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Diagnostic accuracy and cutoff points of Her-2/neu, Cyfra 21-1 and CEA in lung adenocarcinoma-associated malignant pleural effusions

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Background: Cytology fails to detect neoplastic cells in approximately 40–50% of malignant pleural effusions, which commonly accompany lung adenocarcinomas. Published reports of the diagnostic sensitivity of various tumor markers are inconsistent. Reports on Her-2/neu in lung adenocarcinoma-associated malignant pleural effusion, for example, differ markedly (72% vs. 10%). In addition, optimal cutoff points have not been determined. To clarify contrasting reports and maximize diagnostic efforts, we evaluated the diagnostic sensitivity, specificity and optimal cutoff points for Her-2/neu, Cyfra 21−1 and CEA in distinguishing lung adenocarcinoma-associated malignant from benign pleural effusions.
Materials and Methods: Pleural effusion samples were collected from 41 patients with lung adenocarcinoma-associated cytologically malignant effusion, and from 93 with benign conditions including tuberculosis, parapneumonic pleural effusions, congestive heart failure, and liver cirrhosis. We evaluated the diagnostic sensitivity, specificity and cutoff points for tumor markers Her-2/neu, Cyfra 21−1, and carcinoembryonic antigen (CEA) to discrimination lung adenocarcinoma-associated malignant from benign pleural effusions.
Results: Her-2/neu, Cyfra 21−1 and CEA vary in their ability to discriminate lung adenocarcinoma-associated malignant pleural effusion from benign effusion, from 79.85%, to 88.81%, to 94.03% respectively. False-positive rates of these markers in various benign effusions are 4.30%, 7.53% and 3.23% respectively. CEA combined with Cyfra 21−1 increases diagnostic sensitivity to 97.6%. The cutoff points for these markers are optimally set at 3.6 ng/mL, 60 ng/mL, and 6.0 ng/mL respectively.
Conclusions: With appropriate cutoff points, CEA provides the best current diagnostic sensitivity and specificity. Combining CEA with Cyfra 21−1 will obtain the diagnostic sensitivity near 100%.

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Dynamic MR based analysis of tumor movement in upper and mid lobe localized lung cancer

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Background: Tumor motion is a very important factor in the radiotherapy of lung cancer. Uncertainty resulting from tumor movement must be considered in 3D therapy planning especially in case of IMRT or stereotactic therapy. The aim of our dynamic MR based study was to detect tumor movements in upper and mid lobe located lung tumors.
Materials and Methods: Twenty-four patients with newly diagnosed stage II-IV lung cancer were enrolled into the study. According to tumor localization in the right S1-S3 segments 9, in the right S4-S10 segments 2, in the left S1-S3 segments 9 and in the left S4-S10 segments 4 lesions were detected. In normal treatment position individual dynamic MR examinations were performed in axial, sagittal and coronal planes (100 slices/30 s). For tumor motion analysis E-RAD PAC's® software was used.
Results: Movements of the tumor under normal breathing conditions were registered in the three main direction. The mean antero-posterior deviation was 0.109 cm (range: 0.063−0.204 cm), the mean medio-lateral deviation was 0.114 cm (range: 0.06−0.244 cm). The greatest deviation was measured in cranio-caudal direction (mean: 0.27 cm, range: 0.079−0.815 cm). The mean direction-independent deviation was 0.18 cm (range: 0.09−0.48 cm).
Conclusions: Dynamic MR is a sensitive and well tolerable method for tumor motion monitoring for high precision 3D therapy planning in lung cancer. Our results demonstrate that tumors located in the upper and mid lobes have moderate breath synchron movements. The greatest deviation should be considered in craino-caudal direction.

