(42% each). Most of the subjects had not received previous chemotherapy (67%), radiotherapy (83%), or radiosurgery (87.5%). Of the 21 patients that finished the study, 42% showed partial response (8% complete response), 33% improved their performance status, and 33% improved their neurological functional status. The median time to progression was 204 days. The proportion of surviving patients was 0.816 at 99 days and 0.497 at 180 days. As for toxicity, 8% of patients suffered grade III asthenia, and 4% suffered grade III thrombocytopenia.
Conclusions: The treatment of brain metastasis with temozolomide as concomitant treatment is associated to a 50% survival at six months, and a low degree of grade III toxicity.

9111 POSTER

Pathology-validated automated volumetric tumour segmentation in 4D-PET vs 3D-PET of NSCLC

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Background: It has been recommended to use a 42% threshold of maximum intensity to automatically delineate the primary lung tumor on a 3D ^{18}F-FDG-PET scan. However, for radiation treatment planning, 4D-PET scanning is increasingly being used. It is unknown whether the threshold recommended for 3D scans also applies to 4D scans. The aim of the current study was to compare the size of a primary lung tumor on 3D- vs 4D-PET as measured at the 42% threshold level, and to compare these sizes with the gold standard, being the size at pathology.
Methods and Material: 3D- and 4D-PET scans were obtained in 6 patients with NSCLC prior to surgery. The GTV was automatically determined using a 42% threshold level on both the 3D-PET and all 8 respiration phases of the 4D-PET. For the 4D-PET an average volume with standard deviation (SD) was calculated over the 8 phases for each patient. At pathology, the lung lobe was inflated with formalin. The fixated specimen was sectioned in parallel slices of approximately 5 mm, orthogonal to the longest axis. Digital photographs were obtained. About 40 microscopic sections per patient were analyzed encompassing the complete tumor. The area of the tumor on each slice was calculated, and multiplied with the slice thickness to derive the pathologic tumor volume. Both pathologic and PET volumes were converted to an effective diameter (ED) of the GTV, using: ED $((\text{volume} * \frac{3}{4} * (1/p))^{\frac{1}{3}})*2$. Finally, for both the 3D- and the 4D-PET, we calculated the ideal threshold level for each tumor by establishing the threshold value that yielded the volume closest to the pathologic volume.
Results: The ED of the 3D-PET overestimated the pathologic ED (28.4 mm$\pm$15.0 vs 24.4 mm$\pm$16.2, p = 0.046). Only a trend was observed regarding the overestimation of the ED with 4D-PET averaged over all phases compared to pathology (26.7 mm$\pm$14.1 vs 24.4 mm$\pm$16.2, p = 0.063). The ED varied also per respiratory phase, as indicated by the SD over the phases per patient (range: 0.37−2.6 mm). The ideal threshold level for the 4D-PET was 49.8%$\pm$7.8% on average for all phases, and 53%$\pm$8.1% for the 3D-PET. The variation in threshold values between the 4D-PET phases was of the same order of magnitude (range of SD: 0.9−5.8%).
Conclusions: For automatic thresholding of the volume of primary lung tumors on FDG-PET, different threshold levels should be used for 3D- vs 4D-PET. Data of more patients will be analyzed to investigate the optimal method for automatic delineation of lung tumors in 4D-PET.

9112 POSTER

Stereotactic body radiation therapy for peripheral lung tumours: a study in a French cancer center

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Background: The efficiency of Stereotactic Body Radiation Therapy (SBRT) in thoracic tumours becomes well known, while the evaluation of related toxicities is less described. A follow-up of all the pts treated in a French cancer center is described, focusing on the toxicity.
Patients and Methods: From June 2007 to December 2008, 31 pts, median 72 y. [54−86], were treated with SBRT for pulmonary tumour. 23 pts were treated for non-operated peripheral non small cell lung cancer (NSCLC), 3 pts for solitary metastasis (NSCLC n = 2, rectal cancer n = 1) and 5 pts for tumour of doubtful origin (NSCLC-solitary late metastasis of known cancer). 20 pts had histologicaly or cytologicaly proven tumour; in 11 cases, the diagnosis was retained without histological proof if tumour size increased or tumour was highly positive in PET-TDM without argument for another cause. SBRT was performed because of refusal of surgery (n = 1), or contraindications for surgery in 30 pts (comorbidities n = 24, previous surgery n = 6). Median forced expiratory volumes in 1 s (FEV1) before SBRT was 1.6 l [0.48−3.06]. Patients were immobilized in a Stereotactic Body Frame^{TM}. Breathing motion was limited with abdominal compression. Patients were treated with image guidance using Cone-Beam computed tomography before each fraction. 4 fractions of 10 Gy (n = 4), 12 Gy (n = 12) or 15 Gy (n = 13) or 8 fractions of 5 Gy (n = 2) were delivered on the 70% isodose (n = 28), 80% (n = 2) or 95% (n = 1) in 2 weeks, using 10−12 fields.
Results: With a median follow up of 13 months [2−32], 26 pts were alive and 5 had died (2 unknown causes without argument for toxic death, 3 metastatic progressions). Local control at 6 months was obtained for 26 on 28 evaluable pts (92%). During RT, asthenia gr.2 (n = 1), dyspnoea gr.2 (n = 1) and cough gr.2 (n = 1) were noticed. 29 pts were evaluated for acute toxicity (<3 months after the end of SBRT) while 2 pts had died before. 1 dermatitis (gr.2) was reported. After 3 months, 3 pts dyspnoea from gr. 3 to gr.4 (n = 3), from gr.2 to gr.4 (n = 1), and from gr.1 to gr.2 (n = 1), with images compatible with localized radiation pneumonitis on TDM in 3 pts (gr.2−3). No other toxicity was reported. Dosimetric studies for these pts will be presented.
Conclusion: SBRT for thoracic tumours is efficient and well tolerated. It is usually performed in high-risk pts suffering from severe comorbidities but indications must be carefully weighted against the risk of median-term toxicity, in particular for pulmonary function.

