adapted if needed. 724 CT features were calculated using radomics software. To test if features were different for EGFR+, KRAS+ or WT patients one way ANOVA (initially without correction for multiple testing) was performed using a 5% significance level. A pair-wise comparison (t-test) identified significantly different groups.

Results: 51 EGFR+, 47 KRAS+ and 32 WT patients were included. 41 features were significantly different between EGFR+, KRAS+ and WT patients. One feature is a first order gray-level statistics feature (7% of feature subgroup total), two are gray-level co-occurrence matrix based (9%), two gray-level size-zone matrix based (18%), one Laplacian-of-Gaussian transform based (0.5%) and 35 are wavelet transform based features (7%). Statistics for the significant features are shown in Table 1. One easy to interpret significantly different feature for EGFR+ compared to WT patients was the median Hounsfield Unit (HU). EGFR+ patients had a median HU which is on average 54±23 HU higher compared to WT patients, see Figure 1. KRAS+ patients did not have a significantly different median HU compared to EGFR+ or WT patients.

Table 1: Mean value and standard deviation of EGFR+, KRAS+ and WT patients for the gray scale texture features.

<table>
<thead>
<tr>
<th>Feature inside primary tumor</th>
<th>EGFR+</th>
<th>KRAS+</th>
<th>WT type</th>
<th>Different group</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLCM_nbdMean-2</td>
<td>0.125±0.07</td>
<td>0.125±0.06</td>
<td>0.125±0.07</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>GLCM_nbdMean-2</td>
<td>0.125±0.07</td>
<td>0.125±0.06</td>
<td>0.125±0.07</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>GLCM_nbdMean-2</td>
<td>0.57±0.13</td>
<td>0.43±0.16</td>
<td>0.44±0.13</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>GLCM_nbdMean-2</td>
<td>3.5±2.03</td>
<td>1.0±4.01</td>
<td>1.4±3.07</td>
<td>EGFR+ vs. WT</td>
</tr>
<tr>
<td>GLCM_nbdMean-2</td>
<td>5.1±1.07</td>
<td>1.3±2.07</td>
<td>4.1±2.70</td>
<td>EGFR+ vs. WT</td>
</tr>
<tr>
<td>(test)</td>
<td>0.95±25</td>
<td>78±34</td>
<td>80±25</td>
<td>EGFR+ vs. WT</td>
</tr>
<tr>
<td>Median Hounsfield Unit</td>
<td>51.169 HU</td>
<td>51.169 HU</td>
<td>51.169 HU</td>
<td>EGFR+ vs. WT</td>
</tr>
</tbody>
</table>

Conclusion: We showed that there are differences in radiomic CT features between EGFR+, KRAS+ and WT NSCLC. The next step will be to externally validate (work in progress) a robust radiomic signature, based on standard CT imaging. Also this allows to monitor radiomic signature evolvement under treatment.

Symposium: Radiobiology of proton / carbon / heavy ions

SP-0610
Gene expression alterations to carbon ion and X-irradiation

M. Moreels1, K. Konings1, S. Baatout1
1SCK-CEN, Radiobiology Unit, Mol, Belgium

Hadreron therapy is an advanced technique in the field of radiotherapy that makes use of charged particles such as protons and carbon ions. The inverted depth-dose profile and the sharp dose fall-off after the Bragg peak offered by charged particle beams allow for a more precise localization of the radiation dosage to the tumor as compared to the conventional used photons. As a consequence, the surrounding healthy tissue receives a much lower dose. Besides this ballistic advantage, the use of high-linear energy transfer (LET) carbon ion beams offers also a biological advantage, i.e. a higher relative biological effectiveness (RBE) as compared to conventional low-LET photon therapy. Carbon ion radiation is thus more effective in inducing DNA damage, cell cycle arrest and cell death, thereby accounting for highly lethal effects, even in tumors that are resistant to X-ray irradiation.

