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Conformal radiotherapy in radical treatment of stage III non-small cell lung cancer (nsclc)

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Background: Radiotherapy alone or combined with chemotherapy is standard treatment for stage III non-small cell lung (NSCLC) cancer. Conventional schedules of radiotherapy reach doses higher than 40 Gy trying to offer a better survival in these patients. Our objective was to evaluate the overall survival in a population of patients that received 3D conformal external radiotherapy with conventional doses and fractionation schedules.
Materials and Methods: Between 2002 and 2006 75 patients with NSCLC stage III (A/B) were treated in our institution with external radiotherapy (virtual simulation and 3D planning). None of the patients underwent surgery before or after radiotherapy. 70 patients received different schemes of chemotherapy. Aged ranged between 43−83 years. Radiotherapy treatment planning was developed with isocentric and multiple field technique. Total doses were from 42 to 65 Gy, fractionation 1.8−2.0 Gy. Chemotherapy was also administered in 68 of them.
Results: At the end of the study (84 months of follow-up), only 6 patients still alive (8%). Mean survival was 16 months; median, 13m. The value more frequent was 7 months. Survival between 0−6 months was 29%; 6−12 m: 16%; 12−18m: 28%; 18−24m: 12%; >24 m: 15%. 17 patients received doses between 42−50 Gy, with mean survival: 19 m (median: 15); 44 patients, doses = 50−60 Gy, mean survival: 13 (median: 11); 13 patients, doses higher than 60 Gy, mean survival: 25m (median: 21). These results were not comparable because of the different and little number of patients of the groups.
Conclusions: Radical radiation treatment with high doses and conventional fractionation in NSCLC stage III in our institution gives a survival less than 2 years in the majority of patients. We could not observe differences in survival according different total doses because of the little number of patients. Further studies and more patients analyzed could give us more information about this question in order to increase these total doses.

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Role of postoperative radiotherapy for advanced stage non-small cell lung cancer

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Purpose: To evaluate outcomes and prognostic factors of postoperative radiotherapy (PORT) for patients with advanced stage non-small-cell lung cancer (NSCLC) at our institution.
Methods and Materials: From 2000 to 2007, 88 patients had PORT after curative operation for pathologic stage III NSCLC at our institution. At diagnosis, median age was 59 years (range 31−81). There were 80 patients in stage IIIA and 8 patients in stage IIIB. Preoperative nodal stage was as follows: 45 patients in N0, 8 patients in N1, and 35 patients in N2. Among 35 preoperative N2 diseases, 21 patients had single station mediastinal lymph node (LN) metastasis. Eighty three patients had postoperative N2 disease, and 56 patients had single station mediastinal LN metastasis. Surgical types included pneumonectomy (N = 14), bilobectomy (N = 14), or lobectomy (N = 60) with mediastinal lymph node dissection (MLND) (N = 73) or multi-level mediastinal lymph node sampling (N = 15). Seventy six patients had received radiotherapy using conventional technique. Initially 23.4−56 Gy (median 45 Gy) was delivered to mediastinum and bronchial stump area and then tumor bed received additional 3.6−23.4 Gy (median 9 Gy). Thirty six patients had received chemotherapy; 17 patients with adjuvant, 5 patients with neoadjuvant and 14 patients with both.
Results: Median survival was 54 months. 5-yr overall survival (OS) and disease free survival (DFS) rates were 45% and 38% respectively. MLND, total radiation dose greater than 54 Gy and adjuvant chemotherapy did not affect OS (p-value = 0.9525, 0.4160, and 0.8956, respectively). Single station mediastinal LN metastasis is associated with increase in DFS (p-value = 0.0014). 5-yr loco-regional recurrence free survival (LRFS) and distant-metastasis free survival (DMFS) rates were 86% and 48% respectively. Fifty-one relapses occurred at following site: 10 in loco-regional, 11 in lung, 11 in bone, 10 in brain, 4 in kidney, adrenal gland, 3 in non-regional LN, and 2 in liver. Of 10 loco-regional relapses, 6 relapses occurred in radiation field. Total radiation dose greater than 54 Gy did not reduce loco-regional recurrence (p-value = 0.6376). Administration of chemotherapy had no significant effect on distant metastasis (p-value = 0.5583).
Conclusion: PORT after curative operation for resectable advanced stage NSCLC may reduce loco-regional recurrence and increase overall survival. However, criteria for resectability of stage III disease should be further defined because of heterogenous presentation of advanced stage NSCLC. Further efforts are necessary to reduce distant metastasis.

