

## Non small cell lung cancer

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### ENDOBRONCHIAL BRACHYTHERAPY COULD BE CURATIVE

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Brachytherapy is now a widely accepted palliative method for desobstructing the bronchial lumen. However, its place as a curative treatment is still debated. We have tried to distinguish between patients who can be cured with endobrachytherapy and palliative treatments. We report here the results of such a distinction.

**Definition of therapeutic groups:** (1) Curative group (CG), treated with brachytherapy alone: patients who have a small tumor without extrabronchial extension. Surgery or external irradiation (RT) were not possible, because of chronic respiratory failure or previous treatment (previous RT = 87%). (2) Brachytherapy as a local boost after RT (EBRT + BT): initial treatment of lung cancer patients, stages I-IIIb, who have a large endobronchial component at diagnosis. (3) Palliative group (PG): patients with a large obstructing tumor or with metastases.

**Population:** 148 pts have been treated. CG = 69; EBRT + BT = 48; PG = 31. Mean endobronchial tumor length: CG = 2 cm; EBRT + BT = 2.6 cm; PG = 4.5 cm.

**Protocol:** CG: = 6 fractions of 7 Gy in 1 month; EBRT + BT: 2 fractions of 5 or 7 Gy, 15 days after external irradiation; PG: 2 to 6 fractions of 7 Gy.

**Results:** PG: Objective endoscopic response: 71%; Symptomatic improvement: 62% CG; 78% of complete histologic disappearance of the tumor (CHR). 33% of the pts relapse in the treated areas. EBRT + BT: 83% of CHR.

**Survival:** 3-year survivals were: PG: 0%; CG: 51%; EBRT + BT: 69%. Most of the pts in the CG died of local disease.

**Conclusion:** It seems to exist a subgroup of patients, with a low metastatic potential, which can be cured by brachytherapy alone.

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### PRETREATMENT PROGNOSTIC FACTORS IN STAGE III NON-SMALL CELL LUNG CANCER (NSCLC) TREATED WITH HYPERFRACTIONATED RADIOTHERAPY (HFX RT) WITH AND WITHOUT CONCURRENT CHEMOTHERAPY (CHT)

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This study was undertaken to gain insight into those characteristics that could influence survival in 169 pts with Stage III NSCLC treated as follows: HFX RT to a TD of 64.80 Gy (61 pts), HFX RT to the same TD with CHT consisting of 100 mg of CBDCA, d 1&2, and 100 mg of VP16, d 1-3, given every week during RT course (52 pts), and HFX RT to the same TD with CHT consisting of 200 mg of CBDCA, d 1&2, and 100 mg of VP16, d 1-5, during the first third, and fifth weeks of RT course (56 pts). MST for all 169 pts is 13 months, and 1-, 3-, and 5-yr survival is 53%, 15%, and 13%, respectively. Women lived longer than men ( $P = 0.0001$ ), age < 60 yr adversely influenced survival ( $P = 0.0000$ ), Stage IIIA pts had better survival than those in Stage IIIB ( $P = 0.0000$ ), pts with KPS 80-100 had better outcome than those with KPS 50-70, ( $P = 0.0000$ ), and weight loss > 5% adversely influenced survival ( $P = 0.0000$ ). Multivariate analysis confirmed that these five factors independently predict survival, KPS being the strongest, followed by sex and weight loss and age and stage.

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### LYMPHADENECTOMY AS PROGNOSTIC FACTOR IN STAGE III BRONCHIAL CARCINOMA

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Resection therapy in stage I and II bronchial carcinoma is undisputed, but controversially discussed in stage IIIA and IIIB. It is necessary to define those subgroups within this stage that will benefit from surgery.

Lymph node dissection is a cornerstone of oncological surgery. It is particularly important in bronchial carcinoma, where metastatic lymph

node involvement cannot be calculated from location of the primary tumor. Lymphatic manifestation is exactly identified diagnostically in 38% of cases only.

Out of 1951 resections on bronchial carcinoma (2/84-2/93), 361 ( $R_o$ -) resections were carried out on stage IIIA tumors, 5-y survival 24% (31% after complete lymph node dissection). 5-y survival of 18% in stage IIIB ( $n = 201$ ,  $R_o$ ).

These results confirm the relevance of Lymphadenectomy in stage III surgery on bronchial carcinoma.

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### PHASE III STUDY OF NEO-ADJUVANT CHEMOTHERAPY IN RESECTABLE NON-SMALL CELL LUNG CANCER (NSCLC)

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Neo-adjuvant chemotherapy is a promising new concept in the treatment of resectable NSCLC. In 1991, a randomized study was initiated to compare two treatment strategies for patients (pts) with operable stages I (except T1N0), II or IIIa NSCLC. Pts are randomized into two arms. Surgery is performed first in group I. In group 2, pts start with two cycles of chemotherapy; following surgery, two more cycles are administered in responder pts. Chemotherapy is the MIP protocol: mitomycin 6 mg/m<sup>2</sup> day 1, ifosfamide 1.5 g/m<sup>2</sup> days 1 to 3, cisplatin 30 mg/m<sup>2</sup> days 1 to 3. In both groups, if the surgical staging is N2 or T3, a radiotherapy is performed.

From June 1991 until Jan. 1995, 256 pts have been randomized; 35% are stage I, 16% are stage II. 205 pts have completed the treatment. In group 1, 105 out of 106 and in group 2, 91 out of 99 pts underwent thoracotomy. Surgery was complete in 85% of group 1, 83% of group 2, incomplete in 10% of group 1, 5% of group 2. The chemotherapy response rate assessed by surgical evaluation was as follow: complete and subcomplete response. 27%, 18%, partial response 31% (overall: 58%). The study is still ongoing as a total number of 350 patients should be included to reach the required power.

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### A MULTIVARIATE ANALYSIS OF PREDICTIVE FACTORS FOR SURVIVAL AFTER CONCURRENT CHEMORADIOTHERAPY FOR STAGE III NON SMALL CELL LUNG CANCER

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From July 1989 to February 1994, 140 patients (pts) with inoperable stage III non-small-cell lung cancer (NSCLC) were treated with concurrent chemoradiotherapy. Median age was 64 years with a majority of males (93%), WHO status 1 (66.4%), and squamous cell subtype (72%). Clinical stage was IIIA (65.7%), IIIB (34.3%), N0-1 (20.8%), N2 (57.8%) or N3 (21.4%). Using standard fractionation, pts received thoracic radiotherapy (TRT) up to a median dose of 60 grays ( $n = 116$ ), or 45 grays before planned surgery ( $n = 24$ ). 73 pts received concurrent cisplatin at a dose of 20 mg/sqm/d over 5 days for two cycles during TRT. In addition, 67 pts subsequently received etoposide at a dose of 50 mg/sqm/d over 5 days, followed by two additional cycles of the same chemotherapy. With a median F/U of 41 months, overall survival was 60% and 33% at 1 and 2 years respectively. Univariate and multivariate analysis were performed with the aim of identifying characteristics that could predict 2-year survival. Age, sex, performance status and weight loss, as well as histologic subtype, histologic grade, tumor size, and T stage, had no significant predictive value. Difference in 2-year survival for clinical stage IIIA (38%) or IIIB (22.5%) did not reach statistical significance, neither did the degree of clinical nodal involvement (N0-N1 = 47.6%, N2 = 32.3%, N3 = 19.7%). Multivariate analysis identified three highly significant predictive factors with independent prognostic value: addition of etoposide (39.3%,  $P = .008$ ), negative biopsy at the initial tumor site (50.6%,  $P < .0001$ ), and surgery (74%,  $P < .0001$ ).