– **At PET3**: Both SUVmax and MTV decreased DFS ($p = 0.003$ and $p = 0.004$ respectively) in HNC. For cervix cancer, only MTV was correlated with DFS.

Conclusion: 18F-FDG PET at 40 Gy seems to be a prognostic factor of DFS in HNC and cervix cancer, potentially being used to intensify treatment for bad responders.

2001 ORAL

Nanoscale Radiotherapy − NBTXR3 Hafnium Oxide Nanoparticles as Promising Cancer Therapy

L. Maggiorella[1], G. Barouch[2], C. Devaux[3], A. Pottier[4], E. Deutsch[5], J. Bourhis[6], E. Borghi[7], L. Levy[4]. [1]*Nanobiotix, Radiobiology, Paris 12, France;* [2]*CEA, DEN, Cadarache F-13108 Saint-Paul-lez-Durance, France;* [3]*Nanobiotix, Toxicology, Paris 12, France;* [4]*Nanobiotix, Discovery, Paris 12, France;* [5]*IGR, INSERM 1030, Villejuif, France;* [6]*IGR, INSERM 1030 − Radiotherapy, Villejuif, France;* [7]*Nanobiotix, Clinical Development, Paris 12, France*

Background: There is considerable interest in approaches that could improve the therapeutic window of radiotherapy, which represents a crucial modality of treatment in oncology. We present the rationale for designing NBTXR3 nanoparticles activated by radiotherapy and validate the concept. We performed the Monte Carlo calculations for the first time based on the "local model" simulation that showed a dose enhancement of radiation to tumour cells of approximately nine-fold. NBTXR3 was shown to deposit high energy when the ionizing radiation source is "on" and to have chemically inert behavior in cellular and subcellular systems demonstrated by very good systemic tolerance, thus decreasing potential health hazards.

Material and Methods: We used conventional methods, implemented in different ways, to explore interactions of high Z matter and ionizing radiation with biological systems. In addition, microtomography was performed to explore the nanoparticle volume occupancy inside the tumour and its persistence overtime in mouse tumour models. The antitumour activity of NBTXR3 and tolerance were evaluated in Ewing tumour (A673) and fibrosarcoma (HT1080) using high energy source.

Results and Conclusion: We created and developed NBTXR3 nanoparticles with a crystalline hafnium oxide core which provide high electron density structure and inert behavior in biological media. NBTXR3 nanoparticles' characteristics, size, charge and shape, allow for efficient interaction with biological entities, cell membrane binding and cellular uptake. The nanoparticles were shown to form clusters at the subcellular level in tumour models. Of most importance, we show NBTXR3 intratumour bioavailability with dispersion of nanoparticles in the three dimensions and persistence within the tumour structure, supporting the use of NBTXR3 as effective antitumour therapeutic agent. Antitumour activity of NBTXR3 showed marked advantage in terms of survival, tumour specific growth delay and local control in A673 and HT1080 human tumour models. Changing radiotherapy benefit-risk ratio is challenging. These data are supportive for the first clinical development of hafnium oxide nanoparticles, with an on/off mode of action through successive fractions of radiation therapy using current equipment available in hospitals.

2002 ORAL

4D List Mode PET/CT in Free Breathing Stereotactic Radiotherapy

I. Ernst[1], F. Buether[2], C. Moustakis[3], J. Dullat[1], F. Mounessi[1], S. Scobioala[1], T. Boelling[4], N. Willich[1]. [1]*University of Münster, Radiotherapy and Radiooncology, Münster, Germany;* [2]*European Institute for Molecular Imaging, Physics, Münster, Germany;* [3]*University of Münster, Radiotherapy and Radiooncology/Physics, Münster, Germany;* [4]*Paracelsus Hospital, Radiotherapy and Radiooncology, Osnabrück, Germany*

Background: Target movement is still a major problem in high precision radiotherapy like stereotactic body radiotherapy (SBRT). Techniques like gating or tracking can solve this problem but often require invasive intervention or prolonged application time, 4 D CT pictured only few breathing phases, which could be a problem especially for patients with poor lung function.

4D list mode-capable PET/CT allows valid detection of target motion and reduction of planning target volume (PTV) up to 35% compared to planning based on CT in maximal inspiration and exspiration.

The aim of this study was evaluation of this new method particularly with regard to feasibility, local tumour control rate, and toxicity.

