Conclusions: We think a dose of 30 Gy to the axis, with this chemotherapy, is inappropriate because five of the eight patients who received it had treatment failures in the spine, while a dose of 36 Gy seems to be appropriate, even further follow-up is necessary to evaluate the use of HFCSI in childhood medulloblastoma.

912 POSTER

Analysis of proliferation and apoptosis in brain gliomas using MIB-1 monoclonal antibody and tunel labelling

M.A.A.M. Heesters[1], J Koudstaal[2], A.A. Canrinus[2], J. Wiersema[2], K.G. Go[3], W.M. Molenaar[2]. [1]*Department of Radiotherapy;* [2]*Department of Pathology;* [3]*Department of Neurosurgery, Groningen University Hospital, The Netherlands*

Purpose: Histological classification of gliomas is based on cellularity, mitoses, presence of necrosis, microvascular proliferation and nuclear polymorphism. Additional characterization of histopathological grading may be obtained by assessment of the proliferation rate by measuring the Ki-67 labelling index using the monoclonal MIB-1 antibody and the apoptotic ratio by in situ labelling of DNA strand breaks using TdT mediated dUTP/dATP 3'OH end labelling (TUNEL).

Methods: Paraffin sections of 85 supratentorial gliomas including 17 astrocytomas (A), 7 anaplastic astrocytomas (AA), 48 glioblastomas (GBM), 6 oligodendrogliomas (O) and 7 anaplastic oligodendrogliomas (AO) were reacted with MIB-1 and TUNEL. LI were calculated counting labelled nuclei and total tumour cell nuclei. MIB-1 LI and TUNEL-LI were related to histology.

Results: Mean MIB-LI were as follows: A = 0.07, AA = 0.31, GBM = 0.25, O = 0.25, AO = 0.27. Mean TUNEL-LI were as follows A = 0.003, AA = 0.047, GBM = 0.018, O = 0.02, AO = 0.023. MIB1-LI and TUNEL-LI were significantly different between A and all other histological groups ($p < 0.05$ Mann-Whitney). No significant difference was found in MIB-LI and/or TUNEL-LI between AA and GBM, O and AO or GBM and O. No significant correlation was found between MIB-1 index and TUNEL index ($p = 0.17$).

Conclusion: Astrocytomas were characterized by low MIB1-LI and low TUNEL-LI values. Anaplastic astrocytomas have a higher proliferation rate and apoptotic rate and did not differ from glioblastomas. Oligodendrogliomas showed a high proliferation rate and an apoptotic rate equivalent to high grade gliomas.

913 POSTER

Estereotactic, linear acelerator based radiosurgery for brain metastases

S. Rodríguez Villalba, G. Donckaster, F. Sansivirini, M.C. Rubio, J. Samblás, J.C. Bustos, J.A. Gutiérrez, D. Ortiz de Urbina, M.I. García Berrocal, F.A. Calvo, M. Santos Ortega. *Radiosurgery, Radiotherapy and Oncology Unit, San Francisco de Asis Foundation, Madrid, Spain*

Purpose: To describe technique and results of radiosurgery (RS) in patients with brain metastases.

Methods and Material: From Aug 91 to Jun 96, 96 patients with 208 brain metastases were treated with RS (single intracranial lesions 51%). The predominat primary tumor was lung cancer 45 (51%). RS alone was the only component of cranial treatment in 58 cases. Median target volume size was 2157 mm3 (range 62–55968 mm3) Single isocenter was employed in 162 cases (77%). Median RS dose was 1247 cGy (range 900–2000 cGy). Most frequent isodose line selected for dose prescription was 90 (58% cases).

Results: Median survival time for the entire group is 10 months (62% of patients are dead at the time of analysis). Local control in the RS treated areas is projected 76% at 2 years. Actuarial 5 years survival is 23% for the entire group (28% single and 19% multiple lesions).

Conclusions: RS is able to induce high local control rates in brain metastases patients, both as definitive radiotherapy modality or combined with whole brain irradiation. Multifactorial prognostic variable analysis and updated results will be presented.

