Materials & Methods: Between 1998 and 2002 53 patients with complex shaped meningiomas were treated at the dkfz. 34 female and 19 male patient were enrolled. In 34 patient radiotherapy was performed after surgery. In 19 cases radiotherapy was the primary therapy. The diagnosis was established in 18 patients according the imaging studies without a confirming by biopsy. In all cases dosage was performed to the median of the target volume (50% of the volume receive 100% of the dose). For inverse treatment planning the "KonRad® " or the "CORVUS® " system was used. Maximum dose of the brain stem and the spinal cord were constrained to 54 and 45 Gy, respectively. All patients were treated in a patient-specific Scotch-Cast mask. Each plan was verified before treatment by film dosimetry in a head and neck phantom. The "step and shoot" IMRT technique with a multileaf collimator integrated in a Primus (Siemens®) accelerator was used for treatment. Regular follow-up studies at our institution were performed.

Results: The median total dose was 57, 2 Gy (Range: 54 Gy 57,6 Gy). The mean tumor volume was 96,6 cc (Range: 74 - 16 cc). The volume which received less than 90% of dose ranged between 13 and 2% (mean: 6,7%). Treatment time ranged between 5 to 15 minutes. Additionally 5 minutes were needed for patient positioning. With a median follow-up of 25 months except for one patient with a marginal recurrence all patients are local controlled. The 4-year actuarial local control rate was 95%. As acute side effects only a RTOG/EORTC toxicity Grade I of the skin and slight dizziness were seen in 45% of the patients. Additionally a transient alopezia was found in all patient and 10 patients developed a conjunctivitis during therapy. A post-therapeutic cerebral edema in the follow-up MRI could be detected in 4 patients. In all cases the edema were clinically asymptomatic. Until now no late CNS toxicity was seen. The excising pretherapeutic neurological symptoms improved in 34% of the patients.

Conclusion: The use of a inverse planned and intensity modulated "step and shoot" approach is feasible in the clinical routine for complex shaped benign skull base meningiomas. No increased early or late toxicity could be evaluated compared to conventional treatment techniques. IMRT shows advantages in tumor dose and dose at the organs at risk. A longer follow-up is needed to control the success of the treatment.

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First line temozolomide (tmz) in recurrent or progressive oligodendroglioma. a phase II study (Gruppo Italiano Cooperativo Neuro-oncologia).

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Background: Oligodendroglial tumors respond to PCV chemotherapy in 60 to 75% of cases. However, toxicity is not negligible, and frequently imposes delays in re-cycling or early interruptions of treatment. TMZ has shown activity and optimal clinical tolerability as a second line regimen after PCV, but more data are required to establish whether it could replace PCV as standard first line chemotherapy.

Objectives: To evaluate in a phase II study Response Rate (RR), Time to Progression (TTP) and toxicity of TMZ in patients (pts) with oligodendroglioma.

Methods: Eligible were chemonaive pts with oligodendroglioma (OD) or oligo-astrocytoma (OA), progressive or recurrent after radiotherapy, with at least one measurable contrast enhancing lesion (* 1cm of diameter). Pathological diagnosis was centrally reviewed. Pts were treated with 150-200 mg/m^2 TMZ on days 1 to 5, every 28 days. Macdonald's criteria were applied when evaluating tumor response.

Results: Thirty-two pts were included in the study (median age 49 yrs, range 27-63 yrs; KPS 80, range 60-90; 21 OD). To date, twenty-eight pts are evaluable: 4 had Complete Response (CR) (14%), 9 had partial response (PR) (32%), while 9 pts (32%) remained stable for at least two months. Median TTP was 12 months, Progression Free Survival (PFS) at 6 and 12 months was 67% (CI 95%= 52-87%) and 45% (CI 95%= 29-70%), respectively. In responsive pts, PFS-6 and PFS-12 were 83% (CI 95%=64-100%) and 58% (CI 95%= 36-94%), respectively,. A total of 225 cycles of TMZ were administered (on average 7 per pt). Toxicity was mainly hematological, with grade 3-4 neutropenia and thrombocytopenia in 4 (12.5%) and 3 (9.3%) pts, respectively. No extra-hematological grade 3-4 side effects were reported, except for nausea and vomiting G3 in 3 (9.3%) pts. In 6 pts (18.7%) TMZ dosage was reduced to 150 mg/m^2 due to reversible hematological toxicity. Of the progressing 18 pts, 14 have started second line chemotherapy with PCV and 10 are evaluable for response: 1 CR and 2 PR (RR: 33%) plus 4 SD were obtained, with a PFS-6 and PFS-12 of 40 and 30%, respectively.

