907 POSTER

Concomitant chemoradiotherapy (CCR) for brain metastasis. Results of a phase I–II study

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To determine the feasibility and efficacy of CCR we have treated between 3/93 and 2/96, 57 pts = NSCLC: 32 pts, breast: 9 pts, SCLC: 6 pts, ADK without primary: 8 pts, others: 2 pts. Median age was 62 years (39–74); 35 women and 22 men. Brain metastasis were multiple in 31 pts. Treatment consisted of whole brain RT for a total dose of 40 Gy/20 f/26 d. Pts received 3 cycles of chemotherapy with cisplatin 60 mg/m2/d 1 IV and etoposide 60 mg/m2/d × 5 per os each 14 days (d 1 = d 14 = d 28), cycle 1 beginning on d 1 of RT.

For all pts, main toxicities were: *Gr 3:* Hb: 2 pts; PNN: 5 pts; Plq: 2 pts; Mucositis: 1 pt; *Gr4:* Plq: 2 pts; Mucositis: 1 pt. One pt presented septic choc after the third cycle and died. Brain CT scan was performed 1 month following completion of therapy. Major radiological response was observed in 42% of the pts including 5 complete response and 19 pts in partial response. Nine pts were inevaluable for response, 7 of them were died before evaluation, 15 pts were stable and 9 progressed.

This study showed the feasibility of CCR for brain metastasis. Response rate was encouraging. A phase III study comparing CCR vs RT alone merits to be activated referring to the absence of important data in the literature.

908 POSTER

Phase II study of IV RMP-7 + carboplatin in recurrent malignant glioma who grade III–IV previously treated with chemotherapy

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Selective bradykinin analogue RMP-7 transiently increases the permeability of the blood brain barrier and the delivery of hydrophilic agents into brain tumours.

Aim: To assess clinical and 3-D MRI response and toxicity of RMP-7 (300 ng/kg) + carboplatin (AUC 5–7) in the treatment of recurrent glioma, WHO histology III + IV, where patients have had previously received chemotherapy.

Methods: 42 patients (median age 45, Karnofsky 70%) were treated q 28 days. Neurological impairment, performance status and steroid use were measured over 4 cycles, plus tumour volume by 3-D MRI at the end of cycles 2 & 4.

Clinical responders = stable or improved compared to baseline, and steroids stable or reduced, for ≥2 cycles. Primary evaluation of first 4 cycles.

Results:

% Patients Responding By Assessment Tool: Intent To Treat Analysis.

Assessment	All	Grade III	Grade IV
EFIT[1]: improved/stable (n = 40)	7/33	47	38
Karnofsky: stable + improved (n = 41)	49	56	46
MRI volume: PR/SD[2] (n = 37)	3/22	6/38	0/10

[1] an objective, validated measure of neurological impairment. [2] CR ≥ 95% volume reduction + off steroids; PR > 50% reduction + stable or reduced steroids; PD > 50% increase; SD all other situations. All maintained ≥2 cycles.

Toxicity: no deaths, 1 thrombocytopaenic withdrawal. Thrombocytopaenia and/or neutropaenia CTC grades 3/4: 3% at baseline; 36% at cycle 1; 22% at cycle 2; 19% at cycle 3; 7% at cycle 4. 5 patients had treatment associated transient focal seizures.

Conclusions: Clinical and MRI response is promising and toxicity is mild.

909 POSTER

Estereotactic radiosurgery for single brain metastases

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Purpose: To describe technique and results of radiosurgery (RS) in an unselected group of patients with apparent single brain matestases.

Methods and Materials: From Aug 91 to Jun 96, 49 patients were treated with linnear accelerator RS. Patients characteristics were: 33 male, 16 female, median age 56 years (range 29–77 years). Tumors characteristics included: primary site in lung (22), breast (11), melanoma (5), hipernephroma (4), colon (2), and unknown origin (6), breast + colon (1). Supratentorial involvement was present in 42 cases, active extracranial disease was evident in 36 patients (73%). Treatment characteristics. median value of target volume size 9.985 mm3 (range 160–55.968 mm3); single isocenter used in 37 procedures (75%); median RS dose was 1500 cGy (range 900–2.000 cGy); additional whole brain fraccionated radiotherapy was given to 19 patients.

Results: Median survival time is 11 months. At the time of last analysis 59% of patients are dead. Local control rates at 1 and 2 years is 89% and 84% respectively. Actuarial projected survival at 5 years is 28%.

Conclusions: RS is an excellent radiation technique in the treatment of patients with single brain metastases. Updated information will be presented including multifactorial prognostic variable analysis.

910 POSTER

Radiosurgery alternatives and outcomes

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Purpose: To evaluate the role of radiation oncology in case selection in an academic center offering linac-based and gammaknife stereotactic radiosurgery.

Methods: Between Oct 1992–Dec 1994, 90 patients with brain tumors were referred by neurosurgery to radiation oncology for radiosurgery. Twenty three patients (26%) were ultimately observed or treated by other means.

Results: Diagnosis in the 23 patients was meningioma in 7, pituitary adenoma in 8, brain metastases in 3, glioma in 2, glomus jugular in 1, hemangioblastoma in 1, acoustic neuroma in 1. Radiosurgery was not given for the following reasons: 10 patients were given the option of observation, 9 patients opted for fractionated radiation therapy, 4 patients were considered to be at high risk of late complications following radiosurgery, and 1 patient was in poor general condition. Treatment following the radiation oncology consult was fractionated external beam radiation (13 patients), no treatment (9 patients), or surgery (1 patient). Late toxicities have not yet been demonstrated in any patient treated with fractionated radiation therapy. With a median follow up of 24 months, no patient has progressed within the area of treatment. No patient under observation has required treatment for the lesion being followed.

Conclusion: This study demonstrates the need for radiation oncology to work closely with neurosurgeons to present alternatives to radiosurgery.

911 POSTER

Low dose hyperfractionated craniospinal radiation therapy for childhood cerebellar medulloblastoma: Early results of a phase I–II study

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Purpose: To report feasibility and early results of low dose hyperfractionated craniospinal radiation therapy (HFCSI) with chemotherapy for childhood cerebellar medulloblastoma.

Methods and Materials: Twenty-two patients were treated postoperatively for two months with pre-HFCSI chemotherapy (HD-MTX, VCR, CBDCA and VP16). All patients received HFCSI (1 Gy bid, 6 h apart), with 66 Gy to the posterior fossa and 30 Gy to the whole brain; the first 8 patients (Group A) received 30 Gy to the spinal axis, while subsequent 14 patients (Group B) received 36 Gy to the spine. In case of leptomeningeal disease (M1 or M3), 40 Gy were delivered to the spinal axis, with boost on macroscopic lesions up to 50 Gy. All patients were given four "8 drugs in 1 day" cycles after the end of radiotherapy.

Results: During a median of 2 years of follow-up (range 9 months to 6 years), there have been nine treatment failures in 22 patients, seven in the Group A and two in the group B. Five early and isolated spinal failures (range 6 to 18 months after surgery) occurred in patients treated with 30 Gy to the axis. HFCSI, after intensive chemotherapy, was feasible; no patient suffered delays during radiation therapy longer than 7 days. Adjuvant chemotherapy was difficult to give after HFCSI, even in patients treated with 30 Gy to the spine.

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

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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

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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)

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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

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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?

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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