	OS (median, days)		
	RPA1	RPA2	RPA3
p	0.0342	0.0002	n.s.
Breast cancer	422	170	70
Lung adenocarcinoma	289	160	39
Small cell lung cancer	248	119	37
Squamous lung cancer; melanoma; GE cancer; others; primary unknown	144	93	56
Kidney; Ovary/Uterus	324	820	78

Multivariate analysis confirms the impact of histology on overall survival along with the other known prognostic factors (RPA classes, dose of HWBRT, combination of surgery and radiotherapy).
Discussion: Histology of the primary is an independent and strong prognostic factor for OS in BM pts treated with HWBRT. More advanced statistical analysis on larger numbers is needed to confirm these results.

References

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8729 POSTER

The effectiveness of radiosensitized tumor treatment in brain metastases of different histogenesis

L. Bloznelyte-Plesniene[1], D. Sendiuliene[1]. [1]*Institute of Oncology of Vilnius University, Laboratory of Laser and Photodynamic Treatment, Vilnius, Lithuania*

Background: The prognosis of the vast majority of patients who develop brain metastases (BM) is poor. The best treatment strategy remains unknown for a large group of patients affected by BM. The aim of this work was to investigate the possibilities of sensitized malignant tumor treatment using some derivatives of hematoporphyrin (HpD) as a radiosensitizer in brain metastases of different histogenesis.
Material and Methods: From 2000 to 2009 the total of 64 patients with BM underwent radiosensitized tumor treatment (RST). There were 35 patients with previously untreated BM, 12 patients with recurrent BM after neurosurgery and 20 patients underwent radiotherapy until RST. The histological examination of primary (42 patients) or secondary (12 patients) tumor revealed: melanoma in 22 cases, adenocarcinoma in 30, adenoid cystic carcinoma in 5, sarcoma in 4, and other tumors in 3 cases. HpD was injected i.v.; 24, 48 and 72h after injection of the sensitizer tumors were irradiated with gamma rays 2 Gy at a time from radioactive ^{60}Co (the full dose of the course was 6 Gy). At the start of the treatment Karnofsky performance scale index was <70% in 59 patients.
Results: As the immediate result of RST, the Karnofsky performance scale index increased in 52 patients after the treatment. All malignant brain tumors fully disappeared in 14 patients. Among these 14 patients there were 5 patients with adenocarcinoma, 2 patients with melanoma, 1 patient with sarcoma, 1 patient with neuroblastoma and 5 (all treated) patients with adenoid cystic carcinoma. CT or MRI examinations, provided 3−6 weeks after each RST course, revealed the partial regression of tumor in 32 patients. The median survival of 64 patients (from the moment of brain metastases detection) treated by the addition of RST was 12 months. Comparing it with the 4.5 months median survival of 184 control group patients, it was statistically significant longer. The median survival of 22 patients with metastatic melanoma was 10 months, and with metastatic adenocarcinoma (30 patients) – 12 months. The median survival of 64 patients from the first course of RST was 7 months.
Conclusions: RST - effective method of treatment in metastatic brain tumors, especially when it is applied for adenoid cystic carcinoma. The tumors of different histogenesis require some RST modifications.

8730 POSTER

Malignant melanoma brain metastases – a single institution experience

M. Conçalves[1], A. Passos[1], A. Moreira[1], J. Oliveira[1]. [1]*Portuguese Institute of Oncology, Medical Oncology, Lisbon, Portugal*

Background: Brain metastases (BM) develop in nearly half of the patients with advanced melanoma representing the cause of death in up to 54%. The limited array of treatment options and the conflicting data on the role of radiation in this group of patients represents a challenging issue in cancer treatment. The purpose of this study was to analyse cerebral involvement of melanoma according to treatment options.
Materials and Methods: The authors reviewed the records and confirmed survival status of all patients with BM from cutaneous melanoma between 1998 and 2004. Cases were grouped according to the treatment received: 1) Supportive Care (SC), 2) Whole Brain Radiotherapy (WBRT), and 3) Surgery+ Whole Brain Radiotherapy (S+WBRT).
Results: Forty-nine patients were identified, all dead as a result of melanoma progression, with median survival from onset of BM metastases of 12 weeks. Stratifying, 51% patients were in the SC group (n = 25), 34% in the WBRT (n = 17) and 14% S+WBRT(n = 7). The median age of diagnosis was similar in the first two groups (60.7 and 62.6 years) but lower in the third group (48.8 years). Karnovsky performance status was only registered in 15 patients (30%). The majority (n = 44) had systemic disease but in 18 SC cases (72%) more than two sites of metastases were found compared to 35% in the WBRT and 40% in S+WBRT. Multiple metastases (>4 lesions) in 16 patients in the SC (64%) and 11 in WBRT (64%). All the patients in S+WBRT had between 1 and 3 lesions. Median survival was 7 weeks in the SC, 16.7 weeks in WBRT and 24,5 weeks in the S+WBRT group. Neurological improvement was seen in 14 SC cases (56%), 15 WBRT (88%) and in all of S+WBRT cases. Thirty nine patients (80%) were on steroids.
Conclusions: Our median survival depended on the treatment modality which in turn seems to be influenced by patient selection, an important bias in this data. Its is extremely difficult to access the palliative benefit of different treatments since the majority of the patients were on steroid therapy.

