do not differ from adult tumors. However, prepubertal germ cell tumors usually have a different pathogenesis and treatment options are separately defined. Adolescent tumors differ regarding treatment dependent on the primary treating physicion (pediatric oncologist, medical oncologist, urologic oncologist) but the outcome is not different. However, the compliance is much better if the patient is accompanied by parents who take responsibility for the care.

Conclusions: The treatment of germ cell tumors is very much standardized in the pediatric as well as the adult population. For adolescent patients it does not matter who is the primary physician they consult. As long as the treatment follows the published guidelines, an excellent outcome can be achieved in nearly all stages.

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Malignant CNS Germ Cell Tumors (CNS GCTs): A review of the State of Art

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Objectives: Primary CNS GCT account for about 2% of all intracranial neoplasms before 20 years of age. Histologically, CNS GCT are analogous to extracranial GCT. They can be divided into germinoma and non-germinomatous GCT (NGGCT). NGGCT include teratoma, embryonal carcinoma, Yolk sac tumor and choriocarcinoma, occurring as mixed tumors in about 30%. In case of expression of tumour markers (AFP- representing Yolk sac elements, β-HCG- representing choriocarcinoma) in serum/CSF, they are called secreting. Tumor markers therefore can be used for clinically guided diagnosis and treatment response. Germinoma are exquisitely radio- and chemosensitive, NGGCTs are less sensitive to RT. In the past 10 years increased clinical research reflected in institutional as well as multicenter trials in Europa, the United states and Japan was initiated.

Research targets: In germinoma the attempt is to decrease late effects of extensive radiotherapy and in malignant NGGCTs to define risk adapted treatment strategies and increase survival rates. In key publication of the last 5 years and in ongoing multicenter/multinational trials three main issues are targeted: Germinoma: Is chemo +RT equal to craniospinal RT?(Alapetite MPO, Abstr., 2002, Fouladi Childs Nerv Syst,1998): Is chemo equal to RT at all? (Balmaceda JCO, 1999). In case of RT alone, what are the lowest dosages necessary for disease control? (Shibamoto Radiology, 2001; Bamberg JCO, 1999; Hardenbergh Int.J.Rad.Oncol.Biol.Phys.,1997) Malignant NGGCT: what are the most effective drug regimen? (Buckner JCO, 1999, Itoyama Neurosurgery, 1995; Calaminus MPO, Abstr.2002) what is the necessary dosage and extent of RT? (Aoyama JCO, 2002) Are they curable by chemo alone? (Balmaceda JCO, 1999; Baranzelli J Neurooncol.,1998).

Results: For germinoma data of the French SFOP protocol and the ongoing SIOP CNS GCT96 reveal that in localized disease focal RT with chemo is not able to control subclinical ventricular disease and that incomplete staging is a major risk factor. In malignant NGGCTs according to the SIOP data the extend of AFP elevation and residual disease after RT is of prognostic value.

Conclusions: Prognosis of malignant CNS GCTs has dramatically improved. The majority of patients can be cured by combined treatment with lowered RT dosages. Treatment planning has to take into consideration extent of disease, markers, histology and response to treatment.

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Radiotherapy guidelines in the treatment of malignant paediatric CNS Germ Cell Tumors (GCTs)

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The aims of SIOP protocol CNS GCT 96 were to standardise diagnostics and treatment of GCTs in respect to histology: in germinoma to compare in a non-randomized fashion craniospinal radiotherapy (CSI) with chemotherapy followed by focal radiotherapy; in secreting tumors, if AFP > 25 ng/ml and/or β -HCG > 50 IU/l, to evaluate the response to 4xPEI as preoperative chemotherapy, consolidated by radiotherapy tailored to extent of disease (CSI in metastatic patients and focal irradiation in localized disease).

From a radiotherapic point of view, special considerations should be made regarding treatment of localized pure germinoma. In patients with localized disease, the otpimal treatment approach for subclinical disease is still controversial. In order to reduce the potential toxicity associated with craniospinal irradiation, considered as the reference treatment, recent clinical studies tended to limit the radiation volumes, using some courses of chemotherpy followed by focal irradiation only (option B of the SIOP CNS GCT 96 protocol, SFOP protocol TC-90). The combined chemo-radiotherapy approaches yelded excellent cure rates, but the pattern of relapses (9% in option B SIOP series and 14% in SFOP series, occurred mainly in the ventricular system outside the radiation treatment volumes) and the predominance for ventricular subependymal dissemination clearly showed that the chemotherapy was not sufficient to sterilize subclinical ventricular disease. This increased risk of ventricular relapse, marginal to radiation fields, prompted the SIOP CNS GCT group to consider widening the radiation volumes in combined modality treatment from focal to whole ventricular irradiation (WVI) for the forthcoming protocol.

Recommendations for volume definition (third ventricle, lateral ventricles and fourth ventricle) and technical considerations for WVI will be carefully presented: technical guidelines of the SIOP CNS GCT group for optimal WVI will be reported, since the very irregular shape of the planning target volume and the new radiation modalities (such as 3D-conformal and intensity-modulated radiation therapy) make the fields arrangement extremely crucial in order to have the best conformality index.

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Regional deep hyperthermia and pei-chemotherapy in children and adoles-cents with unresectable malignant germ cell tumors: an approach for cure

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Objective: The purpose of the present study in children and adolescents with recur-rent, unresectable GCTs was to improve the efficacy of anticancer drugs by regional deep hyperthermia (RHT) using a non-invasive radio frequency technique.

Patients: From VII/1993 to IV/2002 a total of 25 children and adolescents (21 girls, 4 boys) aged between 13 months and 23 years (median: 3;10 years) with recurrent, unresectable germ cell tumors were treated with chemotherapy and RHT. All patients suffered from either a local relapse (n = 23) or a primary unresectable tumor (n = 2). Tumor site: 21 pelvis, 3 abdomen, 1 head and neck. Histology: 4 teratomas, 1 dys-germinoma, 16 yolk sac tumors, 4 embryonal carcinomas. Therapy: 2000 mg/m2 ifosfamide (with mesna uroprotection), 100 mg/m2 etoposide on days 1 - 4, and 40 mg/m2 cisplatinum (with mannitol diuresis) on days 1 + 4 com-bined with RHT (42 - 44 °C) on days 1 + 4. Side effects and complications: Myelo-suppression WHO grade III/IV in all pts, nephrotoxicity in abdominal tumors WHO grade II-IV. Osteonecrosis in 3 pts, MDS in 1 pt. Tumor response (MRI/CT): 13 CR, 6 PR (response to thermo-chemotherapy 82%). Subsequent surgery led to 13 complete and 3 further incomplete resections. Addi-tional radiotherapy in 7 pts (22 - 44 Gy) ± RHT. Status: In the light of an exceptional late relapse after 56 months Kaplan-Meier-Analysis showed an EFS of 0.42 (14/25 pts) and a survival rate of 0.57 (17/25 pts) with a follow-up from 5 to 102 months (median 29 months).

Conclusion: RHT can increase the efficacy of the multimodal relapse therapy in germ cell tumors. This up-date with a doubled number of patients and a longer fol-low-up period validates previous treatment results (Wessalowski et al. Klin. Pädiatr. 1997, 209:250-6). Supported by Deutsche Krebshilfe, Elterninitiative Kinderkrebsklinik Düsseldorf e.V., and Kinderkrebsfürsorge Wickede e.V.