+ 93 months and "others": + 49 months). Their 5 years survival was similar (65%). BID regimen was elected only in 14% children and induced a higher mucosal toxicity ($p<0.001$) without affecting autcome.

Conclusion: In pediatric STS, in which long term survival and toxicity are equally important, RT can be confined initially to "high-risk" groups only. Delayed RT in "low-risk" ones who failed locally doesn't compromise the outcome.

1263 POSTER

Children osteosarcoma - treatment results and prognostic factors

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Objective: The aim of our study was to evaluate results of treatment and analysis of prognostic factors in children with nonmetastatic osteosarcoma.

Patients and methods: From 1987 to 1999 we treated 90 patients (pts) with classic high-grade osteosarcoma (OS), median age 15 years (range 3 to 18 yrs). 75 pts had large tumours with volume over 150 ml. The majority of pts (86%) had tumour in the region of the knee joint. Adjuvant chemotherapy after amputation was administered in 28 pts. Neoadjuvant chemotherapy was administered in 62 pts - intravenous or intraarterial in 46 and 16 pts, respectively (1 treatment- related death), followed by surgery (amputation in 32 pts, limb salvage in 26 pts, resection in 3 pts) and postoperative chemotherapy. Two- drug regimen (Adr, CDDP) was administered in 43 pts while 47 pts received chemotherapy by other protocols.

Results: During the 18 to 166-months follow-up period (Me=67 mts.), over-all survival rate was 62% and disease-free survival rate was 60%. Over-all survival rate was 49% in the adjuvant grip and 67% in the neoadjuvant group. The most significant prognostic factors were tumour volume (VT) and tumour necrosis. Over - all survival rate was 56% in pts with VT > 150 ml (75 pts) and 92% in pts with VT < 150 ml (15 pts). In the neoadjuvant group, 22 pts (36%) had over 90% tumour necrosis, 20 pts (32%) had 60-90% necrosis, and 20 (32%) had less than 60% necrosis. Over-all survival rates were 91%, 65% and 41% respectively. Significant differences in survival were also in relation to sex, duration of symptoms, LDH and alkaline phosphatase level, but not in relation to the type of chemotherapy applied (two-drug or multi-drug regimen) or the mode of preoperative chemotherapy administration (i.v./i.a.).

Conclusion: Tumour load and responsiveness to chemotherapy are two major prognostic factors in patients with nonmetastatic OS. The effects of Adr, CDDP regimen are similar to those of other more complex and toxic regimens.

1264 POSTER

Natural killer (NK) cell activity, Interleukin-6 (IL-6) and tumor necrosis factor (TNF) in children with brain tumor

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Immunocompetence seems to play an important role in host tumor defense. The aim of this study was to evaluate the number of NK cells, NK cell activity, levels of IL-6 and TNF in patients (pts) with brain tumor (BT).

Patients and Methods: In 12/21 pts with malignant (M) BT and 9/21 pts with benign (B) BT, aged 2–14 years, serum levels of cytokine, number of NK cells and NK cell activity were determined prior to neurosurgery and oncologic treatment. IL-6 and TNF quantification in serum samples enzyme immunoassay was applied. The NK cell activity was measured by cytotoxicity assay with 51Cr-labeled K-562 target cells. The number of NK (CD16+) cells was determined by indirect immunofluorescence with OK-NK monoclonal antibody.

Results: Elevated IL-6 level was found in 83% of examined MBT pts and TNF level in 75% MBT pts ($p < 0.01^*$). Concentration of IL-6 and TNF were elevated in serum of 17% of BBT pts. Serum levels of cytokines are low in healthy control (to <28 pg/ml for IL-6 and <15 pg/ml for TNF). Number of NK cells and NK cell activity were significantly diminished in pts with MBT (see Table).

BT Pts	NK cell activity (%) E:CS** 50:1			CD16+ cells $\times 10^9$/L		IL-6 pg/ml		TNF pg/ml	
	N	x	(range)	x	(range)	x	(range)	x	(range)
Malignant	12	14	(1–39)*	0.06	(0.01–0.18)*	203	(0–500)*	209	(0–880)*
Benign	9	28	(6–53)	0.15	(0.05–0.25)	6	(0–24)	29	(0–190)

**the ratio of effector and target cells

Conclusion: The difference in serum IL-6 and TNF content in malignant and benign BT pts was shown. Number of NK cells and NK cell activity were significantly decreased in pts with malignant brain tumor.

Central nervous system tumours

1265 POSTER

Neurologic function correlates with outcome in patients with non-ependymoma spinal cord gliomas

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Purpose: To identify prognostic factors in patients with non-ependymoma spinal cord gliomas.