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Is there any future of prophylactic cranial irradiation in adenocarcinoma of the lung?

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Background: In this study, we aimed to evaluate the rate of cranial metastases in nonsmall cell-nonsquamous lung cancer patients(NSCLC-NS), refractory to first line platinum based therapy, comparing with small cell lung cancer(SCLC) patients. We argued the role of prophylactic cranial irradiation, especially in patients with adenocarcinoma of the lung that has a high rate of cranial metastasis.
Materials and Methods: Patients who have been treated with a diagnosis of NSCLC-NS and SCLC in our department of oncology between January and December 2008 were retrospectively analyzed. Data have been collected from the patient charts and analyzed by SPSS.
Results: There were 39 patients with NSCLC-NS and 66 patients wih SCLC. Mean ages were 58 and 62, respectively. Most of the caes of NSCLC-NS were adenocarcinoma of the lung. At the time of diagnosis, none of the cases with NSCLC-NS had cranial metastases, while 22.7% (n = 15) of patients with SCLC had cranial metastases at the time of presentation. Howvever, following failure of first line platinum based therapy, cranial metastases have been detected in 35.9% (n = 14) of asymptomatic NSCLC-NS cases. The rate of cranial metastases was even higher than SCLC cases, who had cranial metastases in 22.7% of cases at the time of diagnosis and developed cranial metasases in only one case (3.6%) after failure of first line therapy.
Conclusion: In this single center study, it seems that even though they were asymptomatic, we detected very high rate of cranial metastases at the time of progression in NSCLC-NS, especially in patients with adenocarcinoma of the lung. We can argue that like SCLC, prophylactic cranial irradiation may be part of standard treatment in patients with NSCLC-NS cases, with adenocarcinoma subtype, who progressed under firstline platinum based treatment.

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Induction Docetaxel (D) and Cisplatin (C) plus concurrent Thoracic Radiotherapy (TRT) and biweekly D and C for stage III non-small cell lung cancer (NSCLC) - a Galician Lung Cancer Group study

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Background: Standard treatment of stage III NSCLC remains concurrent chemoradiation, although a clearly superior régimen has not been identified. D has been shown to possess good single agent activity against NSCLC as well as radiosensiziting properties, both alone and sinergisitically with C. The aim of our study is to evaluate the feasibility of induction chemotherapy with D-C followed by biweekly D-C and concurrent TRT.
Methods: 65 patients (p) with inoperable locally advanced NSCLC, stage IIIAN2/IIIB (no pleural T4), were included in a phase II study with induction chemotherapy consisting of three cycles of D 75 mg/m^2 on day 1 and C 40 mg/m^2 days 1−2 every 3 weeks and, if no surgery, then received concurrent TRT with D 30 mg/m^2 and C 30 mg/m^2 every 2 weeks for four courses, during conformal TRT (60−66 Gys, 180 cGy/day). The primary objective: overall survival; secondary: progression free survival, response rate (RR) and toxicity. Median follow-up: 8.8 months.
Results: The p characteristics were: mean age 61.6 years (44−75); male/female 61/4; ECOG PS 0/1 in 15/50 p; squamous/adeno/large cell carcinoma: 53.8%/23.1%/23.1%; stage IIIAN2 16 p (24.7%) and stage IIIB

