**1419** POSTER

**Adrenal cortical tumours in childhood and adolescence, single institution experience**

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Adrenocortical tumors (ACT) are rare in pediatric population. The pathogenesis, prognostic indicators, and management of these tumors are still unclear because of its infrequent occurrence. The Adrenal cortical carcinoma (ACC) accounts for the majority of these tumors often displaying poor prognosis.
Purpose of the study: to review clinical manifestation, genetic predisposition, treatment strategy and outcome for all patients with ACT treated in childhood and adolescence in single institution
**Materials and Methods:** Twelve patients younger than 18 years were treated between 1990–2005 in Faculty Hospital Motol, Prague for ACT. The median patients age was 3.8 years (range 0.8−17.5), there were 7 girls and 5 boys. The majority (58%) were at an advanced stage (stage III and IV) at initial presentation, five had metastatic disease. Virilization alone or in combination with signs of overproduction of other adrenal cortical hormones were present in 10 patients. The majority of patients had positive family history of cancer, 3 families full-filing clinical criteria for Li-Fraumeni (LFS) or Li-Fraumeni-like (LFL) syndromes. The germ-line TP53 mutation was detected in 4 patients with ACT of 6 tested.
**Results:** Five patients (median age 1.5 years at the time of diagnosis) presented with localized, small (<5−10 cm in the largest diameter) tumor which was completely resected. No other treatment was administered and 3 patients are disease free for 15, 14 and 3 years after surgery. Two other patients in this group are survivors of second primary tumors (medulloblastoma and osteosarcoma) developing 4 and 2.5 years after the resection of ACT. Seven patients (median age 11.4 years) had advanced disease at the time of presentation. Six were treated with surgery and chemotherapy (mostly carboplatin/cisplatin, etoposide, mitotan based). One patient presented with respiratory failure requiring mechanical ventilation due to massive metastatic disease to the lungs and was not treated when the diagnosis of ACT was established. One complete and one partial remission to anti-neoplastic chemotherapy were seen, all patients with advanced disease subsequently died of disease progression.
**Conclusions:** Advanced ACT is a consistently lethal neoplasm in childhood and adolescence, localized resectable tumors presenting with virilization in younger children have better prognosis. Genetic counseling and life-long follow up is warranted.
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**1420** POSTER

**Sweeping beam total body irradiation in Chile: technical description and clinical results**

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The aim of this work is to describe our Total Body Irradiation (TBI) technique using a sweeping beam as well as the results in a group of 55 pediatric patients consecutively irradiated between 2000 and 2006.
At Clinica Alemana, TBI irradiation (sweeping beam technique) has been performed since 2000 as part of patient conditioning regime for Bone Marrow Transplant (BMT). Our bunker size dose not allow any stationary beam technique so that a sweeping technique had to be implemented. 12 Gy are prescribed to midline in 3 days, 2 fractions per day (2 Gy/fr). In each fraction (programmed to 25 min), patients lie down on a curved coach, first in supine and then in prone position while the gantry rotates 120º encompassing their entire length ($20 \times 40$ cm$^2$ field size at isocentre). Two of these arcs are used for each position so that 50 cGy are delivered in each arc (100 cGy in each position). With this arc technique is possible to avoid the use of the additional acrylic plates usually needed in other TBI techniques due to the fact that the dose to the surface increases up to 82% of the midline dose (AP and PA incidence). Maximum depth dose is 1.5 cm and dose inhomogeneity is <2% once this point has been reached. Lung customized cerrobend shielding (designed from a portal film in treatment position) is used only in the AP position. In vivo dosimetry measurements carried out with semiconductor diodes revealed average doses to midline lung of 6.75 Gy (which implies an average lung dose rate of 4.5 cGy/min). Average in vivo dosimetry measurements to midline at the level of the pelvis (where dose is prescribed) is 11.5 Gy.
Fifty five children between 3 and 17 years (median, 9 years) with a diagnostic of Acute Lymphoblastic Leukemia (ALL) (45 patients, 52% and 48% first and second remission, respectively), Acute Myeloide Leukemia (AML) (6 patients) and other diseases (4 patients). 38 children received a graft alogenic, 5 autologus, 3 Haploidentico and 9 cord. The chemotherapy conditioning regimens were VP-16 + CY (67%), VP-16 + CY + ATG (15%) and others (18%). The last recruited patient had a 6 months follow up and the average was 21.6 months.
Five patients died from treatment-related complications and ten died from leukemia progression. The average relapse-free and overall survival was 27 and 27.8 months, respectively. The average time in hospital after BMT was 38 days.
Our sweeping beam technique has proved to be very reproducible, simple and comfortable for the patient. Neither veno-occlusive-hepatic disease nor radiation induced intersticial pneumonitis nor cataracts were diagnosed. We have to wait longer to evidence second cancers, endocrinologic or neurologic toxicities. Our clinical results are similar to published data with other traditional TBI technique.