Methods: Twenty-five patients were retrospectively studied from 1970 to 1999 at The University of Texas M. D. Anderson Cancer Center. The median age was 40 years (range, 1 - 58 years). The median follow-up was 54 months (range, 10 - 313 months). Nineteen patients had a biopsy, 5 had a subtotal resection, and 1 had a gross total resection. Twenty-two patients received postoperative radiotherapy (RT) (median dose, 45 Gy; range, 22 - 60 Gy), and 13 patients received adjuvant chemotherapy (median, 6 cycles). A neuropathologic review confirmed the World Health Organization tumor grade. Neurologic Function (NF) was graded as 1 to 4 at diagnosis, postoperatively pre-RT, post-RT, and at follow-up.

Results: Post-RT (within 3 months) NF (1 - 4) predicted for OS (5-yr. rates: 100%, 86%, 14%, and 0%; $p = 0.003$). The change in NF at follow-up from diagnosis ranged from -1 (improvement) to +3 (deterioration), with improvement in NF resulting in superior OS (5-yr. rates: 100%, 42%, 57%, 57%, and 0%; $p = 0.01$) and DMFS (5-yr. rates: 100%, 100%, 51%, 75%, and 0%; $p = 0.02$). NF (1 - 4) at diagnosis predicted for LC (5-yr. rates: 60%, 40%, 27%, and 0%; $p = 0.0001$). The number of grade > 2 tumors did not have a confounding effect on NF at diagnosis (Chi-square test; $p = 0.13$). There was a significant difference in local control (LC) (5-yr. rates: 48% vs. 0%; $p = 0.0005$), progression-free survival (PFS) (5-yr. rates: 43% vs. 0%; $p < 0.0001$), distant metastasis-free survival (DMFS) (5-yr. rates: 67% vs. 50%; $p = 0.006$), and overall survival (OS) (5-yr. rates: 78% vs. 30%; $p = 0.02$) in patients with histologic grade < or = 2 vs. > 2 gliomas. Increase in age adversely affected LC (hazard ratio, 1.07; $p = 0.02$), PFS (hazard ratio, 1.06; $p < 0.01$), and OS (hazard ratio, 1.04; $p < 0.01$). None of the patients developed radiation myelopathy. In a multivariate analysis, tumor grade was the most important predictor of PFS, DMFS, and OS. Gender, duration of symptoms, tumor location, number of involved vertebral segments, degree of resection, and duration of RT delay were not significant in a univariate analysis.

Conclusion: Incremental improvement in neurologic function and younger age may be important favorable prognostic factors for OS. This study confirms tumor grade to be the most important prognostic factor for LC, PFS, DMFS, and OS.

1266 POSTER

Probability and estimation of malignancy in women with pelvic masses, using a logistic model which combines: age, morphological ultrasound pattern and resistance index determination

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Objective: The purpose of this study is to evaluate the potential of a predictive model in characterizing the benign or malignant nature of ovarian tumors, analyzing these variables: age, tumor size, morphological ultrasound pattern, position of the vessels and resistance index (RI) value (last two obtained by *Power* Doppler).

Material and Methods: In this prospective study, 124 women were evaluated pre-operatively using a standard protocol for registering of age (greater or less than 50 years), tumor size (considering the biggest diameter by transvaginal ultrasound [TVUS], and eventually transabdomial ultrasound), morphological ultrasound pattern, position of the vessels (central or peripheral), and RI value obtained by *Power* Doppler.

Results: Pathology revels 90 benign ovarian tumors (72%), and 34 malignant tumors (28%). Twenty patients had ovarian adenocarcinoma; and in only 6 patients FIGO's stages III and IV were found. According to the variables: position of the vessels, and size of the tumor didn't have statistical significance ($p > 0.10$) and were left out from the final analysis. A logistic model showed the best cutoff for RI = 0.35. Using this cutoff, the sensitivity and specificity were 100% and 93%, respectively for diagnosing malignant tumor.

Conclusions: Age in combination with morphological ultrasound pattern, and RI value obtained by *Power* Doppler seem to improve the discrimination between benign and malignant ovarian tumors.

1267 POSTER

Recursive partitioning analysis (RPA) class does not predict survival in patients with four or more brain metastases

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Purpose: To evaluate prognostic factors in patients with four or more brain metastases in order to determine whether intense local treatment might be justified for some of them. If up to three brain metastases are present, surgical resection or radiosurgery are currently being considered in case of favourable prognostic factors.

Methods: Retrospective intention-to-treat analysis of 113 patients who underwent whole-brain radiotherapy without surgical resection or radiosurgery. Standard treatment was given with 10 fractions of 3 Gy. Higher total doses were administered in 13% of patients. RPA classes were defined by the RTOG (class I: KPS $\geq$70%, age <65 years, no extracranial metastases, primary tumor controlled; class III: KPS <70%; class II: others).

Results: Median number of brain metastases was 6 (4-50). Most patients (69%) had extracranial metastases as well. Criteria of RPA class I (II) were met in 4% (41%), whereas 56% had Karnofsky-performance status (KPS) <70% and thus were grouped into class III. Complete or partial remission of brain metastases was found in 46% of patients who underwent computed tomography. Median survival was 4 months, 1-year survival rate 15%. Only age was a borderline-significant prognostic factor in univariate analysis ($\leq$50 years versus >50 years, p=0.05). Strong trends were found for KPS, extracranial metastases, control of the primary tumor, and breast primary. Number of brain metastases, RPA class, and treatment-related factors such as total dose or remission of brain metastases had no appreciable influence on survival. Multivariate analysis failed to identify any significant prognostic factor.