8731 POSTER

Fractionated Stereotactic Radiotherapy (FSRT) in the management of functioning and non-functioning pituitary adenomas

M. Cabeza[1], M.A. Pérez[1], A. Bartolome[1], E. Cabello[2], A. Fernandez[1], R. Díaz[2], V. Rodríguez[1], A. Ruiz[1], J. Pérez-Regadera[1], E. Lanzos[1]. [1]*Hospital 12 Octubre, Radiation Oncology, Madrid, Spain;* [2]*Hospital 12 Octubre, Radiation Physics, Madrid, Spain*

Background: FSRT has been developed as more accurate technique of irradiation with more precise tumor localization and delivery and consequently a reduction in the volume of normal tissue. FSRT is not limited by dimensions or distance from CTV to optic system. The objective was to assess the outcome in a cohort of patients with residual or recurrent pituitary adenoma treated with FSRT.
Materials and Methods: Fifty patients (median age 45 years) with a residual or recurrent nonfunctioning (21) or functioning (19) pituitary adenomas were treated between 1997 and 2007. Fifteen patients had an ACTH-secreting, nine GH-secreting and five PRL-secreting pituitary adenoma. Eleven patients had partial or complete hypopituitarism before FSRT. Visual field defect had 10 patients. The treatment was delivered stereotactically, using a Gill-Thomas-Cosman recolocable guide and four noncoplanar arcs with circular focalized collimators with 6. MV LINAC to a dose of 46 Gy in 23 fractions. PTV was defined as GTV+5 mm margin.
Results: At a median follow-up of 68 months (range 14−143), the 5 and 8 years actuarial progression free survival is 98% and 98%, and overall survival is 98%. One patient relapsed 45 months after FSRT. In secreting adenomas hormone levels declined progressively, with hormonal control actuarial at 5 years in ACTH-secreting adenomas in 61%, GH-secreting adenomas in 46% (GH/IGF-1 levels). The hormone levels become normal in one of five, PRL-secreting pituitary adenoma. Hypopituitarism was the most common long-term effect; Pituitary dysfunction was observed, in different grade in patients with normal pituitary function or with partial hypopituitarism, the rates at 5 and 8 years estimated with Kaplan–Meier survival was 27% and 53%. Non visual complications occurred following FSRT.
Conclusions: FSRT as a high-precision technique of localized irradiation achieves tumor and hormone control of pituitary adenomas comparable with previously published date on the efficacy of conventional radiotherapy, the theoretical benefit over conventional radiotherapy in terms of the reduction in long-term morbidity has not yet been demonstrated and requires longer follow-up

8732 POSTER

Ten years' experience with stereotactic radiotherapy for pituitary adenoma

N. Patil[1], J. Brierley[1], M. van Prooijen[2], M. Heydarian[2], S. Mckinnon[3], S. Ladak[3], S. Fung[4], R. Tsang[1]. [1]*Princess Margaret Hospital University of Toronto, Radiation Oncology, Toronto ON, Canada;* [2]*Princess Margaret Hospital University of Toronto, Radiation Physics, Toronto ON, Canada;* [3]*Princess Margaret Hospital University of Toronto, Radiation Therapy, Toronto ON, Canada;* [4]*Princess Margaret Hospital University of Toronto, Biostatistics, Toronto ON, Canada*

Purpose: To evaluate local control and toxicity for pituitary adenomas treated with stereotactic radiotherapy (SRT).