Conclusions: The activity of temozolomide as a first line chemotherapy appears to be superimposable to that of PCV, with better clinical tolerability and, seemingly, no cross-resistance. Randomized trials are warranted.

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Stereotactic radiosurgery for cerebral melanoma metastases

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Background: To identify prognostic factors for patients with melanoma brain metastases treated with stereotactic radiosurgery (SRS).

Material and Methods: One hundred three patients with 153 intracranial melanoma metastases underwent Linac-based SRS alone or with whole brain irradiation (WBI; n=51) between Nov 1991 and Oct 2001. Median age was 51 years (18-93 years). KPS was > 70 in 78.6% (n=81). Single brain metastasis presentation comprised 58% (n=60). Treatment sequence was SRS alone (n = 78), SRS+WBI (n = 19), WBI+ salvage SRS (n = 29), and SRS + salvage WBI (n = 27). Median tumor volume was 1.9 cm^3 (0.06 76 cm^3). Median SRS minimum peripheral dose was 18 Gy (range, 10-24 Gy). Median patient follow-up was 6 months for all patients and 16 months (range, 2-46 months) for patients alive at time of analysis. Median imaging follow up was 3.2 months for all patients and 10 months (range, 0-37 months) for patients alive. Kaplan-Meier method, log rank test, and Classification and Regression Tree models (CART) were used. Patients were classified according to the Stereotactic Score Index (SIR).

Results: *SRS alone* vs. combined treatment (SRS + WBI, SRS + salvage WBI, WBI + salvage SRS) achieved 63% LC in 1 year vs. 27% respectively (p= 0.009). "SRS first" had higher 1-year LC than "WBI first" (51% vs. 26%; $p < 0.05$). Tumors ≤ 2 cm^3 had better 1-year LC than > 2cm^3 (52% vs. 38% respectively; $p < 0.05$). This is especially true for *SRS alone* treated lesions where smaller tumor volume (≤ 2 cm^3 vs. > 2 cm^3) demonstrated superior 1-year LC (84% vs. 43% respectively; $p < 0.05$). Actuarial median survival for all patients was 7 months and one year OS was 27.8% from time of SRS. Patients with absence of systemic disease demonstrated significantly better survival than those with active systemic disease (8 vs. 5 months respectively; $p < 0.05$). SIR ≥ 6 at presentation predicted significantly longer survival with 29% of patients alive at 1 year compared to 5% for those patients with SIR < 6 ($p < 0.05$).

Conclusions: *SRS alone* is an effective treatment modality for cerebral melanoma metastases achieving 84% 1-year LC for properly selected patients who have small melanoma brain metastasis (≤ 2 cm^3) and should be considered in patients with SIR ≥ 6. Selection bias towards treating patients with more biologically aggressive disease with combined SRS and WBI may have played a role in the inferior LC observed for the combined treatment group (SRS + WBI).

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Temozolomide (TMZ) combined with radiotherapy (RT) versus radiotherapy (RT) alone in newly diagnosed glioblastoma multiforme (GBM): A randomized phase III study

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Background: Despite aggressive treatment glioblastoma multiforme is associated with high rate of recurrence and poor survival. Temozolomide, a new oral alkylating agent, has shown effectiveness in the treatment of malignant gliomas. A multicentric randomized phase III study was conducted