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### Results of Radiotherapy in Cerebral Non-Hodgkin's Lymphoma

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**Purpose:** Prognosis of primary CNS lymphoma is reported in literature with median survival times of 36-70 months and a one-year-survival rate of 8 to 23 %.

**Methods:** We analysed the differences in the course of disease in 49 patients who were treated in 58 series for cerebral Non-Hodgkin's Lymphoma. Of these, 25 were primary CNS lymphomas, 24 cerebral manifestations of systemic disease and 9 treatments were performed for cerebral recurrence (5 after primary and 4 after secondary cerebral disease, none at the same location as the first manifestation). Radiotherapy was regularly performed as whole-brain irradiation in primary treatment (30 Gy midline dose). 13 patients then received an additional 10 Gy boost of the tumor region. Recurrent disease was treated with 20-30 Gy in small fields.

**Results:** One-year-survival rate was 50 % in primary and 10% in secondary cerebral lymphoma, compared to 5 % after cerebral recurrences.

**Conclusions:** Thus, our results suggest that 1. outcome of patients with cerebral manifestations of systemic disease equals that of patients with brain metastases of solid tumors and 2. prognosis of patients with primary cerebral lymphoma might be better than described in literature so far.

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Radiotherapy in the management of invasive thymoma  
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**Purpose:** Clinical and pathological review of 27 patients with invasive thymoma receiving radiotherapy (RT) either as primary treatment or following surgery.

**Material and Methods:** From 1982 to 1996, 27 patients with invasive thymoma (12 men, 15 women; mean age 54.2 years) were irradiated after gross total resection (n=15), partial resection (n=8) or biopsy (n=4) with a mean dose of 50 Gy (30-60 Gy). Associated syndromes were myasthenia gravis in 40.7%, red cell aplasia in 7.4% and hypogammaglobulinemia in 3.7%. Masaoka stage was II in 12 (44.4%) patients, III in 8 (29.6%) patients and IV in 7 (25.9%) patients (IVA, n=6; IVB, n=1). In recent years 5 patients (3 with stage III and 2 with stage IV A) received chemotherapy, three of them in a neoadjuvant setting. Pathologic slides were reviewed by one of the authors.

**Results:** Patients mean survival and 5-year survival rates were 54.7 months and 100% for stage II disease, 48.7 months and 100% for stage III disease and 69 months and 57.1% for stage IV disease. No local recurrence occurred after gross total resection. Local failure was found in 3/27 (11.1%) patients after partial resection (n=2) or biopsy (n=1) of stage IVA disease; distant metastases occurred in 5/27 (18.5%) patients; two of them had distant failure as the first site of relapse without intrathoracic failure. No patient with local or distant failure had received chemotherapy at time of primary treatment.

**Conclusion:** Using external RT after gross total resection of invasive thymoma stage II and III effective local control is achievable. In patients with partial or unresectable tumors, a multimodality approach may be beneficial for long term control.

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### Lymphocyte micronucleus assay does not predict normal tissue reactions in radiotherapy patients

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**Purpose:** The aim of the study was to investigate whether *in vitro* radiosensitivity of lymphocytes evaluated by the micronucleus assay will predict acute and late reactions from radiotherapy in cervical and head and neck cancer patients.

**Methods:** The micronucleus assay was used to measure *in vitro* radiosensitivity of lymphocytes after irradiation with doses of 2 and 4 Gy. Blood samples from 12 cervical cancer patients and 11 head and neck cancer patients were taken before radiotherapy. All 23 patients were treated by radical radiotherapy. The RTOG/EORTC grading system was used to score the acute and late reactions from grade 0 to 4.

**Results:** Significant individual variation in lymphocytes radiosensitivity was found in each group of radiotherapy patients. Since the cluster analysis methodology showed the results to have bimodal distributions we could obtain two subgroups within each group of patients: radioresistant with lower MN frequency and radiosensitive with higher MN frequency. Individual variation was observed in the grade scores of normal tissue reactions in cervical and head and neck cancer patients. MN frequencies obtained *in vitro* for each patient were compared to the acute and late reaction scores. Lymphocytes radiosensitivity did not correlate with either acute or late reactions observed in cervical cancer patients and head and neck cancer patients.

**Conclusion:** Although individuals vary in normal cell radiosensitivity as shown by the lymphocytes micronucleus assay, no significant correlation was found between lymphocytes radiosensitivity and either acute or late effects. We conclude that lymphocyte micronucleus assay is not able to predict normal tissue reactions in radiotherapy patients.

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### ALTERED APOPTOTIC PROFILES IN IRRADIATED PATIENTS WITH INCREASED TOXICITY

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**Purpose:** Using the Leukocyte Apoptosis Assay we have previously demonstrated that mutation of the *Ataxia Telangiectasia* gene results in compromised radiation-induced apoptosis in T-lymphocytes (Ozsahin *et al*; Int J Radiat Oncol Biol Phys 1997; 38: 429-440). A retrospective study of radiation-induced apoptosis in T-lymphocytes from RT patients, who display high acute-toxicity, was performed to test for compromised response.

**Methods:** As described in Menz *et al*. (Radiat Environ Biophys 1997; 36: 175-181), 3 ml of heparinized blood was diluted 1:10 in RPMI medium, irradiated with 0, 2, or 8 Gy; and left to incubate for 24 or 48 h. CD4 and CD8 T-lymphocytes were then labelled using FITC-conjugated antibodies, erythrocytes were lysed, and the DNA stained with propidium iodide. Subsequently, cells were analyzed using a Becton Dickinson FACScan flow cytometer. Radiation-induced apoptosis is recognized in leukocytes as a reduced DNA content attributed to apoptosis-associated changes in chromatin structure. Patients' data was compared to those of 105 healthy blood-donors aged 20 to 70 years. Apoptosis was confirmed by microscopy, electron microscopy, and by the use of commercially available apoptosis detection kits (*in situ* nick translation and Annexin V). To integrate the radiosensitivity values from CD4 and CD8 T-lymphocytes, z-score analysis was performed.

**Results:** A cohort of 12 patients aged 51-75 years who displayed high acute-toxicity was evaluated. The cohort displayed statistically significant less radiation-induced apoptosis (-1.3  $\sigma$ ) than average healthy age-matched donors. Only 1/12 displayed more apoptosis, and 9/12 were more than one standard deviation from the control mean.

**Conclusions:** The Leukocyte Apoptosis Assay could be used to predict individuals likely to display increased acute toxicity to radiation therapy. Validation requires a prospective study.