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Pattern of care and survival in a retrospective analysis of 1866 patients (pts) with glial tumours treated with radiotherapy (RT) in twelve Italian Centres from 1985 to 2003

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End-points: To analyse patterns of clinical presentation, staging and outcome in a multi-institutional series of radiotherapy treated malignant glioma pts and to evaluate actuarial overall survival (OS) in the different clinical and therapeutic subsets.

Materials and methods: Histology was reclassified using WHO system; performance status was defined according to the Karnofsky index and Order scale. Type of surgery, RT volumes, RT techniques and doses, supportive care, chemotherapy were analysed also according to the accrual period (1985–1990, 1991–1996, 1997–2003). Follow-up policies were very different in the different centers ranging from no follow-up to monthly clinical or instrumental evaluation. The OS was calculated only for the pts with G3–4 astrocytoma and considering the centres with active follow-up (1145 pts), using the Kaplan-Meier method. Differences in actuarial overall survival (OS) were analysed with the log-rank test and the Cox-regression test.

Results: Statistically significant differences ($0.000 < p < 0.02$) in clinical, diagnostic and therapeutic features according to the accrual period are evident. In the last period were treated more pts aged plus than 60 years (27%, 42.3% and 50.7% respectively in the 3 groups), with worse Order score (15%, 25%, 32% respectively), with lesions 3–5 cm large (35%, 45% and 50% respectively) with G4 disease (60%, 73%, 73% respectively). As for the diagnostic work up, the number of pts submitted to MRI or CT and MRI significantly increase in the more recent periods both in the pre-surgical and in the post surgical setting ($p = 0.000$). In the last period more pts were submitted to radical surgery ($p = 0.037$), and to conformal radiotherapy ($p = 0.000$), mainly on more limited volumes ($p = 0.000$). The majority of the pts were treated with RT doses > 60 Gy (53.3%). Median OS was 10 and 9 months respectively for the entire series and for G3–G4 patients. The univariate analysis showed a better survival for young pts ($p = 0.0000$), in those with better Order score ($p = 0.0000$), with G3 histology ($p = 0.0000$) and small disease ($p = 0.0027$). Among treatment variables, radical surgery ($p = 0.0001$), high RT dose ($p = 0.0000$), limited treatment volumes ($p = 0.0000$) and the use of chemotherapy ($p = 0.0000$) were related with a better survival. The multivariate analysis confirmed the importance of histology, tumour size, age, neurological performance status, radical surgery, dose of RT and volumes of treatment.

Conclusions: In Italy patterns of practice for malignant gliomas changed significantly during the last two decades. Staging procedures were increasingly accurate, surgery more aggressive and RT techniques more sophisticated. The relevance for OS of age, NPS and WHO histology, radical surgery, high dose radiotherapy on limited volumes is confirmed.

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Radiosurgery vs. hypofractionated stereotactic radiotherapy in patients with high grade gliomas

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Purpose: To compare results using two different approaches of stereotactic radiotherapy after conventional treatment in patients with high grade gliomas (HGG).

Patients and methods: a total of 47 patients with HGG are included. These patients received either boost or treatment in the relapse. In relation to previous well known prognostic factors of these patients, both groups were well balanced (see table).

All patients had KPS equal or superior to 70. Patients with radiosurgery (RS) received a median dose of 17.5 Gy at isocenter and patients with hypofractionated stereotactic radiotherapy (HFSRT) a median of 20 Gy at isocenter.

Results: MST from RS/HFSRT for all group was 18.4 months. The only prognostic factor observed was histology. For GBM group MST for RS and HFSRT were 14.9 and 15.5 months, respectively. And for AA group MST for RS and HFSRT was 24.2 months and not yet reached, respectively. No differences in overall survival (OS) were observed by type of treatment.

