434 POSTER

Intraoperative radiotherapy (IORT) for high grade glioma of the brain – Treatment planning, dose verification, and results

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Introduction: Since May 1992, feasibility, perioperative morbidity, early and long term sequelae as well as survival times following intraoperative radiotherapy are being examined. From our experience, the determination of the correct beam angle and electron energy is difficult by clinical means alone. Therefore, we devised a method for exact pretreatment planning and post-treatment dose verification.

Materials and Methods: From May 1992 to October 1998, 50 patients with malignant gliomas of the brain were treated with IORT at our institution, 47 of which were evaluable at the time of analysis. 31 patients had a primary brain tumor, and 16 patients had recurrent tumors. The histological tumor types were distributed as fol-lows: glioma grade III (n = 22), and glioblastoma (n = 25).

Treatment was carried out as 20 or 25 Gy electron-beam IORT (14 or 18 MeV), followed by 60 Gy postoperative radiation in not previously irradiated patients. The craniotomy was measured in all three dimensions, and the optimal beam angle and the depth of the tumour bed were determined using a neuronavigation system. Afterwards, computerized quality control was carried out by reconstruction of the beam angle and the use of a standard treatment planning system (CadPlan).

Results: Perioperative complications were not increased (2 infections, 1 lethal haemorrhage and 1 malignant edema). 21/22 patients with increased brain pressure showed an improvement. Aphasia, hemiparesis, hemianopsia, psychosyndrom, gyrus angularis syndrom and convulsions were markedly reduced. 1-year survival for all patients was 54%, 2-year survival 14%. Median survival was 12.5 months (glioma III: 13.5 months, glioblastoma IV: 11 months). Median time to progression was 7 months. The only prognostic factor was tumour grade (p = 0.04). Extent of resection, tumour size, age, KPI, and treatment had no significant influence.

Conclusion: By using X-ray verification films, computerized quality control can be carried out after electron IORT. This way we could show that the neuronavigation method of pretreatment planning yields useful results. Side effects were not increased. Most tumour-associated symptoms could be alleviated. Compared to literature, median survival could be slightly improved.

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High-dose chemotherapy (HDCT) with G-CSF support before radiotherapy (RT) in malignant gliomas (MG): Phase II trial

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Purpose: To establish the activity of HDCT in large MG before RT.

Methods: 17 pts with MG less than 60 years and extensive measurable tumor were enrolled. Treatment consisted of carboplatin 200 mg/m^2 (or AUC × 8) plus cyclophosphamide 1000 mg/m^2 days 1–3 and G-CSF 5 mg/kg/day from day 2 (after CT) until hematologic recovery. Two cycles were given before standard RT if stabilization or response were observed after first cycle. Pts characteristics were: male/female 10/7; age 49 (23–59); KF 90% (70–100); GBM/AA, 14/3. Two pts were not assessable for response neither for survival (1 died before and another during the first cycle CT). All patients but one started RT and 11 completed treatment. Response was evaluated according to McDonald,s criteria.

Results: After first cycle of CT 7 pts progressed and 8 stabilized. Seven of them received a second cycle: 1 PR, 1 SD and 5 PD. MST was 7.4 m. Main toxicity was hematologic: in first cycle, neutropenia grade (G) 4 in 100%, thrombocytopenia G 4 in 73% and 3 in 27% and anemia G 3 in 7%. Median neutrophil and platelet recovery were reached on day 11 (8–17) and 13 (0–17), respectively and median number of days under 0.5 × 109/l was 6 (2–10). At second cycle neutropenia was G 4 in 100%, thrombocytopenia G 4 in 100% and anemia G 3 in 50%, and median number of days under 0.5 × 109/l was 7 (4–13). No toxic death was related with treatment.

Conclusions: This regimen showed limited activity in MG with large residual disease at expenses of significant toxicity.

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Treatment of glioblastoma multiforme (GBM) with teniposide (VM26) and lomustine (CCNU) followed by radiotherapy

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Purpose: GBM are frequent neoplasms of adult CNS and exhibit bad prognosis. Nitrosureas and podophylotoxines have some activity against GBM. Here we review our experience from 1996 to 1998.

Methods: Forty three patients (pts) with GBM were seen (23 males, 20 females). Projected treatment included chemotherapy (ChT) (VM26 120 mg/m^2 iv on day 1, and CCNU 120 mg/m^2 orally on day 2, every 28 days, if hematologic count recovery), three cycles in absence of progressive disease, and radiotherapy 60 Gy, after surgery or biopsy. PS <= 2. Thirteen pts did not received ChT (due to bad PS, rapid deterioration or family negative). Of them, four received radiotherapy up to 60 Gy.

Results: Thirty pts received ChT (17 males, 13 females). Mean age 58 y old (36–77). Disease completelly resected: 11, partially resected: 11 and just biopsed: 8. Eleven pts received one cycle of ChT; 9 pts, 2 cycles; 10 pts, 3 cycles. Only 8 pts (27%) completed our projected treatment. No pts without resection completed treatment. Toxicity: Two neutropenia grade 3, one thrombocytopenia grade 3 and three grade 4. One hyperbilirubinemia grade 4. Progressive disease to ChT 15/30 (50%). Survival: Pts treated with ChT ± RT: median survival 6 months (1–19). Alive 10/30 (33%) (mean 8.1 months, range 1–16) (2 biopsed, 8 resected) Dead 20/30 (67%) (mean 4.9 months, range 1–19) (6 biopsed, 14 resected). Pts not treated with ChT: median survival 3 months (1–12). Alive 3/13 (23%), all three resected, one also irradiated (mean 5.6 months, range 2–12).

Conclusions: Although randomized studies have shown benefit with combined therapy, GBM survival is short. Patients not able to end the treatment fared worse. Non resected tumors also fared worse. Although this treatment was well tolerated it seems to bear low activity. New drugs, new strategies and new techniques are needed.

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Radiotherapy in primary spinal cord astrocytoma

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Purpose: Primary spinal cord astrocytoma are rare tumors and the role of radiotherapy remains controversial. This study is a retrospective analysis of patients treated at our department with this diagnosis.

Material and Method: Between May 1975 and December 1997, 24 patients with histologically proven spinal cord astrocytomas were treated with external radiotherapy by either Co-60 or 6 MV photon beam. Median age was 19 years (2–41 years). 11 of them were male and 13 were female. 14 of astroctoma were grade I, 6 of them grade II and 4 grade III. 10 patients had subtotal excision and 14 had only biopsy. Patients were treated with 100–200 cGy daily fractions and given to a median 4950 cGy (3500–6000 cGy) external radiotherapy to primary tumor region with a safety margin at both ends. Chemotherapy was given to 8 patients.

Results: Median follow-up time was 38.6 months ranging between 2–149 months. 17 patients died of their disease. 2 patients have progression and 5 patients are followed with stable disease. Grade, sex, age, duration of symptoms, extent of the surgery were not found as statistically significant prognostic factors. 5 year overall survival was 44.6% and progression free survival was 40.3%.

Conclusion: Our results are in consistent with other retrospective series in the literature and radiotherapy seems to improve the survival as an adjuvant treatment modality especially in subtotally resected tumors.

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Stereotactic radiotherapy for solitary brain metastases as alternative to surgery

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Objectives: To assess efficacy, toxicity and cost-effectiveness of stereotactic radiotherapy (SRT) for solitary brain metastases.

Patients and Methods: Fifty-seven patients with solitary brain metastases (1 to 3 lesions) were treated with SRT with or without whole-brain