CTV-MRI-5 mm were defined as CTV-MRI plus 1 mm, 2 mm, 3 mm and 5 mm margins, respectively.
**Results:** CTV-MRI < 0.5 cc: The sensitivity of tumor detection of MET-PET was 43% (18/42). In 18 lesions, the mean CTV-MRI and CTV-MPET were 0.23 cc and 0.54 cc, respectively. In 18 (100%) of the lesions, the CTV-MPET was located within the CTV-MRI-1 mm.
0.5 cc < CTV-MRI < 2.5 cc: The sensitivity of tumor detection of MET-PET was 95% (18/19). The mean CTV-MRI and CTV-MPET were 1.01 cc and 1.80 cc, respectively. In 17 (95%) lesions, the volume of CTV-MPET extended beyond the CTV-MRI-1 mm was less than 1 cc. In 18 (100%) lesions, CTV-MPET was located within CTV-MRI-2 mm.
2.5 cc < CTV-MRI < 5.0 cc: The sensitivity of tumor detection of MET-PET was 100% (18/18). The mean CTV-MRI and CTV-MPET were 3.36 cc and 4.84 cc, respectively. In 17 (95%) lesions, the volume of CTV-MPET extended beyond the CTV-MRI-2 mm was less than 1 cc.
5 cc < CTV-MRI: The sensitivity of tumor detection of MET-PET was 100% (17/17). The mean CTV-MRI and CTV-MPET were 15.24 cc and 18.41 cc, respectively.
In 14 (82%) lesions, the volume of CTV-MPET extended beyond the CTV-MRI-3 mm was less than 1 cc. In 100% of lesions, CTV-MPET was located within CTV-MRI-5 mm.
**Conclusion:** On defining the target volume definition in the SRS planning of brain metastases, this $^{11}$C-methionine PET study indicates that a margin of 1 mm (CTV-MRI < 0.5 cc), 1−2 mm (0.5 cc < CTV-MRI < 5.0 cc) and 3 mm-5 mm (5 cc < CTV-MRI) should therefore be added to MRI studies.

**2509** POSTER

**Phase II study of fixed dose rate gemcitabine as radiosensitizer for newly diagnosed glioblastoma multiforme (GBM): preliminary results**

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**Background:** Gemcitabine is a deoxycytidine analogue with a wide range of antitumour activity, presenting powerful radiosensitizing activity at non-cytotoxic concentrations. On this basis, several phase I/II studies have presently been designed on different tumours with concurrent radiation therapy. In malignant glioma few data are presently available on the effects of gemcitabine, with unsatisfactory results as a single antiblastic agent. In a previous phase I study, conducted in our Institution, where fixed dose rate (FDR) gemcitabine at 10/mg/m$^2$/min was tested in association with radiotherapy (RT) for the treatment of newly diagnosed GBM, a maximum tolerated dose of 175 mg/m$^2$/wk was identified. Observed activity has been considered interesting enough to support a phase II study.
**Materials and Methods:** After surgery for GBM, patients presenting measurable residual tumour were treated with fractionated focal RT at a daily dose of 2.0 Gy per fraction, five days per week for six weeks (total dose of 60 Gys). FDR gemcitabine at 175 mg/m$^2$/wk was given concomitantly starting 24−72 hours prior to RT, and then for the whole duration of RT. MRI evaluation was performed at 7 and 40 days from the end of chemo-radiotherapy for early therapeutic assessment. Standard oral temozolomide 150–200 mg/m$^2$ was administrated following the combined experimental treatment, at least until tumour progression or relevant side effects. Tumour response rate, progression free survival, and overall survival time have been considered as main objectives.
**Results:** From 07/2004 16 patients (9 male, 7 female) have been enrolled. Characteristics of patients were: median age 57 years (42−72), median KPS at baseline 90 (70–100), surgery/biopsy 14/2. Median time from diagnosis to the initiation of gemcitabine was 45 days (28−54). Among the 14 evaluable patients 3 (21.4%) partial responses, 7 (50%) stable disease and 4 (28.5%) progressive diseases were recorded. At a median follow up of 18 months (2−33) time to tumour progression was 6 months (1.5−24). Toxicity was manageable with only one G3 neutropenia and hypertransaminasemia in two patients respectively. Grade 1 hypertransaminasemia was registered in 6 patients (43%).
**Conclusions:** These preliminary results show that in patients with newly diagnosed GBM, radiosensitizing FDR gemcitabine at 175 mg/m$^2$/wk is a well tolerated regimen with an interesting activity. Accrual is ongoing and more extensive results will be presented.