914 POSTER

Improved survival using fractionated stereotactic radiosurgery (FSR) and concurrent taxol (T) for recurrent glioblastoma multiforme (RGM)

G. Lederman[1], M. Odaimi[2], M. Fine[3], S. Wertheim[3], J. Lowry[3], M. Wrzolek[4], H. Rashid[1], G. Qian[1], E. Lombardi[1], E. Arbit[5]. [1]*Dept Radiation Oncology;* [2]*Dept Medical Oncology;* [3]*Dept Radiology;* [4]*Dept Pathology;* [5]*Dept Surgery, University Hospital, Staten Island, USA*

Purpose: FSR/T was compared to single fraction radiosurgery (SFR) for RGM.

Method: 38 patients (pts) with RGM received 4 fractions FSR/T. Characteristics: tumor volume 3.1–150.3 cc (mean 48.2), FSR dose 450–900 cGy (mean 617.1); Taxol was administered in escalating doses from 80–160 mg/m2; Karnofsky Performance Status (KPS) ranged 50–100 (mean 69.2).

Retrospective analysis of 18 pts treated with SFR was performed. Characteristics: tumor volume 4.1–127 cc (mean 29.4); dose 900–2500 cGy (mean 1816.7); KPS was 50–100 (mean 73.9) with median survival 5.5 months. 21 pts evaluated with tumor volume <30 cc, 12 received FSR/T.

Characteristics: tumor volume 3.1–29.0 (mean 13.5) receiving 450–900 cGy (mean 620.8) weekly times 4; KPS 50–90 (mean 72.5). Compared to 9 pts receiving SFR with tumor volume of 4.1–21.9 cc (mean 11.2), receiving 900–2500 cGy (mean 1922.2); KPS 50–100 (mean 73.3).

Results: The overall 15-month survival for the FSR/T group was 37% compared to 6% in the SFR group. Analysis revealed improved survival for RGM pts with tumor volume of <30 cc receiving FSR/T of 58% compared to 11% in SFR at 15 months ($P = 0.05$).

Conclusion: Survival rates for RGM measuring <30 cc treated with FSR/T are significantly improved compared to SFR. This should encourage treatment approaches using FSR and radiation sensitizers to improve outcome.

915 POSTER

Retrospective analysis of 30 intracranial ependymoma

Z. Koçak[1], M. Garipağaoğlu[1], N. Bozdoğan[2], Binnaz Çelebioğlu[1], Cengiz Kurtman[1], A. Çakmak[1]. [1]*Department of Radiation Oncology;* [2]*Department of Pathology, University of Ankara, Turkey*

Purpose: To analyze of prognostic criteria and recurrences pattern in patients with cranial ependymoma treated by postoperative radiotherapy.

Methods and Materials: Thirty patients with intracranial epandymoma were evaluated retrospectively. Their mean age was 18 years. Male/female ratio was 1. Tumor localization was infratentorial in 15 patients, supratentorial in 15 patients. Surgery was performed in 29 patients, only in one patient biopsy was performed. Postoperative radiotherapy was underwent as a primary treatment in 25 patients and salvage treatment (after relapse) in the remaining 5 patients. Radiation doses were between 4500–6000 cGy. Radiation field was local (n = 17), total cranium (n = 12), craniospinal (n = 1). Median follow-up is 41 (3–144) months.

Results: Three, 5 and 10 year survival rates were 63.5%, 42.45, 42.4% respectively. There were 12 relapses (Primary tumor localization: 11patients and both primary tumor and cerebrospinal fluid: 1 patient). Median Relapse time was 27 (7–60) months. The effect of localization, grade, diameter, age, type of surgery, radiation field and dose on prognosis were studied

Conclusion: The grade ($p = 0.003$) and the diameter of the tumour ($p = 0.05$) was found statistically significant effect on prognosis.

916 POSTER

Is there a role of 3-dimensional conformal boost for the treatment of medulloblastoma?

U. Tiefenbacher[1], J. Debus[1], M. Fuss[1], P. Huber[1], B. Selle[2], M. Wannenmacher[1]. [2]*Department of Pediatric Oncology;* [1]*Department of Radiotherapy, University of Heidelberg, Germany*

Purpose: High-dose radiotherapy alone or in combination with chemotherapy may improve frequency and pattern of relapse in medulloblastoma patients. Combined treatment however maybe associated with clinically significant hearing impairment.