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Adjuvant chemotherapy inelderly patients with non small cell lung cancer (NSCLC)

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Background: Recent trials have shown significant survival benefit from adjuvant chemotherapy after resection of NSCLC. Whether elderly patients tolerate platinum-based adjuvant chemotherapy and derive the same survival advantage is unknown. This retrospective study evaluated the influence of age on survival, chemotherapy delivery and toxicity in patients with NSCLC.
Patients and Methods: Pretreatment characteristics and survival benefit from treatment were compared for patients <65 & >65. Chemotherapy delivery and toxicity were compared for 213 treated patients with NSCLC.
Results: There were 327 young and 155 elderly patients. Baseline prognostic factors by age were similar with the exception of histology (adeno 58% young, 43% elderly; squamous 32% young, 49% elderly; p = 0.001) and PS (PS 0 53% young, 41% elderly; p = 0.01). Overall survival by age showed a trend favoring the young in univariate (HR 0.77, CI 0.58−1.04, p = 0.084) and multivariate analyses (HR 0.75, CI 0.56−1.01, p = 0.059). Patients >75 years had significantly shorter survival than those aged 66−74 (HR 1.95, CI 1.11−3.41, p = 0.02). Overall survival for patients >65 years was significantly better with chemotherapy vs observation (HR 0.61, CI 0.38−0.98, p = 0.04). Chemotherapy administration and toxicity were evaluated in 63 elderly and 150 young patients. Mean dose intensities of vinorelbine (V) and cisplatin (C) were 13.2 and 18.0 in the young and 9.9 and 14.1 in the elderly (V p = 0.0004; C p = 0.001). The elderly received significantly fewer doses of V (p = 0.014) and C (p = 0.006). Fewer elderly patients completed treatment and more refused treatment compared to the young (p = 0.03). There were nï significant differences in toxicities, G-CSF use or hospitalization by age group, except for myalgias and mood alteration (more frequent among the young). Six of 126 deaths (4.8%) in the young were from nonmalignant causes, vs 12 of 71 (16.9%) in the elderly (p = 0.008).
Conclusions: Én spite of receiving less chemotherapy than young patients, adjuvant chemotherapy improves overall survival in patients aged >65 years with acceptable toxicity. Adjuvant chemotherapy should not withheld from elderly patients, although patients >75 years of age require further study.

6598 POSTER

Wait times in early-stage non small cell lung cancer (NSCLC)

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Background: Patients with early-stage (I-III) non small cell lung cancer (NSCLC) who undergo surgical resection represent a potentially-curable population. For those with high-risk disease, adjuvant chemotherapy has become a new standard of care since late 2004. However, the wait-times along this spectrum of care, and their relevance, have yet to be assessed. This study documents wait times at various resolutions of care intervals. Wait times are influenced by a complex interplay of demographic, clinical, epidemiological and system-resource dependant factors. We examine how some of these factors influence access to care, and highlight the use of different care interval definitions to report wait times.
Methods: All patients diagnosed in 2005 with NSCLC who underwent curative-intent surgery in Nova Scotia, Canada were identified through the provincial cancer registry. A retrospective chart review was conducted to abstract patient characteristics and timelines from first suspicious imaging study (detection) to adjuvant chemotherapy treatment (chemotherapy). A general linear model with stepwise selection was used to identify statistically-significant factors (P < .05) that influenced each wait time.
Results: 108 patients were identified, of whom 29 (27%) received adjuvant chemotherapy. The average wait time between detection-chemotherapy was 142 days. At this lowest resolution of care interval, Cancer Centre was the strongest predictor of wait time (Nova Scotia Cancer Centre vs Cape Breton Cancer Centre: 182 vs 60 days). At intermediate resolution of care intervals, detection-surgery and surgery-chemotherapy accounted for 94 and 55 days, respectively. For the former care interval, the strongest predictors of wait times included patient smoking history (current vs former vs never: 102 vs 85 vs 123 days) and surgeon (54–115 days range); for the latter, the strongest determinants were patient age (<60 vs >60 years: 51 vs 61 days) and medical oncologist (37−69 days range). The variables associated with wait times at high resolution of care intervals will be presented.