**2510** POSTER

**Radiosensitized treatment of metastatical brain tumours with hematoporphyrin derivative**

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**Background:** The aim of this work was to investigate and to enlarge the possibilities of sensitized malignant tumor treatment using some derivatives of hematoporphyrin (HpD) as a radiosensitizer. In this paper we have reviewed our results of radiosensitized treatment (RST) of metastatical brain tumors.
**Materials and Methods:** From 2000 to 2006 the total of 33 patients with metastatical brain tumors underwent RST. HpD was injected i.v.; 24, 48 and 72 h after injection of the sensitizer tumors were irradiated with gamma rays 2 Gy at a time from radioactive $^{60}$Co (the full dose of the course was 6 Gy). 7 patients underwent a single course of RST, for the rest RST was repeated.
**Results:** The primary result was already noticeable during the treatment. Especially rapid effect was observed in the patients, who had been in a critical condition. 9 of these 14 patients began to walk, to speak and even to read within two weeks. Nausea disappeared in 8 patients. The Karnofsky performance scale index increased immediately after RST in 29 patients. As the immediate result of RST of metastatical brain tumors all malignant brain tumors (22) in 8 patients fully disappeared. In 6 patients 13 tumors disappeared after a single RST course, and in 2 patients 4 tumors disappeared after some RST courses. However the recurrent disease – new brain metastasis was noticed in three patients. The repeated single RST course was sufficient for the complete regression of all brain metastases in two patients. CT or MRI examinations, provided 3−6 weeks after each RST course, revealed the regression of tumor in 27 patients. As the result of RST, 9 patients were without metastatical brain tumors for 74, 51, 14.5, 12.5, 12, 10, 9, 6 and 5.5 mo. after RST. The median survival of patients (from the moment of brain metastases detection) treated by the addition of RST was 15 mo. Comparing it with the 4.5 mo. median survival of 171 control group patients, it was statistically significant longer. The median survival of patients from the first course of RST was 9 mo.
**Conclusions:** RST is a new and effective method of treatment in metastatical brain tumors. The effectiveness of RST depends on the morphological type of tumor.

**2511** POSTER

**Imatinib plus hydroxyurea in pretreated non-progressive glioblastoma (GBM) – a single center phase II study**

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**Background:** GBM is a highly malignant brain tumor with a median survival of about 15 months. Dysregulated signalling of platelet derived growth factor receptors (PDGF-Rs) is implicated in pathogenesis. The combination therapy of Imatinib (I) plus Hydroxyurea (HU) showed impressive efficacy and tolerability in patients (pts) with recurrent progressing GBM. In a pilot group of 30 pts with recurrent GBM the progression free survival at 6 and 24 months was 32% and 16% respectively. Disease stabilisation (SD) was achieved in 37%. Prolonged disease stabilisation for more than 2 years was possible. Despite the aggressive course of GBM, short periods of disease stabilisation after primary treatment or effective treatment of relapse are observed. The current Phase II study was conducted to analyze the efficacy of I plus HU treatment in GBM pts with documented disease stabilisation for at least 6 weeks as maintenance treatment.
**Methods:** From December 2003 up to June 2005 30 non-progressive GBM pts were included, all of them with SD for more than 6 weeks following effective treatment, including surgery, radiotherapy and at least one chemotherapeutic regimen. No enzyme-inducing anticonvulsive drugs were allowed. I at the dose of 600 mg od and 1000 mg of HU (500 mg bid) were given as a continuous daily treatment, all pts were followed up by blood cell count weekly and magnetic resonance imaging every 6 weeks.
**Results:** All 30 pts are eligible for safety and for 6, 12 and 24 months progression free survival (PFS) and overall survival (OS); 25 pts are male, 5 pts female, the median age is 44 years (32 to 71), 24 pts had primary and 6 pts secondary GBM. All 30 pts had prior radiotherapy, 21 pts had temozolomide containing chemotherapy and 9 pts non-temozolomide containing regimens only. 8 pts were free from relapse, 17 pts after first and 5 pts after second relapse. The median observation time is 31 months. 6, 12 and 24 months PFS is 60% (18/30), 40% (12/30) and 17% (5/30) respectively. 6, 12 and 24 months OS is 90% (27/30), 67% (20/30) and 37% (11/30) so far. PFS for more than 24 months occurred in 3/6 pts with secondary and in 2/24 pts with primary GBM. Hematotoxicity grade 2