9113 POSTER

Palliative radiation oncologic therapy in lung cancer with superior vena cava syndrome

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Background: Lung cancer is the most common cause of superior vena cava syndrome (SVCS) and requires timely recognition and management. Radiotherapy is a succesfully proven, feasible and appropriate antineoplastic treatment for the palliation of this oncologic emergency. In order to study clinical profile of lung cancer with SVCS were studied retrospectively.
Patients and Methods: All lung cancer patients who presented with SVCS during last five years were studied. All 213 patients with SVCS with lung cancer; 194 (91%) male and 19 (9%) female. Age distrubutions were between 35−82 and most patients were in 5. And 6. decade (female median age 44, male 61). Neck edema was found in 177 (83%) patients, 112 (52.5%) had collateral veins and severe dyspnea, cough found in 123 (57.7%) and severe dyspnea were found in all patients. Localization of lesions were right in 188 (88.26%) and left in 25 (11.74%) of cases. Twenty seven were small cell lung cancer (18 disseminated, 9 localized) and 167 (78.40%) were nonsmall cell histology (44 epidermoid, 16 adenocarcinoma, 3 large cell and others nonclassified) and 19 (8.92%) patients were radiologically diagnosed and treated as emergency. According to TNM stage; 37 (17.37%) were in IIIB, 88 (41.34%) were in stage IV and 88 (41.34%) stage not stratified. Cough and dyspnea decreased in 55% of patients. Thirty four patients were died during therapy, 44% were dead in six mounths and only 1 year overall survival rate was 15.6%.
Conclusions: Radiotherapy is effective for paliation in SVCS with lung cancer; in our cases increased amount of patients needed radiotherapy as a firsth treatment especially in nonlocalized group. Nearly 10% of patients were female as an increasing proportion. Overall survival of patients were very poor and symptom control and increasing life quality is important but multimodality new treatments necessary for increasing life span of patients

9114 POSTER

Malignant pleural mesothelioma: the prognostic significance of different surgical treatments. A retrospective study from a single-institution experience

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Backgrounds: Optimal therapy in patients with Malignant Pleural Mesothelioma (MPM) is a matter of debate. Many authors questioned the role of

major surgery in the treatment of MPM. We reviewed our recent experience among different treatment options in patients with MPM to assess their prognostic impact.
Materials and Methods: From 10/97 to 10/08 326 patients were admitted to our Hospital with a diagnosis of MPM (223 men, 103 women, mean age 64 years, range 32−94). Management options included pleural drainage with/without pleurodesis (24 patients), Video-Assisted Thoracic Surgery (VATS) with/without pleurodesis (195), partial pleurectomy (PL) (27), total PL (8), Extrapleural Pneumonectomy (EPP, 72). The last two treatments were intended as maximal debulking procedures before chemotherapy. Chemotherapy and radiotherapy were used when indicated in exclusive or multimodality protocols. Patients receiving total PL and EPP were compared with those receiving palliative procedures (drainage, VATS or partial PL). Survival analysis was performed using univariate and multivariate (Cox regression) models.
Results: Patients receiving PL (partial or total) and EPP were significantly younger than those receiving pleural drainage or VATS (56 vs. 68 years, p = 0.002). Median survival (years) in the different management groups were: pleural drainage (0.97), VATS (0.82), partial PL (1.35), total PL (2.01), EPP (1.73) (p = 0.00001). Two-year survival rates among the groups were: pleural drainage 22%, VATS 18%, partial PL 20%, total PL 50%, EPP 32% (p = 0.00001). A significant survival advantage was observed in patients receiving EPP or total PL vs. those receiving palliative procedures (32% vs.18%, p = 0.0002). In multivariate survival analysis, advanced age was a significant negative prognostic factor (HR 1.02, 95% CI 1.00−1.03, p = 0.007), while EPP or total PL were a significant positive prognostic factor (HR 0.59, 95% CI 0.35−0.99, p = 0.04).
Conclusions: In patients with MPM, different treatment options may be offered with either palliative or maximal cytoreductive intent. Patients receiving major surgery are a selected subset of patients younger than those receiving pleural drainage or VATS. A significant survival advantage was observed in patients after total PL or EPP. Our results indicate that surgery with maximal debulking intent offers a significant survival advantage over palliative procedures and should therefore be considered a valuable option in selected patients with MPM.