**1421** POSTER

**Protontherapy (PT) in pediatric skull base and cervical canal low-grade bone sarcomas. The Centre de Protonthérapie d'Orsay experience**

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Most skull base and spinal canal low-grade bone sarcomas are challenging tumors that require maximal surgical resection, along with high doses of radiations, that usually exceed the tolerance-dose of close critical structures (ie cervical cord, brain stem, optic pathway etc.). We report here on 29 children treated post operatively using PT. One had received gamma knife before, and one chemotherapy due to misdiagnosis. 26 has chordomas (CH), and 3 low-grade (gr I) chondrosarcomas (CS). Mean age was 12 years for both. M/F sex ratio was 1.4. Most common presenting symptoms were headaches, and diplopia. All patients had received previously surgical resection, repeated 1 to 5 times, through an anterior approach in most of them (trans-sphenoidal and/or trans-oral). At the time of radiation, all had gross residue (R2: 29), which was minimal in 4. Anatomical sites affected by CH were the clival area in 13, cervical spine in 1, and both in 12; in CS, they were sphenoid and petrous bones. Mid target volume (PTV) was 173 ccs. Mean total dose was 68.8 CGE (ie Cobalt-Gray equivalent, based on mean 1.1 RBE value), with a 60−70.2 CGE range, administered with a 5 session-per week conventional fractionation. 28/29 received a combination of high energy photons (mean dose: 37.6 Gy), and protons (mean dose: 32 CGE), and one exclusive protons, using highly accurate simulation and alignment-processes, based on the implantation of intra cranial fiducial markers. Treatment was well tolerated in all children, and quality of life deemed satisfactory in all, but failing ones. With a mid 27 months F Up (5–102), 5/29 (17%) children had failed locally: 5/5 were CH, 4/5 Cervical canal primaries, 1/5 female, 194 cc-mid PTV vol. 3 Y-DFS was 80.4%. Long term side-effects were limited to pituitary, and rarely auditory dysfunctions. High dose PT proved highly effective and none toxic in such processes.

**1422** POSTER

**Educational achievement, marital, smoking status, employment, and insurance in long term survivors of Childhood Hodgkin's Disease**

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**Background and Aim:** Treatment advances have led to dramatically improved survival rates for Hodgkin's disease (HD) in children. Social, vocational, and educational adjustments of childhood cancer survivors gained importance in recent years. The aim was to determine educational achievement, marital, smoking, employment, and insurance status in our long-term survivors of childhood HD.
**Patients and Methods:** Children treated for HD at our department between 1979–2002 and followed in remission >4 years were included. Sixty five

cases were interviewed concerning their educational, occupational, marital, parenthood, smoking, and social insurance status. Data were analyzed in relation with gender, age at diagnosis, stage of disease, and follow up duration.
**Results:** All 65 cases (M/F: 50/15) were >18 years of age (median 23, 18−40) at the time of study. Median age at diagnosis was 9 years (2−19). Median follow up time was 16 years (4−26). 12/65 cases (19%) had stage I; 29 (46%), II; 18 (29%), III; and 4 (6%), IV disease. 38/65 (59%) cases had a profession, 27/65 (41%) did not. 34/65 (52%) cases were working at a job. 58% of females didn't work compared to 31% of the male patients didn't ($p = 0.08$). 36/65 (56%) patients were non-smokers, 8 (12%) ex-smokers, and 21 (32%) smokers (3/15 females, 18/50 males; $p = 0.06$). 3 females and 11 males (14/65; 21.5%) were married; 6/14 (43%) (M/F = 3/3) had offsprings. 54/65 (83%) cases had any kind of social insurance; all females had social insurance compared to 74% of the males ($p = 0.02$). There was no significant difference in employment, smoking, marital status, and having social insurance between the cases according to age at diagnosis (<10 or >10 years), and follow up time (<15 or >15 years), and having university education; also between gender and marital status. There was no significant difference between early (I-II) or advanced stages (III-IV) and having higher education, employment, smoking, marital status or having social insurance ($p > 0.05$).
**Conclusions:** That educational status of our patients was not inferior than the normal population is satisfying. All patients should be advised not to smoke. In this series HD survivors did not have important disadvantages in social life. Patients should be encouraged to continue education, work, marry and so have a better quality of life.

