radiation pneumonitis risk with clinical and dosimetric correlations

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Background: The purpose of this study was to examine clinical and dosimetric parameters which correlate with the risk of developing clinically significant radiation pneumonitis (RP) in patients receiving thoracic radiotherapy.
Materials and methods: The records of 99 consecutively treated patients were reviewed. Eligible patients had a malignant lung neoplasm and received conventionally fractionated radiotherapy, either with or without concurrent chemotherapy. Demographic and clinical data were recorded as was the incidence of RP within 6 months from the end of radiotherapy. RP was defined according to the NCI Common Toxicity Criteria version 2.0 pulmonary toxicity scale $\geqslant$grade 2 pneumonitis. Dose-volume histograms were calculated from plans generated with and without heterogeneity corrections for doses to the total lung volume (TL) and TL minus intrapulmonary gross tumor volumes (TL-G). The development of RP was correlated with mean lung dose (MLD), the effective lung volume (Veff), and the percent of total lung (TL or TL-G) receiving greater than, or equal to 10, 13, 15, 20, and 30 Gray (Gy). Logistic regression analysis was performed and p-values of $\leqslant$0.5 were considered statistically significant. Receiver operating characteristic curves were generated and a table to estimate RP risk was constructed.
Results: of 99 reviewed patients, 6 were excluded due to incomplete follow-up and 1 due to death (due to cerebrovascular accident) during radiotherapy. Twelve cases of RP were identified in the remaining 92 patients. The variables significantly correlated with RP were MLD, V10, V13, V15, V20, and Veff. MLD lost significance using TL-G without density correction and V20 and Veff lost significance when intraparenchymal GTV was subtracted from TL. ROC analysis found V10 and V13 the best predictors of RP risk. No baseline clinical or demographic factors were significant correlates with RP.
Conclusions: Clinically relevant radiation pneumonitis is an uncommon side-effect of radiotherapy whose incidence is significantly correlated with MLD, V10, V13, and V15. This correlation is more statistically significant when DVH parameters are calculated using heterogeneity corrections and TL-G. The delivery of intrathoracic radiotherapy should be planned with caution, especially when utilizing intensity-modulated radiotherapeutic techniques which may deliver low, but clinically relevant, doses of radiation to larger lung volumes.

1145 POSTER

Accelerated hypofractionation for early stage non-small cell lung cancer (NSCLC): results of patients treated with 3D conformal radiotherapy alone