Conclusions: This study provides a snap shot of wait times experienced by NSCLC patients undergoing curative-intent surgery and describes how different factors influence timelines based on care interval definitions. In a parallel study we use a subset of these timelines as potential determinants of referral to medical oncology and provision of adjuvant chemotherapy.

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Comparison of cisplatin–paclitaxel combination versus cisplatin-etoposide as first line chemotherapy in SCLC

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Small cell lung cancer is a sensitive tumor to chemotherapy. The initial high response rate is though followed by relapse in nearly 90% of the patients. Cisplatin and Etoposide combination is the standard primary treatment. Other chemotherapy combinations are not often applied. The objectives of the present trial is to compare between two-phase II trials the response rate, time to tumor progression and mainly the median and overall survival.
Material and Methods: Seventy-seven patients with small cell lung cancer were enrolled and divided in two arms. 3 patients were not considered evaluable. 37 patients in each of the two arms were balanced to have the different combination chemotherapy. Arm A patients had the combination of Cisplatin 80 mg/m^2 on day 1 and VP-16 (etoposide) 120 mg/m^2 daily on days 1−3 repeated every 3 weeks. Arm B had Cisplatin 80 mg/m^2 day 1 and Paclitaxel 175 mg/m^2 day 1 repeated every 3 weeks. The median age of the patients was 65 years (range 46−80). There were 61 male and 13 female. Stage of disease: Arm A: Limited disease 15 patients, advanced 22 patients. Arm B: Limited disease 20 and advanced 17 patients. Patients were planned to have 6 courses. 80% of the patients of each arm had completed their courses. Radiation therapy was given to all the patients of limited disease.
Results: Both arms response rates (CR and PR) and survival was similar. In Arm A (with VP-16) it was 65.71% and in Arm B (with Paclitaxel) it was 64.70%. The median survival of Arm A patients was 13 months with range 1−29 and of Arm B the median was 12 and range $\frac{1}{2}$−60+ months. Toxicity was also without difference in respect of myelotoxicity, nephrotoxicity and alopecia.
Conclusions: Comparison of Cisplatin and Etoposide combination versus Cisplatin and Paclitaxel showed no difference in response rate, survival and toxicity. The Cisplatin and Paclitaxel combination could be applied in small cell lung cancer patients as an alternative treatment to the standard one.

6600 POSTER

Risk factors of radiation pneumonitis: a prospective study

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Background: To study the clinical, dosimetric, and biological risk factors of radiation pneumonitis (RP) for lung cancer patients(pts) receiving thoracic radiotherapy (RT) in Taiwan
Materials and Methods: From Jul 2003 to Jun 2005, fifty pts were enrolled to study the clinical, dosimetric, and biological risk factors of RP for lung cancer pts receiving thoracic RT in our institute prospectively. Three of them were ineligible for analysis due to incomplete RT or missing data. The remaining pts (n = 47) constitute our study group. Clinical factors including age, gender, history of smoking, history of pulmonary disease, histology, stage, primary site, operation, chemotherapy, pretreatment albumin, hemoglobulin level, and pretreatment quality of life (QoL) were recorded. QoL was measured by EORTC C30 questionaire. V20 (percentage of total lung receiving more than 20 Gray) and mean lung dose (MLD) were recorded as dosimetric factors. Pretreatment plasma cytokine levels (transforming growth factor beta, TGF-β and interleukin six, IL-6) were recorded as biological factors. Common toxicity criteria v3.0 was used for grading of RP. Uni-variate analysis by Fisher's exact test was used for analysis of risk factors. This study was registered at www.clinicaltrials.gov (NCT00155909).
Results: Most of these pts were male (n = 39) and aged (median age 63 yrs, range: 36−80) at diagnosis. Most of them had stage III non-small cell lung cancer (NSCLC, n = 15) or limited stage small cell lung cancer (SCLC, n = 14) and received definitive RT (n = 37) and concurrent chemotherapy (n = 29). The median RT dose was 54 Gy [range: 36−66, mostly (n = 3) $\geqslant$50]. The median daily fractional size was 2 Gy [range 1.8−3, mostly (n = 45) $\leqslant$2]. The median (range) V20 and MLD were 27% (2−36) and 15 Gy (2.8−21). The median (range) IL-6 and TGF-β levels (pg/ml) were 4.5 (0−71.7) and 1615 (634–3486, missing=14), respectively. At the time of analysis (Mar 2007), the follow-up status were mostly dead (n = 18), followed by lost after disease progression (n = 12), lost with no evidence of disease (NED, n = 1), and regular follow-up with disease (n = 8) and NED (n = 8). Grade II RP was evident in six (13%) pts. The 1 and 3 year overall survival since start of RT for these pts was 59% and 30%. We found gender (female vs male=3/8 vs 3/39, p = 0.05) was the only significant risk factor associated with grade 2 RP.
Conclusions: In this prospective study, no significant risk factor except gender (female) was associated with grade 2 RP.