9115 POSTER

Cisplatin-induced expression of Gb3 enables verotoxin-1 treatment of cisplatin-resistance in malignant pleural mesothelioma cells

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Background: Verotoxin-1 (VT-1) exerts its cytotoxicity by targeting the membrane glycolipid Gb3. We investigated if a sub-toxic concentration of VT-1 could enhance cisplatin-induced apoptosis and overcome acquired cisplatin resistance in cultured cancer cell lines.
Materials and Methods: P31 (mesothelioma) and H1299 (non-small-cell lung cancer) cells with corresponding cisplatin-resistant sub-lines (P31res/H1299res) were incubated with VT-1 and/or cisplatin followed by determination of Gb3-expression, cell viability, apoptosis, and signalling pathways.
Results: Cells from the resistant sub-lines had elevated Gb3 expression compared to the parental cell-lines and cisplatin further increased Gb3 expression whereas VT-1 reduced the percentage of Gb3-expressing cells. Combination of cisplatin and sub-toxic concentrations of VT-1 led to a synergistic increase of cytotoxicity and TUNEL-staining, especially in the cisplatin-resistant sub-lines. Blockade of Gb3 synthesis by a Gb3 synthesis inhibitor led to eradicated TUNEL-staining of MPM cells but also sensitized P31res cells to the induction of apoptosis by cisplatin alone. Cisplatin- and VT-1-induced apoptosis involved the MAPK pathways with increased JNK and MKK3/6 phosphorylation.
Conclusions: We demonstrate presence of Gb3 in acquired cisplatin resistance in P31res and H1299res cells. Cisplatin up-regulated Gb3-expression in all cells and thus sensitized the cells to VT-1-induced cytotoxicity. A strong synergistic effect of combined cisplatin and a sub-toxic concentration of VT-1 in cisplatin-resistant MPM cells were noted leading to a potential synergistic clinical treatment approach.

9116 POSTER

A phase I/II clinical trial of topotecan in combination with cisplatin for extensive-disease small cell lung cancer

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Background: *In-vitro* studies have shown synergistic anti-tumor activity between Topotecan (T) and Cisplatin (CDDP) presumably due to inhibition of DNA repair. We conducted a Phase I/II trial to determine a safe and effective combination regimen of T and CDDP in Extensive-Disease small cell lung cancer (ED-SCLC) patients.
Material and Methods: Patients with histologically diagnosed ED-SCLC, Performance Status 0 or 1 and aged 20−74 were enrolled. The combination was constituted at escalating doses of T on consecutive 5 days at 6 dose levels from 0.50 to 1.40 mg/m^2 and fixed dose of CDDP (60 mg/m^2) either on day1 or day5 every 21days. Phase I: We estimated maximum tolerable dose (MTD) in previously treated patients received T and CDDP on day1 and MTD and recommendable dose (RD) in therapy naive patients received T and CDDP on day1 or day5. Phase II: Each 15 therapy naive patients were randomized into two arms (CDDP on day1 or day5 schedules). The RD of T was administered to patients in each arm (step1). In selected CDDP arm, 15 patients from step 1 and an additional 15 therapy naive patients were evaluated for safety and antitumor effect of T and CDDP combination (step2). Preventive G-CSF was administered on day 6 after T administration.
Results: Phase I: 34 patients were enrolled. Both the MTD and the RD of T in combination with CDDP on day1 schedule were estimated as 0.65 mg/m^2. In CDDP on day5 schedule, the MTD and the RD of T were estimated as 1.4 and 1.0 mg/m^2, respectively. Phase II: 30 and 14 patients were enrolled in step 1 and 2, respectively. The response rates (80% for each) were similar for CDDP on day1 and day5 administration schedules. CDDP on day 5 schedule had a better hematological profile (step1). 29 patients with CDDP on day5 schedule yielded 83% response rate (1CR and 23PR, 95% CI, 64.2- 94.2%). Grade 3/4 hematological adverse events were neutropenia (50%), anemia (58.6%) and thrombocytopenia (44.4%). Non hematological adverse events were anorexia, nausea, vomiting, fatigue, alopecia, AST/ALT increase, as dissolved or improved without influence on clinical trial. Hepatic observations were mainly grade 1 and had a tendency of at first or early period. The median survival time in 29 patients on CDDP day5 schedule was 415 days.
Conclusion: The combination of Topotecan on consecutive 5 days and Cisplatin on day 5 schedule with G-CSF support was a safe and effective regimen option for therapy naive patients with ED-SCLC.

9117 POSTER

A phase I study of amrubicin and carboplatin for previously untreated patients with extensive-disease small-cell lung cancer

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Background: Amrubicin and cisplatin are active in the treatment of small-cell lung cancer (SCLC), and carboplatin is an analogue of cisplatin with less non hematological toxicity. However, the appropriate dose of amrubicin and carboplatin combination chemotherapy for previously