# Breast Cancer

## *Oral presentations* (Mon, 24 Sep, 10.45−12.15)
## Breast cancer – preclinical

**2000** ORAL

**Quantification of free circulating tumor DNA in plasma as a diagnostic marker for breast cancer**

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**Background:** Breast cancer is the leading cause of cancer death in women worldwide. There is a need to develop new approaches that may facilitate earlier diagnosis and more effective treatments. Increased knowledge of molecular pathogenesis of breast cancer offers a basis for the use of molecular markers in biologic fluids for early detection, as well as identification of higher-risk individuals.
The purpose of our study was to determine whether the amounts of circulating DNA could discriminate between breast cancer patients and healthy individuals by using real-time PCR based DNA quantification methodology and determine the kinetics of circulating plasma DNA in surgically treated patients.
**Material and Methods:** Our standard protocol for quantification of cell free plasma DNA involved 175 consecutive patients with breast cancer and 80 healthy controls. The quantification was perfomed by real-time PCR amplification of the human telomerase reverse transcriptase gene (hTERT).
**Results:** We found increased levels of circulating DNA in breast cancer patients compared to control individuals (105.2 vs 77.06 ng/ml, $p < 0.001$). We also found statistically significant differences in circulating DNA amounts in patients before and after breast surgery (105.2 vs 59.0 ng/ml, $p = 0.001$). Increased plasma cell free DNA concentration was a strong risk factor for breast cancer, conferring an increased risk for the development of this disease (OR, 12.32; 95% CI, 2.09−52.28; $p < 0.001$). High levels of plasma DNA were also correlated with a decrease in patients' overall survival ($p = 0.043$). There were no association between clinicopathological parameters and concentrations of cell free circulating DNA.
**Conclusions:** Diagnostic assays based on blood sample analysis are becoming an area of study with growing interest, mainly because of the simplicity of sampling and the future potential of automation of the technical methods for clinical applicability. In conclusion, cell-free DNA is significantly increased in plasma of breast cancer patients, which is associated with an increased risk for the development of this disease and decrease of patient's survival. Therefore, quantification of circulating DNA by real-time PCR may be a good and simple tool for early detection of breast cancer with potential to clinical applicability together with other current methods used for monitoring the disease.

Plasma DNA concentration as a risk factor for breast cancer

| | | Patients (n = 175) N (%) | Controls (n = 80) N (%) | OR* | 95% CI* | P* |
|---|---|---|---|---|---|---|
| High [fcDNA] | Yes | 99 (56.6) | 73 (91.2) | 8.01 | 3.49−18.38 | <0.001 |
| | No | 76 (43.4) | 7 (8.8) | | | |
| Very high [fcDNA] | Yes | 133 (76.0) | 78 (97.5) | 12.32 | 2.90−52.28 | <0.001 |
| | No | 42 (24.0) | 2 (2.5) | | | |

*For High [fcDNA], $P < 0.001$, OR = 6.48 and 95% CI: 2.76−15.20; For Very high [fcDNA], $P = 0.003$, OR = 9.30 and 95% CI: 2.14−40.35, using logistic regression analysis adjusted by age.

**2001** ORAL

**Circulating tumor cells (CTCs) in peripheral blood of primary breast cancer patients – Results from the translational research program of the German SUCCESS-Trial**

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**Background:** In metastatic breast cancer, the presence of CTCs has been shown to be associated with bad prognosis and their persistence predicted lack of treatment efficacy. Only limited data, however, has been published in the adjuvant setting. We evaluated the role of CTCs in peripheral blood at primary diagnosis and during adjuvant chemotherapy, endocrine and bisphosphonate treatment within the SUCCESS-trial (n = 3658 pts.)
**Methods:** We analyzed methods of 23 ml of peripheral blood from 1767 N+ and high risk N− primary breast cancer patients before systemic treatment. 852 of these patients have undergone follow-up blood sampling after completion of chemotherapy. The presence of CTCs was assessed with the CellSearch System (Veridex, Warren, USA). Briefly, after immunomagnetic enrichment with an anti-Epcam-antibody, cells were labeled with anticytokeratin (8, 18, 19) and anti-CD45 antibodies to distinguish epithelial cells and leukocytes.
**Results:** 10% of pts with a blood sampling before systemic treatment (n = 170) showed >1CTC before the start of systemic treatment (mean 13, range 2–827). While we found 2 CTCs in 5% of patients, 3% had 3−5 CTCs and 1% 6−10 and >10 CTCs each. The presence of CTCs did not correlate with tumor size ($p = 0.07$), grading ($p = 0.30$), hormonal status ($p = 0.54$) or Her2-Status of the primary tumor ($p = 0.26$). However, we observed a significant correlation with the presence of lymph node metastases ($p = 0.015$). None of 24 healthy individuals showed more than 1 CTC.
Among those 852 patients with follow-up blood sampling after the completion of cytostatic treatment, 11% were CTC positive before starting systemic treatment (mean 7, range 2–166), while 7% of patients presented with >1CTC after completion of chemotherapy (mean 6, range 2−84). Of those, initially CTC positive, 10% remained positive (n = 9) and 90% had a negative CTC test after chemotherapy (n = 82). Of those initially CTC negative, 93% remained negative (n = 711), whereas 7% returned with a positive CTC test (n = 50) ($p = 0.24$).
**Conclusions:** The SUCCESS-trial is the first trial to perform the detection of CTCs in a large number of primary breast cancer patients with this highly standardized and easily applicable approach. If the observed persistence of CTCs after completion of adjuvant chemotherapy is prognostically relevant, will have be further evaluated with longer follow-up.

**2002** ORAL

**Low SIAH2 expression in breast cancer is associated with resistance to endocrine therapy**

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**Background:** Low expression levels of Seven-in-Absentia Homolog 2 (SIAH2) were observed in our microarray and quantitative real-time PCR