Methods: A total of 30 patients suffering for medulloblastoma (median age 10.2; 2.1–51.3; treated between 1982 and 1996) were enrolled in a retrospective evaluation. 14 patients had craniospinal irradiation after surgery of the primary, 16 were treated with stereotactic radiosurgery for recurrent disease after definitive radiotherapy. FFTF was 60% in the primary situation, median survival after radiotherapy of the recurrent disease was 22

months (7–34). Median doses to the whole brain and the spine were 35 Gy. 29 patients had a boost radiotherapy to the posterior fossa (median dose 20 Gy; 8.0–25 Gy). 21 patients were treated with a standard chemotherapy. Patients were analyzed for the pattern of failure and ototoxicity during the primary treatment.

Results: After treatment of the primary pattern relapse was locally in the posterior fossa in 4 patients. Craniospinal dissemination was found in 2 patients. Hearing toxicity in the combined treatment arm was significantly higher.

Conclusion: Survival after local relapse is poor. The toxicity of the combined modality treatment is significant. 3-D conformal boost treatment should be considered to increase dose to the target and reduce the dose in non-target tissues.

917 POSTER

Phase II trial of topotecan (T) as a continuous intravenous infusion in patients (PTS) with high grade gliomas

A. Kyritsis[1], E.S. Newlands[2], C.S. Brock[2], K. Jaeckle[1], V. Levin[1], M. Bower[2], H. Evans[2], G. Dane[3], M. DeWitte[3], W. Yung[1]. [1]*Department of Neuro-Oncology, MD Anderson Cancer Center, Houston TX 77030;* [3]*SmithKline Beecham Pharmaceuticals, Collegeville PA, USA;* [2]*Department of Medical Oncology, Charing Cross Hospital, London W6 8RF, UK*

Purpose: A Phase II study is currently being conducted to evaluate single agent T as treatment for recurrent progressive high grade gliomas.

Methods: Topotecan is administered as a continuous IV infusion every 28 days, with a starting dose of 0.4 mg/m^2 per day. Pts being treated with a stable dose of dexamethasone (dex) may enter the study, but initiation of dex therapy or increase in dose is not permitted during the study. Twenty-nine pts (20 M, 9 F) have been enrolled and treated at two centers. Twenty-four pts received prior chemotherapy. Lesions measured by CT or MRI scan are assessed after every 2 courses.

Results: Fifty-one courses have been administered at the starting dose level, 7 courses at an increased dose level and 6 courses at a reduced dose level. Twenty-six pts are evaluable for efficacy. There have been 3 (11.5%) pts with documented objective responses, 4 (15.4%) pts with stable disease, and 16 (61.5%) with progressive disease. Three pts are ongoing and too early to evaluate. A total of 62 courses of T in 26 pts are evaluable for toxicity. Documented severe toxicities (pts with NCI Grade 3/4) have been: granulocytopenia 3 (11.5%), infection 2 (7.7%), anemia 2, nausea or vomiting 2, thrombocytopenia 1 (3.8%), leukopenia 1, fever 1 and diarrhea 1.

Conclusion: Continuous IV infusion with T is a well tolerated regimen with activity in recurrent high grade gliomas. Evaluation of topotecan in combination with other agents or with radiotherapy is warranted. Development of an oral formulation of topotecan may facilitate further evaluation for this indication. (Supported by SmithKline Beecham.)

918 POSTER

Modifying the Gill-Thomas-Cosman (GTC) head frame to expand the range of fractionated stereotactic radiosurgery (FSR)

G. Lederman[1], G. Qian[1], P. Hasala[1], H. Rashid[1], T. Costantino[1], L. Cangiane[1], E. Lombardi[1], E. Arbit[2]. [1]*Department of Radiation Oncology;* [2]*Department of Surgery, University Hospital, Staten Island, New York, 10305, USA*

Current relocatable head frames limit the range of FSR. Described is a modification to the GTC head frame which enables stereotactic radiosurgery to be directed to tumors below the base of skull to areas of head and neck and cervical sites while maintaining the accuracy of the original head frame.

The original GTC head frame has two fixation points; anteriorly a custom dental Height of the occipital plate is adjustable in its vertical plane, however the dental piece is fixed. Treatment of head and neck and cervical spine tumors is accomplished by modifying the dental apparatus. Bracket extensions of 3 cm and 8 cm have been engineered to which the dental tray is secured thereby allowing the head frame to be lowered to encompass these regions. The depth helmet is also modified.

