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Individually modified involved field technique of the German/Austrian Pediatric Hodgkin Study (HD90): A way to reduce treatment volume without increase of relaps

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Purpose: Definition of the supra- and infradiaphragmatic involved lymph node area to be irradiated within combined modality of treatment of pediatric Hodgkin's Disease (HD 90) based on clinical examination and modern sectional imaging. Comparison with the classical "involved field"-radiotherapy (1966). Analysis of the location of relaps compared with the modified treatment volume.

Material and Methods: From October 1990 to October 1995 602 patients have been enrolled in the German-Austrian multicenter pediatric HD-study with 73 centres participating. Centralized treatment planning at the study office was performed for 577/602 patients before radiotherapy was started. For each of these patients the individual spread of disease at diagnosis was documented based on the documentation forms filled in by the respective center indicating the extent of disease. A central review of chest X-ray films, Chest and abdominal CT was added. An individual proposal for the radiation field was set up and sent to the respective centre.

The radiation fields proposed were compared to the classical IF-radiotherapy for 577 patients with supra- and infradiaphragmatic disease. Location of tumor recurrence has been analysed.

Results: The individualisation of classical IF-radiotherapy led to changes in altogether 40% of the patients. Most changes were in the supradiaphragmatic involvement: 235/577 changes were volume reduction. The cases of volume enlargement referred to including the thoracic aperture. For the neck and the mediastinum typical patterns of spread resulting in modified IF-radiotherapy could be identified: upper neck: lower neck including the supraclavicular region; upper mediastinum including the thoracic aperture; upper mediastinum including bilateral hili. The proposed radiation fields were in 95% a combination of one or more of these areas. Modified involved field technique with treatment volume reduction could be realised only in a few cases of infradiaphragmatic disease.

Analysis of recurrence (n = 34; 12/96) revealed only one recurrence in a lymph node area treated by a modified radiation field.

Conclusion: Classical IF-radiotherapy can be modified based on modern sectional imaging especially for supradiaphragmatic lymph node involvement. Volume reduction do not jeopardize local control within effective combination treatment.

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Radiotherapy in treatment of Ewing's sarcoma of the chest wall (Askin tumors)

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Purpose: In Askin tumors, radiotherapy is an important modality. In the CESS 81, 86 and EICESS 92 studies it is used as only local treatment or as preoperative or as postoperative irradiation, always in combination with chemotherapy. The results of radiation treatment are evaluated.

Methods: Since 1981, 146 patients with Askin tumors have been treated according to the study protocols CESS 81, CESS 86 and EICESS 92. 119 of them received irradiation as local treatment. 53% of the patients had sarcomas of the ribs, 27% of the scapula, 12% of the spine, 6% of the clavicle and 2% of the sternum. The median follow up is 38 months.

Results: The relapse free survival after 5 years was 46%. It was 66% after operation alone, 75% after preoperative, 48% after postoperative irradiation and 35% after irradiation alone. The difference between the 4 local treatment modalities was not statistically significant (p = 0.16%). Local control was best after operation alone and preoperative irradiation with 100%, it was 81% after postoperative irradiation and 79% after irradiation alone. Again the difference was not statistically significant.

Conclusion: Most patients received radiotherapy. Although there is a tendency of better local control after operation alone, this is partly due to a positive selection. Local control and survival after sole or combined radiation therapy are good.

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The role of radiotherapy in the combined treatment of stage I childhood rhabdomyosarcomas. Results of the german cooperative soft tissue sarcoma study (CWS) in 104 patients

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Purpose: Local radiotherapy in children is to be restricted to indications of proven efficiency due to the impending late radiation sequelae. Is radiotherapy necessary in addition to chemotherapy after initial complete tumor resection (stage I, IRS)?

Methods: From 1981 to 1996 104 stage I patients (pts) were treated with a combined modality regimen according to the CWS protocol. 84 were of embryonal (RME), 20 of alveolar (RMA) histology. Radiotherapy (~45 Gy) was given in 19 pts (18%). The outcome was evaluated after a median follow up of 70 months.

Results: In continuous complete remission/alive are 87/92% of RME and 75/85% of RMA. Local/combined/systemic relapses were to be observed in 5/71% of RME and 5/5/15% of RMA. There were no significant differences between the irradiated and the not irradiated group. The majority of local relapses could be salvaged by second line treatment including radiotherapy or mutilating surgery.

Conclusion: Radiotherapy as an adjunct to multidrug-chemotherapy does not improve further the rather good prognosis in initially completely resected pts. This seems to be true for RME, hopefully even for RMA, but the number of RMA-cases is small. These findings are in keeping with the SIOP, IRS and Italian group data.

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Myeloablative therapy, stem cell rescue and gene transfer in advanced ewing tumors (AET)

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Ewing Tumors (ET) are defined by expression of *ets/ews* chimeric transcription factors and early systemic spread. High dose therapy (HDT) and stem cell rescue has improved the prognosis of AET patients. The European Inter-group (EICESS) has established the following indications for HDT in AET: Patients with primary multifocal bone tumors, patients with early (≤ 2 y after diagnosis) or multiple relapse. As of Nov 1996, probability of EFS for these patients is 32% (n = 50, mean survival time: 52 mo). Results may be affected by histology, transplant type and immunotherapy. Classical Ewing Sarcoma: 35% EFS v.s. MPNT: 27%; autotransplants: 34% v.s. allotransplants: 20% EFS; Patients receiving IL2 post autotransplant: 62% v.s. patients without IL2: 28% EFS. In spite of improved cure rates after HDT, relapse remains a major problem occurring primarily in the lung, within the shielded region, within involved bones outside the radiation field and at the site of lesions detectable only by NMR or PET but not by conventional Tc bone scan. RT-PCR also revealed contamination of both marrow and peripheral grafts with residual ET cells. Based on the IL2 data, we have developed a tumor vaccination strategy utilizing cytokine gene transfer. To this end, we have transfected IL2 as well as other immunostimulatory cytokine genes (IL7, GM-CSF) into ET cell lines derived from transplanted patients as well as into autologous patient fibroblasts. Transgenic IL2 expression in vivo leads to induction of a unique cytokine induced killer cell population, which could not be solicited by treatment with exogenous IL2. We conclude: HDT is efficacious in AET for prevention of relapse. Extension of involved compartment irradiation, post transplant immunotherapy, detection of minimal residual disease and graft purging may further improve the outcome of AET patients.

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Desmoid tumors in children

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Desmoid tumors (DT) belong to fibromatoses, and in TNM classification – to q1 fibrosarcomas. Their rate among soft tissue sarcomas is about 25%, and among all benign and malignant soft tissue tumors – 3%.