The response of an irradiated cell depends on the dose, dose-rate, radiation quality, the lapse between the radiation-induced stress and the analysis, and the cell type. In this context, genome-wide studies can contribute in exploring differences in signaling pathways and to unravel high-LET-specific genes. Several studies within SCK-CEN and outside have already compared changes in gene expression induced by different radiation qualities. Overall, the number of differentially expressed genes as well as the magnitude of (dose-dependent) gene expression changes was found to be more pronounced after irradiation with particle beams.

Currently, the Radiobiology Unit of SCK-CEN is deeply investigating the effect of low- and high-LET radiation on the gene expression of different cancer cell lines in vitro. Our results clearly demonstrate a dose-dependent downregulation in several genes involved in cell migration and motility after carbon ion irradiation. A higher number of genes as well as more pronounced changes in their expression levels were found after carbon ion irradiation compared to X-rays. Further research are currently investigating whether the observed molecular changes also influence the cellular ‘behaviour’ after irradiation in terms of cell migration and motility after irradiation, since these are prominent characteristics of cancer progression and metastasis.

Assessing both the risks and advantages of high-LET irradiation can contribute to the study of the biological effect on the tumor and will lead to further acceptance and improvement of the clinical outcome of hadron therapy.

Acknowledgements: This work is partly supported by the Federal Public Service in the context of the feasibility study ‘Application of hadrontherapy in Belgium’, which is part of action 30 of the Belgian cancer plan. Carbon ion irradiation experiments (P911-H) were performed at the Grand Accélérateur National d’Ions Lourds (Caen, France).

SP-0611
Normal tissue response in particle therapy

B.S. Sørensen1
1Aarhus University Hospital, Exp. Clin. Oncology, Aarhus C, Denmark

Particle therapy as cancer treatment, with either protons or heavier ions, provide a more favourable dose distribution compared to x-rays. While the physical characteristics of the particle radiation have been the aim of intense research, less focus has been on the actual biological responses particle irradiation gives rise to. Protons and high LET radiation have a higher radiobiological effect (RBE), but RBE is a complex quantity, depending on both biological and physical parameters. One of the central questions in particle therapy is whether the tumor and the normal tissue has a differential RBE due to the difference in α/β ratio. Most of the data to enlighten this is in vitro data, and there is very limited in
vivo data available, although this is a more appropriate reflection of the complex biological response.

RBE is often established as measured by cell death, but emerging evidence also demonstrate an altered response in the surviving cells. This is both evident for high LET radiation, but also for proton radiation. This differential biological effect is not only relevant in the tumour, but also in the normal tissue. Current research in particle radiobiology is, in addition to the RBE, focusing on the molecular tissue response, and on the signalling pathways. Gene expression response in a panel of primary human fibroblasts, established from patients with known response to x-ray irradiation in regards to late tissue damage, irradiated in vitro with different radiation qualities, has evaluated the effect of particle irradiation at different positions in the beam. This enlightens the heterogeneity in patient response to proton irradiation, individual biological variations and the differential effect of proton irradiation. This presentation will focus on the available experimental data on normal tissue response after irradiation with protons or heavier ions. Supported by grants from the Danish Cancer Society

SP-0612
Preclinical studies using protons for high-precision irradiation of small animals
P. Van Luik
1University Medical Center Groningen, Department Radiation Oncology, Groningen, The Netherlands

Many technological developments attempt to reduce dose to normal tissues in order to reduce normal tissue damage. However, optimal use of such technologies requires knowledge of mechanisms underlying normal tissue damage. Therefore, normal tissue effects were studied using highly accurate proton irradiation to different regions and volumes in various rat organs.

Rats were irradiated using high-energy protons. Collimator design was based on X-ray imaging (spinal cord), MRI (parotid gland) or CT scans (heart, lung) of age, sex and weight matched rats. This typically resulted in 2-4% uncertainty in irradiated volume of that organ. For partial irradiation of the spinal cord an in-line X-ray imager was used to yield a positioning accuracy of 0.1 mm. Finally, non-uniform irradiations were facilitated by sequential use of different collimators. Hind leg paralysis, breathing frequency chances and salivary flow rate and tissue histo-pathology were used to assess organ response.