The accuracy and reproducibility was performed on the Rando Phantom. Each extension was tested 20 times; for each test 18 depth helmet positions were measured. Standard deviation of the modified head frame ranged 0.05 to 0.35 mm (mean 0.20) and 0.13 to 0.34 mm (mean 0.24) for the original GTC head frame.

The accuracy and reproducibility of the original frame is maintained. This modification facilitates treatment to sites involving the head and neck and cervical area. Ability to localize previously inaccessible sites while maintaining the accuracy and advantages of the non-invasive head frame should stimulate interest in innovative therapy.

919 PUBLICATION

Liposomal daunorubicin in children with brain tumors

R. Lippens. *Center for Pediatric Oncology, University Hospital Nijmegen, The Netherlands*

Purpose: Liposomes can be used as carrier for anthracyclines to pass the blood-brain barrier for chemotherapy of malignant central nervous tissue tumors. In this phase-II study the efficacy of liposomal entrapped daunorubicin (DNX) is studied in children with progressive or recurrent brain tumor.

Method: 14 children with progressive growing or recurrent malignant brain tumor received every 4 weeks DNX (60 mg/m^2 in D5 as one-hour infusion), upto a cumulative dose of 600 mg/m^2. Every 3 months the tumor process was evaluated by CT-scan or MRI. Toxicity was evaluated weekly according to the WHO-grading system.

Results: Six children died during the treatment due to rapid progression of the tumor. In 5 children the tumor reduced in size with 10–40%. In 3 children cysts had to be drained after the 6th 7th and 10th course respectively. and biopsies have been taken from the tumorregion. All 3 biopsies showed inactive tumor remnants without signs of malignancy.

Toxicity: The toxicity of DNX is mild (grade 1–3 hematologic toxicity, grade 1–2 hair loss). In all children the contractibility of the left ventricle (Sf) showed a transient decrease. In 5 of the children the Sf decreased to 20–30%. In one child the Sf decreased to 16%.

Conclusion: Malignant brain tumors in children response to liposomal daunorubicin, but in slowly progressive growing tumors only. The toxicity, including cardiotoxicity, is mild and transient.

920 PUBLICATION

Intraarterial chemotherapy (IACH) in patients with advanced primary central nervous system malignancies (APCNM)

A. Pawelczak[1], J. Korniluk[1], P. Twarkowski, G. Weislo[1], M. Górnasiowa[1], E. Suchcicka[1], M. Wojnarowski, A. Giza, C. Szczylik[1]. [1]*Oncology Dept; Vascular Radiology Dept. Central Clinical Hospital Military Medical Academy, Warsaw, Poland*

Purpose: The intraarterial chemotherapy gives the possibility to elevate the concentration of cytotoxic drugs in the tumor mass and to obtain better results of the local therapy.

Methods: In the period from 06.1993 to 11.1996 11 patients (pts) with primary central nervous system tumors was enrolled to the study due to unsuccessful radiotherapy, systemic chemotherapy treatment or surgery techniques that could not be used because of the advancement of disease (2 pts) with tumors of "butterfly" type. Patients were atheterized with caniula through the femoral artery. Then dependently on the tumor localization the appriopriate brain arteries were microcatheterized. The BCNU was dissolved in 5% glucose solution (vol.50 ml) and subsequently administered in the range of doses 160–180 mg/m^2. After the third course of such a treatment the BCNU doses to the values of 120–140 mg/m^2 have been reduced. The maximum tolerated dose (MTD) was completed to the value of 600 mg/m^2. The drug was injected with constant infusion (10 ml/min.) in order to avoid the "stream effect". Courses were repeated every 6–8 weeks.

Results: The response to the IACH by the mean of the axial computed tomography 24 hours before, 24 hours and 3 weeks after were evaluated. In the evaluated patients side effects like: pyrexia (2 pts), sensory aphasia (1 pts), headaches (3 pts), transient blindness (1 pts), hemiparesis (1 pts), enlargement of oedemal zone around the tumor in ACT (1 pts), narrow of the artery after microcatheterization (1 pts). The results of the therapy are following: CR-0, PR + SD-8, PD-3. From this studied group 9 (87.3%) died of the APCNM, and 2 (12.7%) are alive. The time of survival was 5.4 months (range 0.5–29.6).

Conclusion: Intraarterial BCNU chth with the highly selective microcatheterization of brain arteries in patients with advanced CNS malignancies can be useful when other therapeutic procedures cannot be applied.