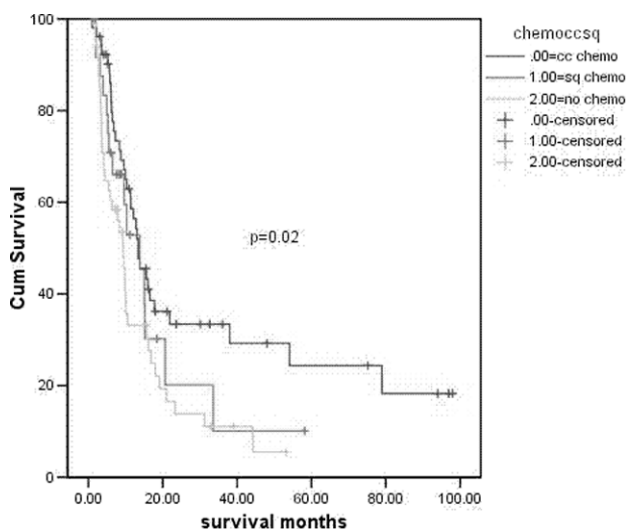


and B2: <130 patients), and conducted an extramural audit survey for 627 stage I-III NSCLC patients.

**Results:** Ninety-nine (16%) NSCLC patients had received PORT between 1999 and 2001. The median age was 65 years (range, 39–82). The preceding surgery was pneumonectomy in 12%, lobectomy in 79%, and segmentectomy in 9%. Histopathology was squamous cell carcinoma in 46%, adenocarcinoma in 43%, large cell carcinoma in 7%, and adenosquamous carcinoma in 2%. The clinical stage was stage IA in 14%, IB in 13%, IIA in 7%, IIB in 7%, IIIA in 42%, and IIIB in 16%. Location of the primary tumor was the upper lobe in 63%, the middle lobe in 7%, and the lower lobe in 28%. Predominantly involved mediastinal nodes were 7 (34%), 4 (34%), 5 (28%), and 3 (26%) according to the mapping system of Japan Lung Cancer Society. The pathological stage was stage I in 8%, II in 17%, IIIA in 44%, and IIIB in 20%. The median field size of PORT was 9×11 cm, whilst the median total dose was 50 Gy. The photon energy of ≥6 MV was used for 71% of patients in A1, 78% in A2, and 80% in B1, whereas only 23% in B2 institutions ( $p < 0.0001$ ). The planning target volume included the contralateral mediastinum for more than 70% in A1 to B1 institutions, whereas only 46% in B2 ( $p = 0.011$ ). Thirty patients (31%) received systemic chemotherapy. For 70% of these patients, chemotherapy and PORT were administered concurrently, mainly using platinum based 2-drug combination. For 9 patients, platinum-based chemotherapy was used as an induction therapy. Oral fluorouracil was used in 9 patients. First failure sites were local in 6, regional in 5, and distant metastases in 31, with a median time to first failure of 7 months. Overall survival 3-year for the entire group was 63%.

**Conclusions:** During the study period, PORT was used mainly for pathologic stage III NSCLC. Obsolete equipments such as Cobalt-60 unit were still used, especially in non-academic institutions treating small patient number/year.



Survival functions

1142

POSTER

**Radiation pneumonitis following combined modality therapy in the treatment of locally advanced non-small cell lung cancer (LAD-NSCLC) including three-dimensional conformal radiation therapy (3D-CRT): analysis of clinical and dosimetric prognostic factors**

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**Background:** Radiation pneumonitis is the most prominent dose-limiting complication in LAD-NSCLC irradiation. 3D-CRT is a high precision radiation technique that represents a significant advance in the delivery of radiotherapy for LAD-NSCLC, minimizing the exposure to the surrounding normal tissues. This study attempted to identify clinical and dosimetric parameters associated with the development of severe radiation pneumonitis (RP) in patients (pts) with LAD-NSCLC treated with combined modality therapy.

**Material and methods:** 80 pts (72 males and 8 females; median age: 58 years, range: 32–78) with stage IIIA (20%) and IIIB (80%)

NSCLC treated between April 1995 and March 2001 with cisplatin-based induction chemotherapy (IQT) followed by concurrent chemotherapy and hyperfractionated 3D-CRT (1.2 Gy b.i.d.; median dose: 72.41 Gy, range: 54.13–85.89), were evaluated retrospectively. Acute and late (>3 months) RP were scored using the RTOG classification. Potential predictive factors evaluated included clinical parameters (sex, age, performance status, stage, histology, weight loss >5%, tumor site, pre-existing lung disease), therapeutic factors (IQT schedule, 3D-CRT dose, treatment response), and dosimetric factors according to the ICRU definitions (volume and dose of GTV, PTV-2, CTV and PTV-1; pulmonary V20, V30, mean lung dose (MLD) and normal tissue complication probability (NTCP)). The lungs were defined as a whole organ. Univariate and multivariate analyses were performed.

