activity was decreased with increasing the concentration of aminotriazole (ATZ; 0.1, 1, 10 mM) dose-dependently. ROS was increased with ATRA and it was augmented by the combination with radiation. ATZ decreased ROS production and increased cell survival by ATRA alone or ATRA combined with radiation despite the reduction of catalase. The catalase that is induced by ATRA increases ROS production and radiosensitivity, and excess catalase would be one of the mechanisms for antiproliferaive effect of ATRA.
This study shows new mechanism of antiproliferaive effect of ATRA and will give a basis for cancer treatment in using ATRA alone or combined with radiation therapy through the elucidation of the role of antioxidant enzymes.

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Erythropoietin in patients with malignant extradural spinal cord compression: functional and pharmacokinetic outcomes

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Background: Erythropoietin has shown neuroprotectant properties in preclinical and randomized studies. There have been no studies showing that erythropoietin enters the central nervous system in patients with extracranial disease.
Methods: Ten paraparetic patients with malignant extradural spinal cord compression who were eligible for radiotherapy, lumbar puncture and intravenous epoetin alfa were enrolled. Patients received epoetin alfa 1500 U/kg intravenously over 30 minutes followed by a standardized dexamethasone and radiotherapy protocol. A lumbar puncture and venipuncture were performed 24–30 hour post-epoetin alfa infusion. Patients were followed daily during radiotherapy, at weeks 2, 3, 4, 8, 12 and at months 6, 9 and 12.
Results: There were no apparent acute toxicities from the epoetin alfa infusion. Erythropoietin was detectable (range 17–214 mIU/ml) in the cerebrospinal fluid in all 8 patients sampled. Before treatment, 8 patients were non-ambulatory and 2 patients were weak but ambulatory. After treatment, 6 (75%) and 2 (100%) recovered or maintained ambulation and improved at least one functional class after a median time of 15 and 18 days, respectively. Five of seven patients with objective sensory deficits and one of seven catheter-dependent patients recovered. Fifty-five percent had a complete pain response and 22% had a partial response. Eight patients have died with a median survival of 1.5 months.
Conclusions: After an intravenous infusion of epoetin alfa, radiotherapy and steroids, high concentrations of erythropoietin were detectable in the cerebrospinal fluid. Patients with malignant extradural spinal cord compression demonstrated encouraging improvements in neurologic function and pain.

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Combined treatment of experimental gliomas with radiotherapy, radiosensitizing and chemosensitizing gene therapy

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Background: The aim of this work was to improve the chemotherapeutic and radiosensitising effects of gemcitabine. Our hypothesis was that increasing the deoxycytidine kinase (dCK) enzyme level that activates gemcitabine within the cells, will lead to increased gemcitabine effects, which could improve the efficacy of chemo- and radiotherapy.
Material and methods: Murine Gl261, rat C6 and 9L and human U373 glioma models were used. The dCK gene was cloned into an adenoviral vector (Ad-dCK). For in vitro proliferation assay cells were transduced with Ad-dCK, treated with Gemcitabine and irradiated. Subcutaneous Gl261 tumors were established in C57BL/6 mice using either wild type or Ad-dCK infected tumor cells. Tumor bearing mice were treated with intraperitoneal injection of Gemcitabine and local tumor irradiation. Tumor growth and survival were followed.
Results: Strong differences were seen in the basal dCK activities of the different glioma cell lines: the murine Gl261 cells showed ten fold higher enzyme activities, than the human and rat glioma cell lines. Intracellular dCK activity was raised by infecting the cells with increasing multiplicities of infection (MOI) of Ad-dCK. Ad-dCK at high MOI was very toxic for Gl261 cells, but did not affect the viability of the other glioma cell lines. The in vitro data showed that increased dCK enzyme activities could not further increase gemcitabine toxicity in Gl261 cells, but gemcitabine itself had a minor radiosensitizing effect. On the contrary, in rat C6 and 9L glioma cells elevated dCK levels could substantially improve both gemcitabine toxicity and the radiosensitising effect. In the case of Gl261 cells, in vivo data are in concordance with the in vitro data: although the combined effect of gemcitabine and radiotherapy has a pronounced synergistic effect (60% tumor free animals after 100 days) compared to mono-therapies (no tumor free animals), increasing dCK levels in the tumor cells did not affect tumor growth or survival. Experiments with C6 and 9L rat models are undergoing.
Conclusions: In the Gl261 model increasing intracellular dCK levels could not improve the chemo- or radio-sensitizing effect of gemcitabine. In the C6 and 9L models elevated dCK levels could increase both the chemo- and radio-sensitizing effect of gemcitabine.

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Potential interest in integrating functional MRI (f MRI) in high-precision RT planning for WHO grade 2 unfavorable and grade 3 supra-tentorial gliomas: first experience with 10 consecutive patients

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Introduction: Among new imaging techniques potentially useful in radiotherapy (RT) of patients (pts) with brain gliomas, fMRI is supposed to add informations to conventional MRI (cMRI). fMRI could modify Gross Tumor Volume (GTV) delineation, visualize inside a low-grade glioma small focuses of higher activity (for an RT boost) and identify sites essential for memory and language, to be eventually avoided, these functions being potentially altered by RT. Here, fMRI was evaluated for adults with gliomas of intermediate prognosis, in addition with computed tomography (CT) scan and cMRI, routinely used for RT planning (RTP). The main goal was to evaluate if fMRI could modify CT/cMRI-based RTP.
Description: After biopsy/surgery, 10 adult pts with gr. 2 unfavorable or gr. 3 supra-tentorial glioma were entered in the study. CT scan and cMRI (T1 Gado, T2-weighted sequences) were performed in RT position. fMRI was subsequently performed in the same position using 1) a diffusion tensor imaging (DTI)-based fiber tracking technique, visualizing major white matter tracts, 2) a perfusion-weighted imaging identifying higher perfused areas, 3) cortical activation with memory and language paradigms.
Firstly, only CT scan and cMRI were used for RTP, contouring of GTV was based on T1 Gado for gr. 3 and T2 for gr. 2 gliomas, organs at risks (OaR) were delineated. Then, RTP was made, optimizing GTV coverage and mimimizing irradiation of OaR. Pts were treated according to the conventional RTP and baseline neurocognitive functions were evaluated before RT, then bi-annually.
Secondly, fMRI images were analysed and used to define a "functional" GTV for comparison with the conventional one.
Results: 10 adult pts (mean age of 42 yrs) were included in 6 months, all with an oligodendroglioma component. First symptom was epileptic seizure in 8 pts. In 6 pts, glioma was located in the left-temporal area with a mean size of 6 cm in T2-cMRI, 6 showed a mild signal enhancement. In 7 pts, highly active focuses were identified, within homogenous T2 hypersignal areas. In 5 patients, DTI fiber-tracking showed warped white matter fibers, strongly suggesting brain infiltration beyond cMRI images. Overall, the balistic of RT could be potentially modified in 4 pts.
Conclusion: The preliminary results of this study strongly suggest that the entire spectrum of fMRI can play a major contribution to improve the accuracy of high precision RT in adult pts with non-glioblastoma gliomas.

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p53 and RB suppressor pathways deregulation by HDM2 overexpression in human meningeal hemangiopericytomas. double immunofluorescence and laser scanning confocal microscopy study.

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Meningeal hemangiopericytomas (MHPC's) are slow growing tumors, that in spite of complete surgical removal followed by radiation, recur and