Methods: The SRT program to treat pituitary adenomas was initiated in 1997. The clinical outcome of all patients treated with SRT up to 2007 were retrospectively reviewed (n = 83). Median age was 47 years (range: 14−73), with 46 males and 37 females. Twenty patients had functional and 63 had non-functional tumors. Median follow up was 42 months (range: 1−137). Two patients received SRT as their primary treatment, 38 received it postoperatively and 9 for raised hormones. Thirty-four patients received SRT for radiological progression despite prior surgery with median time to progression following surgery being 12 months (range 1−275). Before SRT, hormone replacement therapy was observed in 37% (thyroid), 35% (cortisol), and 30% (testosterone, males only). SRT dose was 50 Gy in 25 daily fractions using the GTC frame, and CT-MR fusion for planning (Radionics^{TM}). Arcs were used in 66 patients and stationary 4−6 non coplanar fields in 17. The GTV and sella contents were treated, with no expansion from CTV for PTV margin. The prescription guideline was > 95% coverage of the CTV by a minimum dose of 47.5 Gy, and maximum dose <52.5 Gy.
Results: The 3-year progression free survival rates for functional and non-functional adenomas were 94% and 92% respectively (p = 0.90). Four patients had progression (3 nonfunctional and 1 functional); among these, 2 had metastatic spread. One patient had salvage excision, 1 had radiosurgery, 1 patient required temozolamide for lepto-meningial disease and 1 required palliative radiation to treat lumbar bony metastases. Post SRT 43 patients (52%) had hypothyroidism, 35 (42%) required cortisol and 20 (24%) required testosterone. 1 patient had severe optic neuropathy. To date there were no second cancers.
Conclusion: Though with a relatively short follow up, this study suggests fractionated stereotactic radiotherapy with a narrow margin is safe and effective for the treatment of pituitary adenomas. The results compare favorably with historical outcomes achieved with conventional 2 or 3-field techniques.

8733 POSTER

Atypical meningioma: outcomes and prognostic factors

H.J. Park[1], I.H. Kim[1], H.W. Jung[2]. [1]*Seoul National University Hospital, Radiaton Oncology, Seoul, Korea;* [2]*Seoul National University Hospital, Neurosurgery, Seoul, Korea*

Background: To retrospectively analyze and assess the outcomes and prognostic factors in atypical meningioma.
Methods and Materials: From April 1990 through April 2008, 45 patients with histologically confirmed atypical meningioma(WHO Grade ll) were treated with surgery and/or radiotherapy as a primary therapy at our institution. Of 45 evaluable patients, 21 patients were treated with surgery alone and 24 patients received surgery plus postoperative EBRT. Fifteen out of 21 patients who had a gross total resection(GTR) and nine out of 16 patients who had other than GTR received adjuvant EBRT. The median postoperative radiation dose was 61.2 Gy (range, 54−61.2 Gy). The median age at presentation was 52 years (range, 13−75 years) and the male:female ratio was 18:27.
Results: The 10-year cause-specific survival rate was 96.6% and 3- and 5-year progression-free survival(PFS) rates were 73.7% and 56.7%, with a median follow-up of 37.4 months (range, 6.1−217.8 months). Only one patient died from local failure and no one had distant failure. The 5-year PFS rates of patients treated with GTR only, GTR plus EBRT, other resection only, and other resection plus EBRT were 46.4%, 77.9%, 0% and 55.6%, respectively. Better PFS was significantly influenced by initial postoperative EBRT ($p = 0.025$), GTR ($p = 0.002$), male ($p = 0.033$) and Ki-67 <5% ($p = 0.002$) on univariate analysis. By multivariate analysis, postoperative EBRT, GTR, and male were associated with better outcomes.
Conclusions: In patients with atypical meningioma, postoperative radiotherapy improved progression-free survival, regardless of the extent of surgical resection. Besides adjuvant radiotherapy, GTR, male, and low Ki-67 proliferative index were independent predictors of the successful local control.

8734 POSTER

Oncolytic virotherapy of malignant glioma in an animal model using parvovirus H-1 (H-1PV)

I. Kiprijanova[1], K. Geletneky[2], A. Ayache[2], B. Leuchs[1], J. Schlehofer[1], J. Rommelaere[1]. [1]*Deutsches Krebsforschungszentrum, Tumorvirology, Heidelberg, Germany;* [2]*University of Heidelberg, Neurosurgery, Heidelberg, Germany*