49 p (75.3%). 60 p were evaluables for response and 62 p for toxicity. Induction D-C response: 33 PR (RR 55%; 95% CI:43−77), 18 SD (30%) and 9 PD (15%). 4 p went to surgery: 3 pPR and 1 pPD (unresectable). 40 p completed CChRT (5 p in treatment) with 5 CR, 23 PR, 4 SD and 8 PD (RR 70%; 95% CI:56−84). The median to PFS was 11 months (95% CI:7−15) and median OS was 12 months (95% CI:8−16). The PFS and OS at 1 year was 44.5%/48.1% respectively. A total of 175 cycles of D-C were administered (2.8 per p), with the main toxicity (NCI-CTC 3.0) per p Grade (g) 1−2/3−4 (%) was as follows: neutropenia 11.3/29; anemia 30.6/0.5; nausea/vomiting 30.6/4.8; fatigue 27.4/0; diarrhea 14.5/11.2; there were nine episodes of febrile neutropenia and there were one treatment-related death. The main toxicities per p in CChRT (D-C doses: 143, 3.5 per p) were: g1−2 neutropenia/anemia 13/34.7%; g1−2/3 esophagitis in 45.6/2.1% and g1−2 pneumonitis in 26%; there were one treatment-related death.
Conclusions: Induction chemotherapy with D-C plus concurrent TRT and biweekly D-C is a feasible treatment option for locally advanced NSCLC, showing good clinical activity and tolerability with promising survival.

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Toxicity report of a phase I/II dose escalation study in inoperable locally advanced non-small cell lung cancer with helical tomotherapy and concurrent chemotherapy

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Purpose: To evaluate the feasibility and toxicity of radiation dose escalation using helical tomotherapy (HT) in patients with inoperable stage III non-small cell lung cancer (LANSCLC) with concurrent chemotherapy.
Patients and Methods: This phase I/II study was designed to determine the maximum tolerated dose (MTD) of radiotherapy in patients with LANSCLC, concurrently with docetaxel and cisplatin. Radiotherapy was delivered using HT. A dose per fraction escalation was applied starting at 2 Gy, with an increase of 6% per dose cohort (DC). The RTOG acute radiation morbidity score was used to monitor pulmonary, esophageal and cardiac toxicity. All other adverse events were scored using the NCI CTC version 3.0.
Results: Dose escalation was performed in 34 patients over 5 DCs to a dose per fraction of 2.48 Gy. No differences were found in acute toxicity between the different DCs, but a significant increase in late lung toxicity in DC IV, using a fraction size of 2.36 Gy, necessitated a halt in further dose escalation with the MTD being defined as 2.24 Gy per fraction. The overall incidence of acute $\geqslant$grade 3 esophageal and pulmonary toxicity is 24% and 3% respectively. Overall late lung toxicity was 21%, but an acceptable 13% in DC I-III. Local response rate was 61% on computed tomography.
Conclusion: The use of helical tomotherapy to 67.2 Gy with concurrent cisplatin/docetaxel is feasible and resulted in acceptable toxicity. A full phase II study has been initiated to establish the true local response rate at the MTD of 2.24 Gy per fraction.

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Toxicity and outcome results of a class solution with moderately hypofractionated radiotherapy in inoperable stage III non-small cell lung cancer using helical tomotherapy

