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.