Toxicity: four groups of side effects were established; 1) seizures (15% for RS and 23% for SHFRT). 2) focal damage in radiotherapy field (8.8% for RS and 30% for SHFRT). 3) Neurocognitive damage (8.8% for RS and 0% for SHFRT). 4) Radiation necrosis (15% for RS and 0% for SHFRT).

Table: patients characteristics before radiotherapy (RS and SHFRT)

Variables	Radiosurgery	Stereotactic HF RT	P value
Age (median)	50	44	0.81
Sex: male/female	25/9	7/6	0.34
Tumour size (mm)	30	27	0.93
Surgery: Resect/Bx	33/1	10/2	0.32
Histology: GBM/AA	21/13	4/9	0.11
Chemo: yes/no	24/10	10/3	0.94

Conclusions: In spite of limited number of patients, we can conclude that the two modalities of high precision radiotherapy for HGG do not show differences in OS. Histology remains the most important factor. However, side effects could be more important in terms of radiation necrosis and neurocognitive damage in patients treated by single dose.

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Craniospinal radiotherapy in adult medulloblastoma

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Purpose: To evaluate the outcome and prognostic factors of adult patients with medulloblastoma.

Materials and methods: We evaluated 26 adult (≥ 17 years old) medulloblastoma patients with a median age of 27 (range, 17–42 years) treated between April 1994 and September 2003 at Hacettepe University, Radiation Oncology Department. All patients' pathology slides were centrally reviewed. The Radiation Therapy Oncology Group (RTOG) "Late radiation morbidity scoring schema" was used in our review to grade severe complications. The standard-risk stratification for analysis was defined as a reported gross total resection ($< 1.5 \text{ cm}^2$ residual) and no evidence of metastatic tumor outside the posterior fossa on both CSF analysis and complete spine imaging. Staging was retrospectively verified according to the Chang Classification system. All patients were treated with craniospinal fractionated external beam radiotherapy (EBRT). A dose of 30.6 Gy with 1.8 Gy/fraction/day was prescribed for M0 patients; while 36 Gy was adjusted for patients with positive CSF findings. Posterior fossa was boosted to a total dose of 54 Gy. Spinal seeding metastasis was also boosted to a total dose of 50 Gy. While 20 (77%) patients were treated with EBRT alone, only 6 (23%) patients received sequential adjuvant chemotherapy. Survival time was calculated from the date of completion of radiotherapy.

Results: Male/female ratio was 1.2 (14/12). Preradiotherapy Karnofsky Performance Scale (KPS) was recorded as median 100 (range 70–100). Patients were staged as: T1 = 1; T2 = 15; T3 = 5; T4 = 1; T-unknown = 4; M0 = 23; M+ = 3 (M1 = 1, M2 = 2). Thirteen patients (50%) were classified as poor risk (10, STE; 3, M+). The median follow-up time was 46.5 months (range, 5–126 months). Majority of the patients had gross total excision (GTE) of the primary tumor (GTE: 16 patients, Subtotal excision-STE: 10 patients). Patients were referred to radiation oncology after a median duration of 1 month (range 1–3 months). Median radiotherapy treatment duration was 42 days (range 36–51 days). The 5-year actuarial recurrence free survival rates for recurrence free, distant metastasis free, disease free and overall survival were 82.5%, 90.8%, 73.5% and 89.7% respectively. Univariate analysis of variables including patient characteristics (age, gender, Karnofsky performance status-KPS), treatment modalities and factors (surgical extension: gross total versus subtotal – residual disease $> 1.5 \text{ cm}^2$; radiotherapy alone versus sequential chemotherapy; overall radiation treatment time; time to radiotherapy), and tumor characteristics (standard versus poor risk; Chang classification: T-stage, M-stage) failed to show an association with recurrence free, distant metastasis free and overall survival. The 5-year actuarial recurrence free survival rates for recurrence free, distant metastasis free, disease free and overall survival were 82.5%, 90.8%, 73.5% and 89.7% respectively. None of our patients experienced grade 3 or 4 late morbidities in their follow up period.