receiving pCRT experienced fewer locoregional recurrences without higher severe treatment-related toxicity compared with the pCHT group. Although there were not significant differences in terms of OS and PFS in our series, it can not be ruled out significant differences with a longer follow-up.

EP-1360 Heat shock Protein 70 serum levels as a predictor of clinical response in non-small-cell lung cancer

C. Ostheimer[1], S. Gunther[2], M. Bache[1], D. Vordermark[1], G. Multhoff[2]
[1]*Universitaetsklinikum HalleSaale, Radiation Oncology, Halle, Germany*
[2]*Ludwigs-Maximilian-Universitaet Muenchen, Radiation Oncology, Munich, Germany*

Purpose or Objective
Hypoxia mediates resistance to radio(chemo)therapy (RT) by stimulating the synthesis of hypoxia-related genes, such as osteopontin (OPN) and stress proteins, including the major stress-inducible heat shock protein 70 (Hsp70). Apart from its intracellular localization, Hsp70 is also present on the plasma membrane of viable tumor cells that actively release it in lipid vesicles with biophysical characteristics of exosomes. Exosomal Hsp70 contributes to radioresistance while Hsp70 derived from dying tumor cells can serve as a stimulator of immune cells.
Material and Methods
We investigated the prognostic and predictive role of Hsp70 in the plasma in n=44 patients with advanced, non-metastasized (M0) non-small-cell lung cancer (NSCLC) before (T1) and 4–6 weeks after RT (T2) in relation to OPN as potential biomarkers for clinical response and compared plasma levels with a control group of n=114 healthy individuals. Plasma biomarker concentration was determined with commercially available ELISA.
Results
Plasma levels of Hsp70 correlated with those of OPN at T1 ($r = 0.422$, $p = 0.005$) and high OPN levels were significantly associated with a decreased overall survival (high OPN: 13 vs. low OPN: 23 months; $p < 0.05$). Hsp70 plasma levels dropped significantly after RT, i.e. from 10.35 ng/ml before RT to 6.05 ng/ml after RT ($p = 0.016$). A significant positive correlation was determined between HSP70 levels before and after RT ($r = 0.659$, $p < 0.0001$). Compared to the cohort of 114 healthy donors (7.8 ng/ml), mean Hsp70 values in NSCLC patients remained to be significantly upregulated before (T1) and after (T2) RT ($p < 0.05$). Patients who responded to radiotherapy had significantly higher median Hsp70 plasma levels after RT (8.6 ng/ml) compared to those who showed no response after therapy (2.8 ng/ml, $p = 0.013$) and responding patients had a superior OS compared to non-responding patients (23 vs. 9 months, $p = 0.026$) who had an increased risk of death ($rr = 2.11$). The related ROC curve analysis showed a significant predictive function ($p = 0.014$) of plasma Hsp70 levels after RT for therapy response with an area under the curve (AUC) of 0.82 and an optimal cutoff value determining a positive therapy response at ≤4.35 ng/ml (sensitivity = 0.895; false positive rate = 0.143).
Conclusion
In summary, high OPN plasma levels at before RT are indicative for poor OS, whereas elevated post-therapeutic Hsp70 plasma levels together with a drop of Hsp70 between T1 and T2, successfully predict favorable responses to RT. Monitoring the dynamics of Hsp70 in NSCLC patients during and after RT can provide additional predictive information for clinical outcome and therefore might support the therapeutic decision-making process and allow a more rapid therapy adaptation after radiotherapy.

EP-1361 Upfront cranial radiotherapy for EGFR mutant non-small cell lung cancer with brain metastases

M.Y. Kim[1], M.K. Kang[2]
[1]*Kyungpook National University Chilgok Hospital, Radiation Oncology, Daegu, Korea Republic of*
[2]*Kyungpook National University School of Medicine, Radiation Oncology, Daegu, Korea Republic of*

