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 xray radiation 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 Luijk1
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 changes and salivary flow rate and tissue histo-pathology were used to assess organ response.

Spinal cord: Next to irradiated volume, low doses surrounding small volumes with a high dose effects were found to strongly impact the tolerance dose. In addition, the tolerance dose strongly depended on the shape of the dose distribution, independent of irradiated volume. Taken together this indicates that irradiated volume is not good predictor of toxicity. However, a model including tissue repair originating from non-irradiated tissue over a limited distance could explain the observed effects. Taken together these results suggest that regeneration plays an important role in the response of the spinal cord.

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. Bize1
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. Vertebraplasty 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 obtained in 100% of cases after successful vertebroplasty (ref 2). When combined with thermal ablation (RFA or Cryoablation) the local recurrence 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. Zairi1
1CHRU Lille Hôpital Salengro, Department of Neurosurgery, Lille, France

Abstract not received

SP-0615 How to optimise the potential of SBRT
P. Ost1
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. NRP 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