The current standard of care for malignant gliomas is surgical resection and radiotherapy followed by extended adjuvant treatment with the alkylating agent temozolomide. Regrettably, this standard treatment paradigm has only a modest effect on patient survival. Resistance to radiation and chemotherapy remains an obstacle to the treatment of brain tumours. We have demonstrated that rodent H-1 Parvovirus (H-1PV) wild type, replicating efficiently in glioma cells, may overcome the limitations of conventional therapies by its oncolytic activity. This hypothesis is supported by findings on the sensitivity to the killing effect of the virus. Normal (non-tumor) cells were found to be unsensitive to the oncolytic effect of H-1PV. In vivo, H-1PV was tested for its efficacy and safety in treatment of a rat glioma in an animal model. A single stereotactic intratumoural injection of wild-type H-1PV was sufficient for remission of intracranial gliomas (established from RG2 cells in Wistar rats) without any damage of normal brain tissue or other organs. Similarly, intravenous injection of H-1PV led to complete cure of the brain tumours with no side effects. Furthemore, tumors derived from human glioma cells in immunodeficient rats could also been shown to be sensitive to H-1PV. The contribution of immunological factors to the oncolytic activity of H-1PV is currently under investigation.
These results are the basis of a planned clinical trials on H-1PV virotherapy.

8735 POSTER

Selection of candidate genes involved in glioma pathogenesis using bioinformatics tools

C. Diez-Tascón[1], J.M. López-Martí[1], O.M. Rivero-Lezcano[2], G. Santín-Piedrafita[1], C. González-Cortés[2], T. Ribas-Ariño[1]. [1]*Hospital de León, Servicio de Anatomía Patológica, León, Spain;* [2]*Hospital de León, Unidad de Investigación, León, Spain*

Human malignant gliomas are the most frequent form of brain tumours. They are commonly resistant to chemotherapeutic and radiotherapeutic treatments and their diffuse or infiltrative nature prevents surgical cure. The discovery during the last decade of molecular and epigenetic alterations have proven prognostically useful, but few advances have been made in the understanding of the complex mechanisms of tumour pathogenesis.
The present work deals with the selection of candidate genes potentially involved in the origin or progression of astrocytoma, the most frequent diffuse glioma. Our working hypothesis is that low and high grade astrocytoma should show differences in the expression of genes involved in biological functions that participate in tumour pathogenesis. In order to identify those functions, we used the bioinformatics tool “Gene Set Enrichment Analysis (GSEA)” to compare the following microarray experiments available in public databases: GSE4290, GSE3185, GSE1993, GSE2223 (from GEO database) and E-MEXP-597 (from ArrayExpress database). Results were obtained in terms of Gene Ontology (GO) categories (Biological process, Metabolic process and Cellular Component). Next, we selected the GSEA high scoring genes (“core enrichment”) associated to high grade (54 genes) and low grade (55 genes) tumours, in at least four of the experiments. Results were verified by the comparison of both gene lists using Fatigo+, a functional profiling method. In general, differentially expressed functions (GO hierarchy level 3) were (a) Biological process: “Cellular metabolic process”, “Macromolecule metabolic process” and “Primary metabolic process”; (b) Molecular functions: “Ion transporter activity”, “Nucleic acid binding” and “Hidrolase activity”; (c) Cellular component: “Membrane bound organelle”. We observed that specific high grade tumours share common functions with low grade tumours. This is consistent with the hypothesis that secondary tumours are generated by the evolution of low grade tumours, while primary tumours arise de novo.
Results of differential expression experiments using low and high grade tumour samples for two of the identified genes are presented.

8736 POSTER

Correlation between immunoreactivity of monocarboxylate transporter 1 in malignant glioma and tumor response to continuous intrathecal infusion of sodium butyrate

H. Nakagawa[1], M. Yoshida[1], M. Shindo[1], H. Nishiyama[1], T. Motozaki[1], K. Yoshioka[2], K. Itoh[2]. [1]*Nozaki Tokushukai Hospital, Neurosurgery, Osaka, Japan;* [2]*Osaka Medical Center for Cancer & Cardiovascular Diseases, Biology, Osaka, Japan*

Background: It has been suggested that the monocarboxylate transporter 1 (MCT1), which is part of the monocarboxylate transporter family, plays a major role in the uptake of butyrate. MCT1 in glial limiting membranes may play a role in equilibrating monocarboxylates between the brain cortex and the cerebrospinal fluid (CSF). Moreover, MCT1 immunoreactivity was strongest in high-grade glial neoplasma. However, sodium butyrate (NaB) is expected to be clinically useful because of its biological effects on cellular proliferation, differentiation, apoptosis and invasive metastasis. Therefore, NaB administered via the CSF enters the brain by abundant MCT1 in the glial limiting membrane, and then is distributed in the brain, where NaB is associated with MCT1 in the tumor itself. Thus, abundant MCT1 expression not only by tumor cells but also by the glial limiting membrane and ependym is supposed to facilitate a positive treatment effect of continuous intrathecal administration (CIA) of NaB for malignant glioma (MG).