Spinal cord: Next to irradiated volume, low doses surrounding irradiation, individual biological variations and the differential effect of proton irradiation. This presentation will focus on the available experimental data on normal tissue response after irradiation with protons or heavier ions. Supported by grants from the Danish Cancer Society

PAROTID GLAND: We demonstrated that the response of the parotid gland critically depends on dose to its stem cells, mainly located in its major ducts. The importance of this anatomical location was confirmed in a retrospective analysis of clinical data. A prospective clinical trial to validate this finding is in progress.

Lung: Volume dependent mechanisms of lung toxicities were observed, where high volumes with low dose limiting early vascular/inflammatory responses inducing pulmonary hypertension and consequential cardiac problems, whereas low volumes displayed high or even no dose limiting late fibrotic response. Moreover, inclusion of the heart in the irradiation field strongly enhanced early lung responses.

In summary, using high-precision proton irradiation of rat organs we elucidated several mechanisms and critical targets for normal tissue damage. In general we found that, rather than dose to the organ, the development of toxicity strongly related to dose to functional sub-structures within the organ or even in other organs. In general, in more parallel organized tissues it seems that a high dose to a small volume is better that a low dose to a large volume. Maintaining or enhancing the regenerating potential of the normal tissue seems warranted to further optimize radiation therapy.

Symposium: New insights in treating vertebral metastases

SP-0613
Recent progresses in interventional radiology
P. Bize
1Centre Hospitalier Universitaire Vaudois, Department of Diagnostic and Interventional Radiology, Lausanne Vaud, Switzerland

Treatment of vertebral metastasis can be complex, involving medical treatment, radiotherapy, surgery or newer technique such as thermal ablation and vertebroplasty. The purpose of vertebral metastasis treatment is to rapidly improve the quality of life of the patients and to restore the mechanical properties of the spinal column and to a lesser extend to prevent local tumor growth.

Minimally invasive treatment such as vertebroplasty, combined or not, with thermal ablation fulfill all these purposes with minimal impact on the patient’s quality of life. Vertebronplasty is efficient in controlling the patient’s pain in 89.7% at 1 month and 86.9% at 6 months (ref 1). Restoration of the mechanical properties of the spinal column is obtaind in 100% of cases after successful vertebroplasty (ref 2) When combined with thermal ablation (RFA or Cryoablation) the local recurence rate is very low (ref 3)

While radiation therapy remains the mainstay in the treatment of vertebral metastasis, it does not improve the stability of the vertebral column. A complimentary surgery is often necessary to ensure stability of the treated vertebra. Minimally invasive procedure such as thermal ablation combined with vertebroplasty do offer immediate pain control in addition to local tumor control and restoration of mechanical stability with a minimal impact on the patient’s quality of life.

SP-0614
What are the limits of minimally invasive surgery?
F. Zairi
1CHRU Lille Hôpital Salgreno, Department of Neurosurgery, Lille, France

Abstract not received

SP-0615
How to optimise the potential of SBRT
P. Oud
1University Hospital Ghent, Ghent, Belgium

Radiotherapy is a well-established treatment for painful vertebral metastases. Multiple prospective studies report pain response rates of 50 to 90%. Based on randomized studies, 8 Gy in a single fraction is the standard of care for painful uncomplicated bone metastases. Despite the lack of a dose response relationship for pain control, there is good rationale for dose escalation with the aim to improve upon existing rates of local tumour control and pain control. Stereotactic body radiotherapy is ideally suited to safely escalate the dose and improve tumour control. In order to optimize the potential of SBRT, adequate patient selection and specific technical considerations should be taken into account.

PATIENT SELECTION
Several considerations should be taken into account before delivering SBRT for vertebral metastases. A first consideration is the life expectancy of the patient, which should be evaluated with validated scoring systems (e.g. MRF score, Recursive partitioning analysis index, PRISM). Patients with a short life expectancy in need for palliative radiotherapy should be managed with short effective radiotherapy courses. In patients with longer life expectancy local control might be an important end point potentially