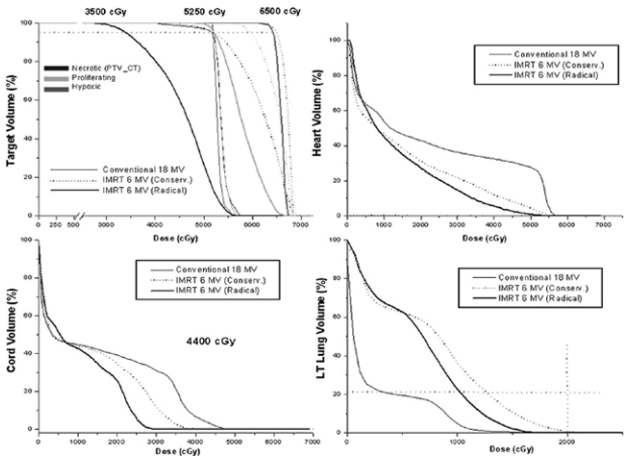
redone with fusion of PET/CT data and 3D CT. Three target volumes were created: necrotic BTV (same as seen in CT), proliferating BTV (based on PET signal to background ratio 1:3) and hypoxic BTV (based on PET signal to background ratio of 1:19, believed to be related to anaerobic glycolisis inefficacy in ATP production). Two IMRT plans were created based on these three BTVs. The first plan ("conservative plan") delivers 52.5 Gy to the necrotic BTV and 65 Gy to the hypoxic BTV. The second plan ("radical change") delivers 30 Gy to the necrotic BTV, 52.5 Gy to proliferating BTV and 65 Gy to hypoxic BTV.
Results: Impact of different target volumes on DVH curves for the three BTVs and the critical structures are shown in Figure 1. The use of BTVs in IMRT plan seems attractive because it increases dose to targets considered to need higher doses. It reduces considerably dose to the heart and spinal cord, organs considered to limit dose escalation approaches in NSCLC treatment. However, lower dose to the spinal cord comes at the expense of slight increase in the contra lateral lung dose, still way below V20 limit.



Conclusions: The "conservative" IMRT approach can be understood as a PET/CT based concomitant boost to the tumor expressing the highest FDG uptake. The "radical" IMRT delivery implies a deviation from the traditional uniform dose target coverage approach, with the intention of achieving a better surrounding tissue sparing and ultimately allowing for dose escalation protocols in NSCLC patients. Several issues should be considered before treating patients using PET/CT based BTVs: tumor motion (4D PET/CT scanning and gated RT), dose calculation accuracy with Monte Carlo based treatment planning, and specific tumor metabolic activity imaged with better radiopharmaceutical markers. We also intend to present four current recommendations for tumor outlining using PET: Qualitative Visual Method (Ciernik), CTV = 2.5 SUV units (Paulino and Johnstone), CTV = 40% Iso of max Uptake Value (Erdi) and Linear SUV threshold function method (Black).

1159 POSTER

Insulin-like growth factor receptor 1 (IGFR-1) expression is significantly associated with longer survival in non-small cell lung cancer (NSCLC) patients treated with gefitinib