Conclusion: Patients with four or more brain metastases seem to represent a group with unfavourable prognosis where remission of brain metastases or administration of more than 30 Gy were not associated with increased survival. The number of patients in RPA class I was too small to draw final conclusions. However, there was absolutely no survival difference between patients in class II (median survival 3.6 months) and III (median 4.2 months).

CNS tumours in adults

1268 POSTER

Evaluation of the adenoviral mediated tranduction of antisense RNA to O6-methylguanine-DNA methyltransferase (MGMT) into nitrosourea-resistant 9L brain tumor model

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Purpose: Chloroethyl-nitrosourea (ACNU in Japan) is one of the most potent chemotherapeutic agents for brain tumors. However, acquired resistance to this drug has become a serious problem for treatment of patients with these tumors. Previously, we established a syngenic animal model resistant to nitrosurea (9L rat gliosarcoma cell line retrovirally transfected with MGMT cDNA (9L-MGMT); Abstract No.431, ECCO10, 1999) and distributed it to researchers developing therapies to subdue the resistance. In this study, we evaluated the efficacy of antisense RNA transduction by adenoviral vector encoding antisense to MGMT in our model.

Method: The 9L MGMT cells and Fisher 344 rats were used in this study. Replication defective adenoviral vector encoding antisense RNA to MGMT was constructed by homologous recombination in HEK 293 cells. The 9L-MGMT cells were infected with the virus and drug sensitivity of ACNU was quantified.

Results: The adenoviral transfer of antisense RNA down-regulated the transcription of the MGMT in 9L-MGMT cells in vitro. Cellular levels of MGMT also decreased. However, it did not confer the sensitivity to nitrosourea by cytotoxic assay (IC50=260ug/ml, infected; vs. =330, uninfected). When we stereotactically implanted the 9L-MGMT cells into the rat brain and treated with adenoviral vector, it did not significantly prolong survival with ACNU treatment (survivals; mean+-S.D.=15.33+-1.00 days, n=9, control vector; vs. =18.30+-2.83, n=10, antisense RNA).

Conclusion: Adenoviral transduction of antisense RNA did not confer the enough sensitivity to nitrosourea both in vitro and in vivo, although it clearly inhibited the MGMT transcription and expression. These data suggest that incomplete depletion of the MGMT is not sufficient to conquer the resistance.

1269 POSTER

Early non-invasive detection of brain tumor response to radiation therapy using diffusion weighted MRI

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Introduction: Diffusion weighted MRI (DWMRI) is sensitive to the biophysical characteristics of tissues, including the slow/fast water volume fraction (R) and apparent diffusion coefficients (ADCs) of water. DWMRI has been shown to detect early changes in brain water diffusion associated with several pathologies such as cell membrane permeability, cell swelling and cell lysis. We studied the use of DWMRI to detect early changes in brain lesions after radiation and chemotherapy.

Methods: We present 7 patients with various brain metastases and 1 with acoustic neuroma treated with single fraction stereotactic irradiation, and 2 patients with primary brain tumors and 1 with brain metastases treated with fractionated irradiation. Line Scan DWMRI, and contrast enhanced T1 weighted and T2 weighted MRI were used to monitor prior to, and at regular intervals during and following treatment. All images were acquired with 5mm slices, 2-signal averages and a 22x16cm field of view. T1 and T2 weighted images were acquired with a 256x128 matrix and with TE/TR=16/500 ms and TE/TR=102/3000 ms, respectively. DWMRI were acquired with a 128x64 matrix, b=1000 s/mm2 (b is a parameter used for evaluating the intensity of the diffusion weighting) and TE/TR=105.2/2907 ms. Diffusion curves were calculated from additional DWMRI obtained with 14 b values ranging from 15 to 4000 s/mm2. Data were acquired using a 0.5T interventional MRI machine. ADCs and Rs and their change in time were calculated for regions of interest chosen after comparing the DWMRI images with T1 and T2 images.

Results: Changes in diffusion parameters recorded one week after starting radiation correlated with changes in tumor volumes as measured 2 months after treatment. Several patterns of response were seen: (a) significant increase in ADCs and decrease in R were followed by a decrease in lesion size; (b) unchanged ADCs and Rs were observed for stable lesions; (c) decreased ADCs and increased Rs were followed by tumor growth. In 3 patients treated with intratumoral taxol, significant changes were seen within 24 hr after treatment began. The shape, magnitude and nature of this effect changed during the 5-day treatment period. No similar changes were observed in conventional MRI.

Conclusions: These results demonstrate the feasibility of using DWMRI for early, non-invasive prediction and monitoring of response of brain tumors to radiation and chemotherapy. This study is ongoing.