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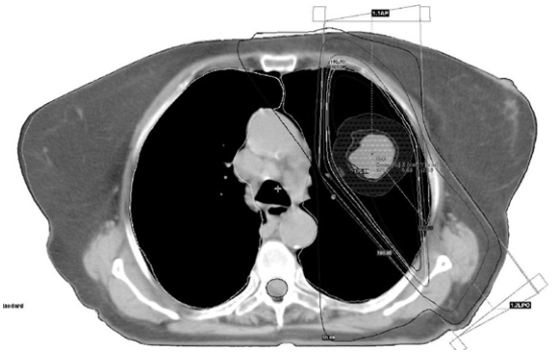
Purpose/Objective: Accelerated hypofractionated radiotherapy (AHRT) is an attractive option for patients with early stage NSCLC unfit for surgery because it may overcome repopulation in rapidly growing tumors, as is the case for non-small cell lung cancer. Furthermore, it is more convenient for sick/elderly patients who have difficulty with numerous daily hospital visits. It can also lead to a reduction in health care costs. We report our preliminary results with this approach.
Material/Methods: Between August/2002 and May/2004, 32 patients with clinical stage I NSCLC (T1 and T2), who were deemed by their treating physician to be unfit for surgery, were treated with curative AHRT, with 3D conformal planning using 18 MV photons. Inspiratory motion was monitored by fluoroscopy or electronic cine-portals in all patients. PTV encompassed the radiologically visible tumor with an additional 10−15mm margin in all directions. Planning ensured that the esophagus and spinal cord received <50% of total dose. Fractionation of 52.5 Gy in 15 daily treatments of 3.5 Gy given over 3 weeks was chosen. This is considered to be biologically equivalent to 76 Gy in 38 fractions of 2 Gy given over 8 weeks. The dose was prescribed in the isocenter without lung correction for inhomogeneity. Acute and late toxicity was prospectively evaluated using the RTOG/CTC morbidity criteria. Radiographic abnormalities alone in asymptomatic patients were not considered to represent late toxicity. Local control was evaluated with chest x-rays and CT scans performed every 3 to 6 months.
Results: There were 23 males and 9 females with a median age of 76 years. Fifteen patients were staged as T1 and 17 as T2. The median PTV volume was 150 cc. The median V20 of both lungs was 13%. In 22 patients the tumor was located in the upper lobes. Radiotherapy planning included two fields in 17 patients (Figure) and 3 fields in 13. The acute toxicity was minimal. Two patients experienced lung toxicity (one grade 1 and another grade 2) and 3 patients sustained grade 1 acute esophagitis. There was no skin toxicity observed. To date, no late toxicity has been observed. As of May 2005, with a median follow-up of 16 months, 11 patients have died but only 3 of these had demonstrated a component of local cancer progression. Actuarial 1 and 2 year overall survival is 79.2% and 59.1%, cancer specific survival (CSS) is 91.3% and 81.1%, and local relapsefree survival is 100% and 80% respectively.



Conclusions: AHRT using 52.5 Gy in 3 weeks, given with 3D conformal planning, appears to be safe and well tolerated in NSCLC patients with severe co-morbid diseases. It shortens by half the traditional treatment duration. Preliminary CSS is encouraging but further follow-up is needed to evaluate long-term outcome.

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Chemotherapy of topotecan combined with paclitaxel in advanced or metastatic non-small cell lung cancer

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Background: There are several trials that combine new non-cisplatinum agents for the treatment of advanced non-small-cell lung cancer (NSCLC). One of these agents is topotecan, which is mainly used in SCLC and ovarian cancer and very little tested in NSCLC. Having the experience based on a phase I-II trial we combined Topotecan with paclitaxel in a phase II trial with weekly administration. Objectives were mainly the response rate and secondary, safety and duration of response.
Material and Methods: From September 2003, till March 2005, 45 patients entered in the study. They were all diagnosed by cytology or histology as NSCLC, adenocarcinomas, squamous cell and undifferentiated of stage IIIb and IV. There were 35 males 10 females of median age 65 (range 48−80). Performance status (WHO) 0−2. All patients were chemotherapy naïve. Treatment: Both agents were infused on day 1 repeated once every week for three consecutive weeks every 28 days. Three infusions were considered as one course. The treatment plan was to give 3 courses (9 infusions) and then to evaluate the response. Drug dosis was of topotecan 1.75 mg/m^2 infused for 30 min. and of Paclitaxel 70 mg/m^2 infused for 90 min. These doses were established as MTD in the previous phase I trial. Total number of courses were 115, 25 patients had 3 courses each and 20 patients had 2 courses each. Toxicity: Treatment was quite well tolerated. Neutropenia of Grade III was observed in 6 patients, thrombocytopenia grade II in 2 patients, Anemia in 3 patients. The non-hematological side effects seen were asthenia, nausea, allergy, neuropathy, alopecia in a small minority of the patients.
Results: Out of 45 patients 18 (40%) responded, 3 with CR (6.66%) and 15 with PR (33.33%). 22 had stable disease (48.88%) and 5 patients disease progression (11.11%). The median duration of response was 6 mo (2−10+) and TTP median 7 months (3−9).
Conclusion: The novel combination of Topotecan-Paclitaxel in a weekly administration is quite active with a 40% RR and with very low toxicity in untreated patients, stage IIIb-IV of NSCLC.