**Results:** All pts were evaluated for acute RP and 78 pts could be evaluated for late RP. RP (early and late) grade ≥3 occurred in two pts (2%) and 10 pts (12%), respectively. Five pts (6%) died of pulmonary toxicity, with 3 of them having pre-existing moderate-severe cardiopulmonary disease. The median time to diagnosis of late RP was 4.5 months (range: 3–8). Multivariate analysis showed that, pre-existing lung disease (*Odds ratio* = 10.12,  $p = 0.01$ ) and NTCP >30% (*OR* = 10.54,  $p = 0.007$ ) were independently associated with late pulmonary toxicity grade ≥3. The incidence of RP grade ≥3 for pts with pre-existing lung disease and/or NTCP >30% was 25% vs. 4% for pts without pre-existing lung disease or NTCP <30% ( $p = 0.01$ ). The risk of severe RP was higher for pts with pre-existing lung disease and/or NTCP >30% (*Odds ratio* = 7.33; I.C. 95% = 1.44–37.33,  $p = 0.016$ ).

**Conclusions:** In this study, pre-existing lung disease and NTCP were the best predictors of late severe pulmonary toxicity (grade ≥3), and should be evaluated in all patients undergoing high-dose 3D-CRT prior to treatment.

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POSTER

**Lung and heart toxicity analysis of a combined 3D high dose chemoradiation protocol. Recommendations for further studies**

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**Background:** This work analyzes the toxicity of lung and heart irradiation in patients (pts) presenting with a NSCLC, treated with 3D conformal therapy (74 Gy), in terms of relationship between  $V_{20}$  and the incidence and grade of radiation pneumonitis (RP), as well as the assessment of heart events. The ultimate goal is to elaborate recommendations for a future escalation dose phase I trial, based on the observed toxicities.

**Patients and Methods:** Fifty pts, 41 men, 9 female, median age 63 years (27–80), stage I/II 7%, IIIA 51% and IIIB 42%, squamous carcinoma 58%, adenocarcinoma 24%, large cell undifferentiated 12% and neuroendocrine 6%, have been treated between June 1998 and April 2002. Radiotherapy delivered a mean dose of 72 Gy (range 68–74 Gy), using 3D conformal therapy (2 Gy/day, ICRU point, 5 days/week). The mean PTV was 648 cc (range 220–1876), the mean lung  $V_{20}$  38% (range 19–68%),  $V_{25}$  31%,  $V_{30}$  27.5%. Thirty nine pts (78%) received platinum-based chemotherapy, as an induction (25 pts) and/or as a concurrent (14 pts) scheme. Acute toxicity was scored according to the NCI criteria, late effects using the SOMA/LENT scoring system.

**Results:** Eight pts experienced a grade 3–4 acute lung toxicity, all of them had a  $V_{20} \geq 25\%$ , 3 of them presented a late grade 3 fibrosis, with a  $V_{20}$  superior 35%. Pts with low FEV1 (<1.5l) presented more frequently a lung toxicity without clear correlation. Three pts died of acute cardiac failure during the first 3 months of the treatment. Grade 4 acute heart toxicity occurred in 1 pt, G3 esophagitis in 3 pts. Eighteen months complete response rate was 45%, median overall survival time 17.3 months, the 12 and 24 months overall survival rates 72% and 37% respectively. A local failure occurred in 55% of pts, either as sole site (21%) or as a component of distant failure. Metastatic rate is 49%, with 18% brain metastases. Four patients are still alive.

**Conclusions:** The results show a relationship between the  $V_{20}$  value and the risk for occurrence of radiation induced lung toxicity. Parameters like FEV1, and  $V_{20}$ ,  $V_{30}$  for heart and lung will be integrated in the dose level choice of the future protocol. The heart toxicity is highly difficult to precisely assess, late deaths are rarely documented, responsibility of the treatment is often under-estimated, in smoking patients. These results form a basis for an escalating dose phase I trial, which is under elaboration, integrating these predictive toxicity parameters.