Material and Methods: 140 patients with 167 lesions were enrolled. They suffered from primary or secondary thoracal or abdominal cancer. Planning procedure included free breathing contrast enhanced PET/CT with list mode-based reconstruction. For liver lesions, accuracy was improved by additional MRI with different contrast enhanced phases. Planning target volume (PTV) contained gross tumour volume (GTV), 2 mm set-up margin and safety margins based on list mode detected motion. All patients underwent SBRT with prescribed radiation dose to the 65% enclosing isodose. Normally, 3 x 12.5 Gy were delivered. Tumours close to lung hilus, stomach, or small bowel received 7.0 Gy in 5 fractions. All patients received prophylactic antiemetic medication one hour before starting SBRT. In case of radiotherapy close to the stomach, patients got proton pump inhibitors for three months starting with first SBRT.

Clinical history, laboratory findings, early and late toxicity scores, PET/CT, and MRI in cases of liver lesions were gathered at the 6-week follow-up visit and then at 3-month, 6-month, 9-month, and 12-month follow-ups.

Results: All lesions were visible in PET and movement was detected by list mode PET/CT in all cases. The patients tolerated planning procedure and SBRT very well. No early or late toxicity $\geqslant$ grade 2 (CTCAE v.3.0) was reported.

1/167 lesions showed an in field relapse, local control is 98.5% (2 to 23 months observation time, mean 7.9).

Conclusion: Good tumour control rate and low toxicity demonstrate excellent applicability of 4D list mode-based target delineation in free breathing high precision radiotherapy.

2003 ORAL

Perfusion and Permeability Study in High Grade Glioma Patients: Implications on Outcome and Importance of Steroids Uptake Before Radiotherapy

M. dos Santos[1], F. Fayard[2], I. Ghorbel[1], A. Frattici[1], J. Domont[3], A. Laplanche[2], F. Bidault[3], D. Ducreux[3], F. Dhermain[1], J. Bourhis[1]. [1]*Institut Gustave Roussy, Radiotherapy, Paris, France;* [2]*Institut Gustave Roussy, Epidemiology, Paris, France;* [3]*Institut Gustave Roussy, Medical Oncology, Paris, France*

Background: High grade gliomas (HGG) represent the most frequent group of primary malignant brain neoplasm. Conventional imaging evaluation is not a direct measurement of tumour aggressiveness. Evaluation of microvascular characteristics as Perfusion and Permeability could be more appropriate.

Material and Methods: At Institut Gustave Roussy, since January 2008 and up to December 2010, all patients diagnosed with HGG and residual disease 1 week before Radiotherapy (RT) were evaluated with perfusion and permeability magnetic resonance imaging, and treated either to Stupp protocol (60 Gy in 30 fractions plus concomitant temozolomide (TMZ) 75 mg/m^2, then adjuvant TMZ, 150–200 mg/m^2) for grade IV or RT alone in grade III gliomas (with TMZ after failure). Disease free survival (DFS) was estimated using the Kaplan–Meier method; comparison between groups was performed using the log-rank test. Multivariate analysis was performed by Cox model. Chi-square tests were used to analyze the relationship between variables of interest.

Results: Median follow up was of 15 months and 79 patients were studied. Median age was 60 years (range: 17−82), there were 15 grade III and 64 grade IV gliomas (81%). A total of 49 patients was under steroids (64%) just before RT. There were 42 patients with tumours presenting detectable permeability (53%) and median relative cerebral blood volume estimate (r-CBV) was 4 (range: 1.7 to 8.3). Median DFS was 9 months. There was no difference between the high perfusion (r-CBV > 4) and the low perfusion group (r-CBV $\leqslant$ 4) with a HR of 0.78. Patients with detectable permeability had a worse DFS when compared to "no permeability" group (respectively 22% vs. 38% at 1 yr, with a HR of 1.32), but without statistical significance ($p = 0.3$). There was no correlation between permeability and perfusion ($p = 0.85$). Patients under steroids had a worst DFS ($p = 0.04$) and this item was not correlated to bulk of residual tumour. Multivariate analysis confirmed this result ($p = 0.03$).

Conclusions: Patients under steroids before RT presented a worse prognosis. In our series, no correlation was shown between perfusion and permeability in HGG with residual disease, and higher values of rCBV had no impact on outcome. High permeability could be still interesting to study in the future as a possible independent prognostic marker, even if no definitive assumption could be made because of the limited number of patients studied.

2004 ORAL

Rosiglitazone(RGZ) Attenuates Pulmonary Fibrosis and Radiation-induced Intestinal Damage

M. Mangoni[1], M. Sottili[1], C. Gerini[1], F. Castiglione[2], S. Gelmini[1], E. Vanzi[1], A. Bottoncetti[1], A. Pupi[1], L. Livi[1], G.P. Biti[1]. [1]*University of Florence, Clinical Physiopathology Department, Firenze, Italy;* [2]*University of Florence, Department of Human Pathology and Oncology, Firenze, Italy*

Background: Rosiglitazone (RGZ) is a peroxisome proliferator activated receptor (PPAR) gamma agonist with anti-inflammatory, anti-fibrotic