and 3 occurred in 11 out of 30 pts (anemia grade 3: 2 pt; anemia grade 2: 4 pts; leucocytopenia grade 3:2 pts; leucocytopenia grade 2: 7 pts; thrombocytopenia grade 2: 4 pts) and required dose reduction of HU in 8 pts, dose reduction of I in 1 patient and G-CSF subcutaniously in 8 pts. No febrile neutropenia, no interruption of the treatment due to toxicity and no treatment related death occurred.
**Conclusion:** The combination of I (600 mg/d) and HU (1000 mg/d) was well tolerated and effective as maintenance treatment in this study. Pts with secondary GBM seem to be more likely to benefit.

**2512** POSTER

**Predicting survival in an unselected glioblastoma multiforme population – use of the RTOG recursive partitioning analysis**

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**Background:** Glioblastoma multiforme (GBM) is associated with median survival of 6−12 months. Curran et al [1] used recursive partitioning analysis to identify patients with significant differences in survival. Scott et al [2] used the technique to re-analyse data from RTOG 83−02 and found that 72 Gy hyperfractionated radiotherapy (HRT) was not superior to database estimates, correctly predicting the negative outcome of RTOG 90−06 illustrating the utility of this technique.
We postulate that recursive partitioning analysis may facilitate patient selection for intensive treatment in a general clinic setting. We designed a retrospective study to investigate whether groups with significant differences in median survival were identified in our unselected clinic population.
**Materials and Methods:** Patients with a histological diagnosis of GBM referred between January 1998 and December 2005 were eligible. Clinical notes, operative notes and radiotherapy prescriptions and plans were analysed. Patients were assigned to an RTOG class and median survival was calculated for each RTOG class. The Kaplan Meier method was used to calculate the median survival. The log rank test was used to examine if the survival times in the different RTOG groups were significantly different.
**Results:** 188 patients were identified. In 12 cases there was insufficient information available to assign an RTOG class. An accurate date of death could not be established for 26 of the patients who were known to have died – these patients were excluded from the survival analysis. Median survival in each RTOG class is listed in table 1. At the time of analysis 6 (3%) patients were alive with a median survival in the range of 21−50 months. Median survival times for the four RTOG classes were significantly different with $p < 0.001$.
**Conclusion:** The classification of patients with malignant glioma according to the RTOG recursive partitioning analysis produces patient subgroups with significantly different median survival figures in a general clinic population. This is the first time the RTOG classes have been validated outside a trial environment. The RTOG recursive partitioning analysis is a useful tool when assessing patients in the clinic for radical treatments.

Table 1. Median survival according to RTOG class

| RTOG class | No. of patients (%) [Total N = 176] | Median survival (mo) |
|---|---|---|
| 3 | 22 (13) | 10.72 |
| 4 | 61 (35) | 8.11 |
| 5 | 48 (27) | 6.72 |
| 6 | 45 (25) | 5.62 |

**References**

[1] Curran et al. J Natl Cancer Inst. 1993 May 5;85(9):704−10.
[2] Scott et al. Int J Radiat Oncol Biol Phys. 1998 Jan 1;40(1):51−5.