Purpose or Objective
Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are now used as first line therapy in patients with metastatic non-small cell lung cancer (NSCLC) with an EGFR mutation. This study aimed to evaluate the impact of upfront cranial radiotherapy with TKIs or TKIs alone on outcomes of patients with brain metastases from EGFR mutant NSCLC.
Material and Methods
This single center retrospective review included 53 patients with brain metastasis from EGFR mutant NSCLC at the time of the diagnosis, between Jan 2012 to Mar 2017.
Results
First line treatment for brain metastases consisted of upfront cranial radiotherapy with TKIs in 25 patients and TKIs alone in 28 patients. Patients receiving upfront cranial radiotherapy with TKIs were more likely to be symptomatic from brain metastasis and have more brain metastases. The 1-year intracranial progression-free survival was 100% for upfront cranial radiotherapy and 73% for TKIs alone, respectively (p-value=0.016). The median overall survival (OS) and 1-year OS rate was 17 months, 72% for upfront cranial radiotherapy and 24 months, 84% for TKIs alone, respectively (p-value= 0.054). In multivariate analysis, poor performance status (ECOG scale, 2,3 vs. 0,1, HR 9.676, p-value= 0.0008), greater number of extracranial metastasis (≥2 vs. 0-1, HR 3.530, p-value= 0.010) were associated with shorter OS.
Table. Multivariate analysis of overall survival

Variables	Hazard Ratio	95% confidence interval	p-value
ECOG performance status(2,3 vs. 0,1)	9.676	3.128-29.928	0.00008
Number of extracranial metastasis (≥2 vs. 0,1)	3.530	1.344-9.269	0.010
Treatment (Upfront cranial radiotherapy vs. TKIs alone)	-	-	0.226
Number of brain metastasis (≥2 vs. 1)	-	-	0.928

Conclusion
Upfront cranial radiotherapy with TKIs for brain metastasis from EGFR mutant NSCLC improved intracranial progression-free survival, with no difference in OS.

EP-1362 Random forest analysis to predict Disease-Free Survival using FDG-PET and CT in Lung Cancer

M. Kirienko[1], L. Lozza[2], L. Cozzi[3], N. Gennaro[1], A. Rossi[4], E. Voulaz[5], A. Chiti[6], M. Sollini[7]
[1]*Humanitas University, Department of Biomedical Sciences, Milan, Italy*
[2]*Orobix spa, Orobix Spa, Bergamo, Italy*
[3]*Humanitas Research Hospital, Radiotherapy, Milan, Italy*
[4]*Humanitas University/Humanitas Research Hospital, Department of Biomedical Sciences/Radiology, Milan, Italy*
[5]*Humanitas Research Hospital, Thoracic Surgery, Milan, Italy*
[6]*Humanitas University/Humanitas Research Hospital,*

Department of Biomedical Sciences/Nuclear Medicine, Milan, Italy
[7]*Sollini Martina, Department of Biomedical Sciences, Milan, Italy*

Purpose or Objective
We previously identified a radiomic signature capable of predicting disease-free survival (DFS) in non-small cell lung cancer (NSCLC) patients undergoing surgery. In this study, we evaluated the same population with a non-parametric, multivariate analysis using a random forest model, aimed at predicting DFS from a combination of input variables.
Material and Methods
Random forests for classification were developed keeping the same training and validation sets as for the parametric analysis, to predict DFS. Seven different combinations of variables were considered: Clinical (263 patients, 5 features), CT (295, 41), PET (258, 43), PET+CT (258, 84), CT+Clinical (263, 46), PET+Clinical (231, 48), PET+CT+Clinical (231, 89). For each dataset, a random forest model was built considering different number of trees and different split dimensions. Moreover, the relative weight assigned to the output classes was explored. Once hyper-parameters with a better performance in terms of AUC were identified, feature importance was extracted for the optimal models. Additional models were created considering the features with importance greater than the 25th, 50th, 75th and 80th quantiles, respectively. The search of the best split dimension was performed again on these new trees.
Results
The highest AUC obtained on the validation set was 0.79. The corresponding model was a forest with 10000 trees, 6 split dimensions, 0.25/0.75 relative weight and on the dataset containing CT+clinical features. The dataset was the one with only the features with importance greater than the 80th quantile, out of which nine variables were selected.
Conclusion
Innovative statistics analysis are a promising tool to select robust radionics signatures.

EP-1363 Intensity modulated radiotherapy with simultaneous integrated boost for non-small cell lung cancer

A. Fondevilla[1], J.L. López-Guerra[2], M. Dzugashvili[3], P. Sempere Rincón[3], A. Sautbaet[4], P. Castañeda[5], J.M. Díaz[5], J.M. Praena-Fernandez[6], E. Rivin del Campo[7], I. Azinovic[8]
[1]*Instituto Oncológico del Sureste, Radiation Oncologist, Murcia, Spain*
[2]*University Hospital Virgen del Rocio, Department of Radiation Oncology, Seville, Spain*
[3]*Imoncology, Department of Radiation Oncology, Murcia, Spain*
[4]*Imoncology Fundación, Máster Internacional en Aplicaciones Tecnológicas Avanzadas en Oncología Radioterápica de la Universidad de Murcia, Madrid, Spain*
[5]*Imoncology, Radiation Physics, Murcia, Spain*
[6]*University Hospital Virgen del Rocio, Methodology Unit, Seville, Spain*
[7]*Gustave Roussy Cancer Campus, Department of Radiation Oncology, Villejuif, France*
[8]*Imoncology, Department of Radiation Oncology, Madrid, Spain*