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Purpose: To assess feasibility, toxicity and local control of a class solution protocol of hypofractionated tomotherapy in stage III, inoperable, locally advanced non small cell lung cancer (LANSCLC) patients.
Patients and Methods: Eligible patients were treated according to a uniform class solution (70.5 Gy in 30 fractions) with fixed constraints and priorities using helical tomotherapy (TT). Toxicity monitoring was performed using the RTOG criteria and the NCI CTCAE version 3.0. Pulmonary function tests (PFT) were measured at start and repeated at three months after treatment.
Results: Our class solution resulted in a deliverable plan in all 40 consecutive patients. Acute grade 3 lung toxicity was seen in 10% of patients. Two patients died during acute follow-up with pulmonary toxicity. Correlations were found between changes in PFT and mean lung dose (MLD) or the lung volume receiving 20 Gy (V_{20}). The correlation was strongest for lung diffusion capacity for carbon monoxide (DLCO). A V_{20} of >27% and >32% were predictive for grade 2 and 3 acute lung toxicity respectively ($p < 0.05$). Late grade 3 toxicity was exclusively pulmonary, with an incidence of 16%. Overall grade 3 lung toxicity correlated with a MLD >18 Gy and a median lung dose of > 15 Gy ($p < 0.05$). Median survival was 17 months and the 1y/2y local progression-free survival (LPFS) were 66% and 50% respectively.
Conclusion: The current class solution using hypofractionated TT in patients with LANSCLC is feasible. Toxicity was acceptable and in line with other reports on intensity-modulated radiotherapy. The LPFS was encouraging considering the unselected population.

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The radioprotective effect of dimethyl sulfoxide in radiation induced acute pulmonary injury: detection by Tc99m-DTPA transalveolar clearance scintigraphy and histopathology

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Purpose: to investigate if radical scavenger and antiapoptotic agent dimethyl sulfoxide can prevent radiation-induced pulmonary injury by Tc^{99m}-DTPA transalveolar clearance scintigraphy, histopathologic assessment, and by TUNEL staining in an animal model.
Material and Method: Twenty white New-Zealand rabbits were grouped as: 1) control (CONT), 2) radiation alone (RT), 3) dimethyl sulfoxide plus radiation (DMSO+RT), and 4) dimethyl sulfoxide, alone (DMSO). Right hemithoraxes of the RT and DMSO+RT groups were irradiated with a single dose of 20 Gy by a Co^{60} treatment unit. Dimethyl sulfoxide (4.5 gr/kg) was given i.p. 30 minutes before irradiation. The Tc^{99m}-DTPA transalveolar clearance scintigraphy was performed on 14^{th} day after irradiation. The rabbits were sacrificed on 15^{th} day and lungs were removed for histopathologic evaluation. Evaluation was performed for the presence of peribronchial inflammatory cell infiltration (PIHI), alveolar septal infiltration (ASI), alveolar exudate (AEX), alveolar edema (AED) interstitial fibrosis (IF), and necrosis formation (NEC) by using a 4-point scale. Apoptotic cells were assessed by TUNEL staining. The reactivity of TUNEL positive cells is scored by 5-point scale.
Results: Administration of dimethyl sulfoxide prior to irradiation caused a marked prolongation in the transalveolar clearance rate of DTPA through the alveolocapillary membrane ($p = 0.028$). In addition, dimethyl sulfoxide administration prior to irradiation revealed better scores for pulmonary parenchyma in histopathologic evaluation compared to radiation alone group. Dimethyl sulfoxide given prior to irradiation markedly decreased the severity of alveolar exudate ($p = 0.042$). TUNEL staining scores of the apoptotic cells in the DMSO administered group prior to irradiation were better than radiation alone group at a statistically significant level ($p = 0.018$).
Conclusion: The results of our study suggest that dimethyl sulfoxide appears to be a protective agent against radiation-induced lung injury. Additional work is needed to better identify the effectiveness of dimethyl sulfoxide as radioprotective agent in radiation associated lung injury.

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Randomized phase III study of mitomycin/vindesine/cisplatin (MVP) versus weekly irinotecan/carboplatin (IC) or weekly paclitaxel/carboplatin (PC) with concurrent thoracic radiotherapy (CTR) for patients (pts) with unresectable stage III non-small cell lung cancer (NSCLC): West Japan Thoracic Oncology Group (WJTOG) 0105

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Background: Concurrent chemoradiotherapy has become standard treatment of unresectable stage III NSCLC. However, the optimal regimen of concurrent chemoradiotherapy including radiation dose, schedule and chemotherapeutic agents has not been defined. We conducted a