**2513** POSTER

**Radiation brain necrosis after stereotactic radiosurgery of the intra-cranial lesion**

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**Background:** Stereotactic radiosurgery (SRS) has become an important therapeutic approach for the treatment of not only malignant brain tumors but also benign tumors or other intracranial diseases such as arteriovenous malformation (AVM). Because this treatment allows a dose increase in the target volume and a reduction of normal tissue exposure, it can improve patient quality of life and control disease. However, high radiation doses bear an increased risk of radiation brain necrosis as late sequelae.
We analyzed the characteristics of cases of radiation necrosis as late sequelae after SRS in our institute and clarified the risk factors of radiation necrosis.
**Methods:** We treated 360 cases of intracranial disease by SRS between December 1998 and March 2007 in our institute. We regarded as radiation brain necrosis if the patient had some radiological abnormal findings around the irradiated field, and deteriorated some neurological complaints required medical care at three months or more after SRS. Cases of local recurrence, defined as increasing the lesions consecutively, were left out of this study. Using the above criteria, 18 patients were classified as having radiation brain necrosis, and we analyzed the backgrounds, methods of irradiation, and characteristics of these patients, retrospectively.
**Results:** The rate of radiation injury after SRS was 5.1% (18/360). The mean age of these 15 patients was 58.3 years old (range: 30−74). Nine cases were male and 9 were female. Ten cases were treated for brain metastases (7: lung cancer, 2: breast cancer, 1: hepatic cell carcinoma), 5 cases for meningioma, 2 cases for glioblastoma, and 1 case for AVM. The regions of the lesions were the frontal lobe: 1 case, the temporal lobe: 5 cases, the occipital lobe: 2 cases, the parietal lobe: 4 cases, the basal skull: 4 cases, and the cerebellum: 2 cases. Six cases had past histories of irradiation of the same area of SRS treatment. The mean peripheral dose (D95) was $18.4 \pm 3.6$ Gy, and the mean maximum dose of the target (Dmax) was $26.3 \pm 8.3$ Gy. The value of Dmax/D95 was more than 2 in 3 cases. Late toxicity occurred 5 to 36 months after SRS (mean: 13.1 months, median: 12 months). Headache was experienced by 2 patients, dizziness and convulsion by 1 patient, motor paralysis by 8 patients, numbness by 3 patients, and disturbances of cranial nerves by 5 patients. In magnetic resonance imaging, expansion of the peritumoral high signal areas on T2-weighted images was shown in all patients, and an increase of enhanced lesion on Gd-MRI was shown in 8 cases. In 4 cases, craniotomy was performed and the lesions were determined pathologically to be radiation necrosis.
**Conclusion:** The rate of radiation brain necrosis as late sequelae after SRS was 5.1%. Meningioma, past irradiation history and a Dmax/D95 value of over 2 were the important risk factors of radiation injury.

**2514** POSTER

**Contribution of $^{18}$F-FET PET in radiation therapy planning of high-grade gliomas**

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**Background:** The aim of this study was to assess the contribution of $^{18}$F-fluoro-ethyl-tyrosine ($^{18}$F-FET) PET/CT to 3D conformal radiation therapy (3DCRT) planning of high grade gliomas.
**Materials and Methods:** A total of 6 high-grade glioma patients (grade III, 3 patients and IV, 3 patients) underwent 3DCRT planning using dynamic PET/CT studies (0−30 min. after injection of 200 MBq of $^{18}$F-FET). A set of 3 triangulation lasers identical, to those used on linacs, were used for patient positioning. The CT descended from the PET/CT was used for radiotherapy planning and dose calibration without fusion of an additional simulation CT. In 3 patients PET/CT was performed median 14 days (range, 10−20) after partial resection and 3 had the PET/CT after biopsy. The target volumes were defined by 2 experienced radiation oncologists based on CT/MRI and PET/CT datasets, and by simple segmentation of the PET images.
**Results:** Dynamic PET imaging ($3 \times 10$ min.) was evaluated and all tumors showed clearly a rapidly and significant tracer uptake exceeding uptake in normal brain (median SUVmax. 1.22). The uptake peak was observed between 10 and 20 min. after injection. The median SUVmax. was 4.33 (range 3.56−4.74) and the median SUVmean was 3.38 (range 3.08−3.59). $^{18}$F-FET PET/CT allowed unequivocal identification of all high grade gliomas. In 3 patients $^{18}$F-FET PET/CT detected multicentric tumors. In one of these patients MRI showed 3 suspected lesions while PET/CT indicated only 2. This result was confirmed by follow-up imaging. The MRI of the other 2 patients visualized only 1 tumor lesion in each case while PET/CT uptake detected a second tumor of 1.5 cm and 2.0 cm of diameter, respectively. The $^{18}$F-FET PET/CT findings let to significant changes in the PTV in 4 patients compared with CT/MRI imaging alone. Interobserver variability for tumor volume delineation was smaller using additional PET/CT in all cases, when compared to CT/MRI-based target volumes.
**Conclusions:** The use of $^{18}$F-FET PET/CT had an important impact on the 3DCRT planning of high-grade gliomas. This imagery modality led to significant modification of 3DCRT techniques in a majority of patients.