Purpose or Objective
The aim of this study was to assess the feasibility and treatment outcome of intensity modulated radiation therapy with simultaneous integrated boost (SIB-IMRT) in locally advanced non-small cell lung cancer (NSCLC) patients.
Material and Methods
A total of 64 NSCLC patients (mean age was 64 years, ranging from 32 to 81 years) with stage IIB (3%), IIIA (36%), and IIIB (61%) were treated with concomitant (N=47; 73%) or sequential (N=9; 14%) chemotherapy between February 2009 and January 2014. Eight patients (13%) received RT alone. Five out of 64 (8%) patients did not complete the planned radiation therapy due to progression disease (N=1), haematological toxicity (N=1) or death shortly after starting the treatment (N=3). All patients received the same irradiation scheme: prophylactic dose for mediastinum was 56 Gy and SIB up to 68 Gy in 34 fractions. In the planning process, we aimed for 95% of prescribed dose to cover at least 95% of the PTV.
Results
The median follow up was 16 months (range, 1-70 months). The overall survival rate for all patients was 79% after one year and 46% after two years. Disease-free survival (DFS) was 81% and 45% after one and two years, respectively, resulting in a median DFS of 16 months. Patients receiving radiation doses above the mean (66Gy; N=56) associated with a lower risk of distant metastasis (HR: 0.25; P=0.017), but this did not remain significant after adjusting for other covariates. Multivariate analysis showed a statistically significant association between stage IIIB patients and a higher risk of mortality (HR: 2.11, 95% CI 1.13-3.96, P = 0.019) compared with stages IIB-IIIA. In addition, T4 stage associated with higher risk of any recurrence (HR: 2.98, 95% CI 1.43-6.22, P = 0.004). Patients receiving chemotherapy were associated with lower risk of locoregional recurrence (HR: 0.27, 95% CI 0.11-0.73, P = 0.009) and those with concomitant chemoradiation were associated with lower risk of any recurrence (HR: 0.25, 95% CI 0.12-0.56, P = 0.001), and mortality (HR: 0.48, 95% CI 0.24-0.95, P = 0.036) compared with sequential treatment and radiation therapy alone. Fourteen patients (22%) experienced acute grade 1 esophagitis and 26 (40%) grade 2. There were no grade ≥3 cases and late oesophageal toxicity was negligible (3 cases had grade 1). Pneumonitis was observed in 10 patients (16%) being grade ≥3 in 6 cases (9%). Although receiving a higher maximum dose to the lungs (P=0.022), having a higher volume of normal lungs receiving 20 Gy or more radiation (P=0.046), and having higher volume of lungs (P=0.045) associated with higher risk of pneumonitis only the last one retained significance in the multivariate analysis (HR 16.21, 95% CI 1.51-174.57, P=0.022).
Conclusion
SIB IMRT can safely increase the radiation dose to the gross tumor volume in patients with NSCLC, while maintaining tolerable doses to adjacent organs, and it has a low pneumonitis rate. We believe that our results should encourage further evaluations in future prospective clinical trials.

EP-1364 Methylenetetrahydrofolate Reductase C677T polymorphism in lung, rectal and breast cancer

K. Boudaoud[1], S. Taleb[2], A. Boucenna[3], K. Sifi[4], K. Benmbarek[4], T. Filali[5], N. Abadi[4]
[1]*University Farhat Abbes Setif. Scientific research laboratory of molecular biolo, Radiation Oncology, Setif, Algeria*
[2]*CHUC, Department of radiation oncology, Constantine, Algeria*
[3]*UC1, Departement of animal biology, Constantine, Algeria*
[4]*Scientific research laboratory of molecular biology-UC3, Biochemistry, Constantine, Algeria*
[5]*Scientific research laboratory of molecular biology-UC3, Medical oncology, Constantine, Algeria*

Purpose or Objective
Methylenetetrahydrofolate reductase (MTHFR) enzyme plays an important role in folate metabolism which is involved in DNA methylation, repair, and synthesis. We