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Background: Clinical data have already demonstrated that the prevention of Epidermal Growth factor Receptor (EGFR) mediated signal transduction by the small molecule inhibitor gefitinib provides a promising new treatment option for patients with NSCLC, especially for those with specific EGFR gene mutations or amplification. IGFR-1 is a transmembrane Tyrosine Kinase (TK) receptor implicated in promoting oncogenic transformation, growth, and survival of cancer cells. Data on cell lines suggested that IGRF-1 mediate resistance to anti-EGFR therapy through continued activation of the antiapoptotic PI3K-akt pathway. In NSCLC no data exists on IGFR-1 expression and on its effects on gefitinib therapy.
Materials and Methods: A total of 77 NSCLC patients treated with gefitinib were evaluated for IGFR-1 expression by immunohistochemistry in tumor samples collected at the time of original diagnosis. Using a semiquantitative scoring system, patients were classified as IGFR-1− (score <100) or IGFR-1+ (score 100 to 400). This cohort included 59 patients previously evaluated for EGFR, HER2, HER3, and Phospho-Akt.
Results: IGFR-1 resulted positive in 30 and negative in 47 cases. IGFR-1 expression was not significantly associated with any clinical characteristic, such as gender, histology, or smoking history. No association was also found with other biological markers, such as EGFR gene mutation, amplification or expression, HER2 amplification, HER3 amplification and Phospho-Akt expression. No difference in response (16.7% versus 12.8%, $p = 0.74$) and time to progression (2.6 versus 3.06 months, $p = 0.83$) were observed in IGFR-1+ and IGFR-1−. Median survival was significantly longer in IGFR-1+ patients (17.8 versus 7.3 months, $p = 0.013$). Multivariable analysis confirmed that IGFR-1 negative status was significantly associated with higher risk of death (Hazard Ratio 2.21, $p = 0.012$).
Conclusions: In NSCLC patients treated with gefitinib, IGFR-1 expression is not associated with gefitinib sensitivity in terms of response and time to progression but significantly associated with longer survival. The role of IGFR-1 as independent prognostic factor should be validated in a cohort of NSCLC not treated with TK inhibitors.

1160 POSTER

CXCL12−3'A polymorphism and Lung Cancer metastases protection: new perspectives in immunotherapy?

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Background: The Stromal Derived Factor-1 (SDF-1/CXCL12) chemokine and its receptor CXCR4 have been implied in the development of long distance metastases of several types of cancers, including Non-Small Cell Lung Cancer (NSCLC). A single nucleotide polymorphism consisting in a G to A transition in the UTR3' of *CXCL12* gene, *CXCL12−3'A* polymorphism, and its allelic frequencies were associated with breast cancer and melanoma. The objective of this study was the evaluation of the genetic influence of the *CXCL12−3'A* polymorphism in the susceptibility to lung cancer development.
Material and methods: DNA samples were extracted from peripheral blood cells of 403 patients (154 patients diagnosed with lung cancer and 249 healthy individuals). The *CXCL12−3'A* polymorphism was analyzed through PCR-RFLP (*MspI*). Analysis of data was performed using the computer software SPSS for windows. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measure of the association between *CXCL12−3'A* genotypes and lung cancer risk.
Results: Our data showed that the presence of A carrier genotypes was more frequent in patients with epidermoid NSCLC without long distance metastases, (46.6%), than in patients with epidermoid NSCLC with long distant metastases, (20%). This difference is statistically significant ($P = 0.036$) and suggests that patients with epidermoid NSCLC carrying the A allele present almost 3.5 times less risk of developing long distance metastases (OR = 0.29; 95%CI = 0.09−0.97). Multivariate logistic regression analysis indicates that the A allele presence (aOR = 0.221; 95%IC 0.056−0.877; $P = 0.032$) and age at diagnosis above 66 years (aOR = 0.220; 95%IC 0.067−0.728; $P = 0.013$) are significantly associated with the development of epidermoid NSCLC with long distance metastases.
Conclusions: Our findings suggest that *CXCL12−3'A* polymorphism has a protective role in the development of NSCLC metastases and the elucidation of the molecular mechanisms underlying this protective effect could open the possibility of creating an effective immunotherapeutical approach that mimicries the effects of the polymorphism.

1161 POSTER

VEGF and S100 beta serum levels in advanced non-small cell lung cancer (NSCLC) patients with and withour brain metastases (BM) at diagnosis

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Background: BM at diagnosis is found in 25−30% of NSCLC patients (pts) and are frequently associated with abnormal blood-brain barrier (BBB) function. Serum levels of calcium-binding, astro-glial protein S-100 beta are suggested to be an important marker of BBB-integrity. Data have also shown the role of VEGF in BBB-integrity and in BM growth. The study is aimed to explore if there is any difference between serum levels of S100B and VEGF in advanced NSCLC pts with and without BM at diagnosis.
Patients and Methods: Peripheral blood samples from 73 metastatic NSCLC pts (37 without and 36 with BM) were collected. Pts in both