6601 POSTER

A pilot study of topotecan in patients with irinotecan-refractory small cell lung cancer

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Background: Although the efficacy of topotecan as second-line chemotherapy for small cell lung cancer (SCLC) has been consistently demonstrated in clinical trials, the choice of irinotecan as first-line therapy prevented use of the evidence-based option. This pilot study was conducted to determine the activity and safety of topotecan in SCLC patients refractory to first-line therapy with irinotecan/platinum combination.
Materials and Methods: Patients with primary refractory (no response, or progression during or $\leqslant$90 days after last chemotherapy) SCLC after treatment with irinotecan/platinum received topotecan 1.5 mg/m^2 as a 30-min infusion daily for 5 days every 3 weeks. Given a threshold response rate of 10%, at least 18 patients were required to be treated with topotecan in the first stage.
Results: Of 18 eligible patients, 11 patients were previously treated with irinotecan/cisplatin and 7 were treated with irinotecan/carboplatin. The median age was 68 years (range, 44−75) and the median interval from the last chemotherapy was 50 days (range, 21−89). A total of 38 chemotherapy cycles were administered (median, 2; range, 1−5). Causes of therapy discontinuation were disease progression in 11 patients, toxicity in 6 patients, and one patient's refusal. Toxic effects were mainly hematologic (grade $\geqslant$3 neutropenia in 67% of patients) and fatigue (grade 3 in 44%). One (6%) patient had a confirmed partial response and 5 patients achieved stable disease. Median progression-free and overall survivals were 1.8 months (95% CI, 1.5−2.1) and 8.3 months (95% CI, 0−18.6), respectively. Palliative radiotherapy and third-line chemotherapy was offered to 4 and 3 patients, respectively, after failure.
Conclusions: The limited antitumor activity of second-line topotecan prompted no further evaluation in patients with irinotecan-refractory SCLC.

6602 POSTER

Induction docetaxel and cisplatin followed by bi-weekly docetaxel with concurrent thoracic radiotherapy for stage III non-small cell lung cancer (NSCLC). A phase II study conducted by the Galician Lung Cancer Group (GLCG)

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Background: The most satisfactory treatment for patients with locally advanced NSCLC is combination chemotherapy-radiotherapy (CT-RT). The optimal treatment modalities remain to be determined.
Methods: 60 patients (pts) with inoperable stage locally advanced NSCLC, stage IIIAN2/IIIB (no pleural T4), were included in a phase II study with induction chemotherapy consisting of three cycles of Docetaxel 75 mg/m^2 on D1 and Cisplatin 40 mg/m^2 D1−2 every 3 weeks and, if no surgery, then received concurrent CT-RT with Docetaxel 30 mg/m^2 every 2 weeks for four courses, during thoracic conformal radiotherapy (60−66 Gys, 180 cGy/day). The primary objective: overall survival; secondary: progression free survival, response rate (RR) and toxicity. Median follow-up: 9.1 mo.
Results: The pts characteristics were: mean age 62.9 yrs (43−74); male/female: 56/4; ECOG 0/1 in 17/43 pts; stage IIIAN2: 17 pts (28.3%) and